**A meta-analysis of previous falls and subsequent fracture risk in cohort studies**

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**Abstract**

***Summary***

The relationship between self-reported falls and fracture risk was estimated in an international meta-analysis of individual-level data from 46 prospective cohorts. Previous falls were associated with an increased fracture risk in women and men and should be considered as an additional risk factor in the FRAX® algorithm.

***Introduction***Previous falls are a well-documented risk factor for subsequent fracture but have not yet been incorporated into the FRAX algorithm. The aim of this study was to evaluate, in an international meta-analysis, the association between previous falls and subsequent fracture risk and its relation to sex, age, duration of follow-up, and bone mineral density (BMD).

***Methods***The resource comprised 906,359 women and men (66.9% female) from 46 prospective cohorts. Previous falls were uniformly defined as any fall occurring during the previous year in 43 cohorts; the remaining three cohorts had a different question construct.The association between previous falls and fracture risk (any clinical fracture, osteoporotic fracture, major osteoporotic fracture, and hip fracture) was examined using an extension of the Poisson regression model in each cohort and each sex, followed by random-effects meta-analyses of the weighted beta coefficients.

***Results***Falls in the past year were reported in 21.4% of individuals. During a follow-up of 9,102,207 person-years, 87,352 fractures occurred of which 19,509 were hip fractures. A previous fall was associated with a significantly increased risk of any clinical fracture both in women (hazard ratio [HR] 1.42, 95% confidence interval [CI] 1.33-1.51) and men (HR 1.53, 95% CI 1.41-1.67). The HRs were of similar magnitude for osteoporotic, major osteoporotic fracture, and hip fracture. Sex significantly modified the association between previous fall and fracture risk, with predictive values being higher in men than in women (e.g., for major osteoporotic fracture, HR 1.53 (95% CI 1.27-1.84) in men vs. HR 1.32 (95% CI 1.20-1.45) in women, P for interaction = 0.013). The HRs associated with previous falls decreased with age in women and with duration of follow-up in men and women for most fracture outcomes. There was no evidence of an interaction between falls and BMD for fracture risk. Subsequent risk for a major osteoporotic fracture increased with each additional previous fall in women and men.

***Conclusions***A previous self-reported fall confers an increased risk of fracture that is largely independent of BMD. Previous falls should be considered as an additional risk factor in future iterations of FRAX to improve fracture risk prediction.

**Keywords:** previous falls – fracture risk – hip fracture – major osteoporotic fracture – meta-analysis – risk factors

**Introduction**

Falls are common in the aging population, with more than one third of community-dwelling adults above the age of 75 years experiencing a fall every year [1]. Falls are a leading cause of injury, disability, and death with around 10-15% of falls in older adults resulting in a fracture [2, 3]. Indeed, many epidemiological studies have shown that falls history is associated with an increase in fracture risk [4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19]. In addition, a fall within the past 4 months appears to confer a similarly high fracture risk as a recent fracture [20].

The FRAX® tool, released in 2008 by the then World Health Organization (WHO) Collaborating Centre at Sheffield, UK, is a fracture risk assessment tool for estimating individualized 10-year probability of hip and major osteoporotic fracture (MOF: hip, clinical spine, distal forearm or proximal humerus) [21]. The algorithm integrates seven dichotomous clinical risk factors (prior fragility fracture, parental hip fracture, smoking, systemic glucocorticoid use, excess alcohol intake, rheumatoid arthritis, and other secondary causes of osteoporosis) with age, sex, and body mass index and optionally, a femoral neck bone mineral density (BMD) measurement.

Despite being a well-known risk factor for fracture, previous falls were not included as a risk factor in the original FRAX algorithm [22, 23], whereas fall history is an input variable in other risk engines such as the Garvan fracture risk calculator [24] and the QFracture algorithm [25]. At the time of the launch of the FRAX calculator, there was a lack of reliable data with a uniform question construct [22, 23] and it remained unclear whether the fracture risk attributable to previous falls was amenable to pharmacological intervention [26]. Since 2008, assessment of previous falls has been shown to improve fracture prediction in addition to FRAX clinical risk factors and BMD in women and men [27, 28]. Moreover, pharmacological interventions, including menopausal hormone treatment [29, 30], clodronate [31], zoledronate [32] and omega-3 fatty acids [33] as well as non-pharmacological interventions [34, 35, 36] have been shown to have a beneficial effect in lowering the increased fracture risk associated with previous falls. Evidence that fall prevention interventions reduce subsequent fracture risk remains, however, limited [37, 38, 39, 40, 41, 42, 43]. With the update of the FRAX tool currently under development and the associated large resource assembled [44], data on previous falls are available both in a larger number of cohorts and with a uniform question construct, making it possible to consider falls history a new candidate input variable. The aim of the present study was to examine the risk of fracture associated with previous falls in an international setting and to determine its dependence on age, sex, duration of follow-up, and BMD.

**Methods**

The study population was derived from a systematic review that identified prospective cohort studies for the update of FRAX. The study was registered with the International prospective register of systematic reviews, PROSPERO (CRD42021227266), and followed the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines. Studies were eligible if the cohort was prospective, included at least 200 participants, assessed an adequate number of clinical risk factors and reported an adequate number of incident fracture outcomes. We analysed baseline and follow-up data from 906,359 women and men from 46 prospective cohorts, the majority of which were population-based. Of these 46 cohorts, 17 included only female participants, 6 included only male participants, whereas the remaining 23 included both. Details of each of the cohorts have been published previously [44] and are summarised in Table 1.

*Identifying falls*

A history of falls was obtained through questionnaires and was available in 46 cohorts that were assembled to construct the update of the FRAX algorithm. The question to ascertain self-reported falls was uniformly defined in 43 out of the 46 cohorts as “Have you fallen during the past year/12 months”. The remaining three cohorts had a different question construct for previous falls (Bern, “2 or more falls in the last 12 months”; CaMos, “falls in the last month”; Sheffield, “2 or more falls within the previous months”) (Table 1). Information on the number of previous falls was available in 30 cohorts. The number of previous falls was examined as a categorical variable (0, 1, 2 >3 falls in the past year).

*Identifying fractures*

Ascertainment of incident clinical fractures was undertaken by self-report and/or verified from hospital or central databases. Clinical fracture outcomes comprised any clinical fracture, osteoporotic fracture (defined according to Kanis et al. [45] as clinical vertebral, ribs, pelvis, humerus, clavicle, scapula, sternum, hip, other femoral fractures, tibia, fibula, distal forearm/wrist), MOF, and hip fracture.

*Other variables of interest*

Covariates of interest included current age since start of follow-up, current time since start of follow-up, and BMD at the femoral neck. Femoral neck BMD measurements were only available in a subset of individuals. Standardised BMD values were utilised to accommodate different DXA equipment. Corresponding femoral neck T-scores were calculated as previously described [46, 47].

*Statistical methods*

The association between previous falls and the risk of fracture was estimated using an extension of the Poisson regression model [48, 49] applied separately to each cohort, irrespective of risk factor definition, and separately by sex for those cohorts contributing both women and men. Because of an embargo on transfer of primary data from Manitoba, Cox regression was used on the Manitoba cohort on site and beta coefficients, variances, and co-variances forwarded to the analysis team. The associations between previous falls and risk of fracture were described as hazard ratio (HR) for fracture with 95% confidence intervals (CIs) for any fall versus no fall. The number of falls in the previous year was also compared to no falls. The observation period of each participant was divided in intervals of 1 month. The first incident fracture per participant was counted for each relevant outcome. Covariates examined were current age at the start of follow-up, current time since start of follow-up, and BMD T-score at the femoral neck. The estimated value of the beta-coefficients and their variance was determined from the Poisson model for each age from 40 years. The results of each cohort and both sexes were weighted according to the variance and merged to determine the weighted means and standard deviations. Interaction terms were used to determine whether the strength of the association of previous falls and fracture risk changed with age, duration of follow-up, sex, or femoral neck T-score. Interactions with age, duration of follow-up, and femoral neck BMD were also explored using piecewise linear regression to check the adequacy of the Poisson model.

Heterogeneity between cohorts was tested by the I2 statistic [50]. Random-effects models were used in the meta-analysis as moderate (I2=50) to high (I2=75) heterogeneity was noted between cohorts. Individuals with missing data were excluded. No data were imputed.

*Sensitivity analyses*

As indicated above, the effect of sex on the risk of fracture was computed in those cohorts that contributed both women and men. Similarly, differences in fracture risk with and without BMD were additionally explored in those cohorts that contributed probabilities both with and without BMD. Results were also computed for those cohorts with a uniformly defined question construct for previous falls (i.e., excluding the Bern, CaMos, and Sheffield cohorts). The evaluation of the effects of race and ethnicity was restricted to those cohorts recording more than one race or ethnic group (Asian, Black, Hispanic, and Caucasian), comprising CaMos, Health ABC, LASA, Manitoba, MrOS USA, SOF, UK Biobank and WHI. Finally, fracture risk associated with a previous fall was explored according to study quality. Quality was based on a 0/1 score for four criteria: Population-based cohort (yes scores 1); Fracture ascertainment (self-report scores 0, others score 1); Duration of follow-up (> 2 years, scores 1); Average loss to follow-up/year (< 10%, scores 1). This gives a maximum score of 4 and a minimum of 0. A quality score of 0 or 1 was designated as poor quality, a score of 2 or 3 categorised as intermediate quality, and a score of 4 designated as high quality [44].

**Results**

The analysis population comprised 606,715 women and 299,644 men, aged 20-111 years, who were followed for 5.9 million person-years and 3.2 million person-years, respectively (Table 1, Appendix Table 1 and 2). During an average follow-up of 10.0 years, 67,308 women and 20,044 men sustained at least one fracture; 58,375 and 15,713 were characterized as a MOF in women and men, respectively, and 14,829 and 4680 were hip fractures. BMD measurements were available in 160,580 (17.7%) individuals. A previous fall was reported in 21.4% of individuals (148,382 women and 45,345 men). Falls were reported more frequently in women than in men (24.5% vs. 15.1%, respectively). The risk factor was uniformly defined in 43 out of 46 cohorts (Table 1). The prevalence of a previous fall among the cohorts increased (almost linearly) with age, being 16.3% at 20-29 years, to 22.2% at 50-59 years, and up to 45.8% at 90-99 years.

*Previous falls and fracture*

A previous fall in the past year was associated with a significantly increased risk of any subsequent fracture in both women (HR 1.42, 95% CI 1.33-1.51) and men (HR 1.53, 95% CI 1.41-1.67) (Table 2). The HRs were of similar magnitude for the specific fracture outcomes, ranging from 1.36 to 1.42 and 1.50 to 1.59 in women and men, respectively. Forest plots showing the effect size associated with a previous fall on the risk of a MOF and a hip fracture in women and men are shown in Figure 1.

*Previous falls and sex*

Taking all cohorts into account, the HRs for the association between previous falls in the past year and fracture risk were consistently higher for men compared with women for all fracture outcomes (Table 2). When estimating the models using only those cohorts that contributed both women and men, a significant interaction between previous falls and sex was observed, with the predictive value of previous falls for fracture risk higher in men than in women by approximately 10-30% (Table 3). For example, in the case of the outcome MOF, the HR for previous falls was 1.32 (95% CI 1.20-1.45) for women and 1.53 (95% CI 1.27-1.84) for men (P-value for the interaction, P=0.013).

*Previous falls and age*

At all ages, previous falls in the past year were a risk factor for subsequent fracture. The HRs were highest at younger ages and decreased progressively with age (Table 4). A significant interaction between previous falls and age was observed in women for all fracture outcomes (Table 4). For hip fracture, the HR associated with previous falls decreased from 2.63 (95% CI 1.85-3.76) at the age of 40 years to 1.09 (95% CI 1.00-1.19) at the age of 90 years (P<0.001) (Figure 2). In contrast, in men, the interaction term with age was not significant (Table 4). Similar relationships were observed using piecewise linear regression models (data not shown).

*Previous falls and duration of follow-up*

For all fracture outcomes, the risk following a previous fall in the past year decreased slowly over time since the start of follow-up (Table 5). A significant interaction was observed between previous falls and duration of follow-up for all fracture outcomes in women. In men, the interaction term was only significant for any and osteoporotic fractures. An almost identical relationship was observed using piecewise linear regression models (data not shown).

*Previous falls and BMD*

The predictive value of a previous fall on incident fracture risk was only marginally downward adjusted or not affected by the inclusion of femoral neck BMD in the models depending on the fracture outcome. In particular, the HRs from the models including only those cohorts contributing to both scenarios (i.e. in which femoral neck BMD had been measured) did not substantially differ (Appendix Table 3). When analysing the interaction between previous falls and femoral neck T-score, the HRs tended to increase as the BMD increased in both women and men for all fracture outcomes (Table 6). The interaction terms were, however, not significant. Piecewise linear regression models with a knot at T-score -2.5 largely confirmed these results (data not shown).

*Number of previous falls and fracture*

Information on the number of self-reported previous falls in the past year was available in 30 cohorts (Table 1). Fracture risk increased progressively with an increasing number of previous falls (Table 7). The HR for a MOF increased from 1.27 (95% CI 1.19-1.36) for one fall to 1.48 (95% CI 1.30-1.68) for two falls to 1.68 (95% CI 1.51-1.87) for >3 falls in women. The increment in risk for each additional fall was greater in men than in women. The HR for a MOF in men increased from 1.48 (95% CI 1.30-1.69) for one fall to 2.13 (95% CI 1.69-2.68) for two falls to 2.45 (95% CI 1.65-3.63) for >3 falls. Similar HRs were observed for the other fracture outcomes.

*Previous falls and risk of death*

One or more previous falls was significantly associated with an increased risk of death in both women (HR 1.15, 95% CI 1.09-1.22) and men (HR 1.20, 95% CI 1.09-1.33). HRs remained essentially unchanged when femoral neck T-score was added to the models.

*Sensitivity analyses*

In sensitivity analyses, the association between a previous fall and subsequent fracture risk did not materially change when the analyses were restricted to those cohorts with a uniform risk factor definition (n=43 cohorts, Appendix Table 4). No significant differences in HRs were observed according to race and ethnicity in those cohorts with these characteristics documented (Appendix Table 5). When analysing the cohorts according to quality score, fracture risk was significantly increased following a previous fall in cohorts of intermediate quality (a quality score of 2 or 3) and cohorts of high quality (a quality score of 4), while this association did not reach statistical significance in the cohorts of poor quality (Appendix Table 6). Moreover, the predictive value of previous falls for fracture risk was significantly larger in cohorts of intermediate quality compared with cohorts of high quality for all fracture outcomes in women and all but MOF in men.

**Discussion**

With the second iteration of FRAX currently under development and the corresponding largest resource available to date, the predictive value of previous falls for subsequent fracture risk was investigated in 46 prospective cohorts. Our findings show that a previous fall in the past year confers a significantly increased risk of any clinical fracture, osteoporotic fracture, MOF, and hip fracture with the increase in risk varying between 36% and 59% depending on the fracture outcome and sex. Notably, the effect size was largely unaffected by race and ethnicity. Previous studies have similarly shown that assessment of falls history predicts fracture risk [5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20] and improves fracture risk prediction in addition to FRAX clinical risk factors and BMD [27, 28] in both women and men. Moreover, the availability of a standardized question construct in a large majority of the contributing cohorts and the increased risk of fractures associated with previous falls being amenable to pharmacological treatment of the underlying bone fragility [29, 30, 31, 32] support the consideration of falls history as an additional clinical risk factor in the update of the FRAX tool.

A significant interaction was observed between previous falls and sex for incident fracture risk with the predictive value of previous falls higher in men than in women. Also, in women, the increased risk mediated by previous falls decreased with age whereas the risk was not significantly associated with age in men such that it remained significantly increased at the age of 80 and 90 years. As previously reported [51], women fell more frequently than men. This suggests that the more frequent falls in women are less injurious than in men despite the fact they occur more often in older women. Thus, previous falls are an important risk factor for fracture in older men but less so for older women, i.e., those individuals who most often present with fractures in daily practice. This finding is in accordance with recent findings from the Osteoporotic Fractures in Men study showing fall history (previous year) is a strong risk factor for clinical fracture and hip fracture in late-life (over 80 years of age) men [52]. In addition, we observed a significant interaction between previous falls and follow-up time for the prediction of incident fractures with the risk diminishing over time. A previous study of elderly men showed that the association between previous falls and fracture risk decreased progressively with increasing follow-up time [27]. This may be a possible concern with the incorporation of previous falls into FRAX as falls history may provide less predictive power over longer periods. As with all risk variables to be used in FRAX, any interaction of effect over time is also important to incorporate in future probability models. Similarly, previous falls are associated with increased mortality, an important consideration when modelling 10-year fracture probability which, in the case of FRAX, is based on the hazards of both death and fracture [21].

Our findings indicate that the increased fracture risk mediated by previous falls is largely independent of BMD as the point estimates did not materially change after accounting for this measure. The predictive value of previous falls tended to increase with each unit increase in femoral neck T-score; the interaction terms were, however, not significant for the fracture outcomes investigated. The mechanism for the BMD-independent increase in fracture risk associated with falls history could not be determined from this study.

The predictive value of previous falls increased progressively with additional falls reported in the previous year in women and men. Our results are in line with previous findings of the risk of fracture increasing with the number of reported falls [6, 16, 28, 53] although the point estimates in this study were smaller compared with those previously reported. The clear dose-response indicates that the next generation of FRAX should incorporate the number of previous falls in the past year as an input variable. In the interim, conventional estimates of FRAX can be adjusted by hand [53] or electronically through the FRAXplus portal [54] (<https://www.fraxplus.org/>).

A particular strength of this study is that the estimates of fracture risk for previous falls are derived from the largest international resource available to date. The participating cohorts were identified partly through collaboration and through a systematic search of potentially available cohorts [44]. Computations were based on individual-level data, decreasing the risk of publication biases, and the extent of the data resource allowed for additional analyses such as interactions. We also acknowledge several limitations. Falls history was based on recall, which may not be accurate, especially since older adults who experience a fall may fear institutionalization, resulting in under reporting. This bias would most likely weaken rather than strengthen any associations with incident fractures. Also, it is not possible to examine all potential confounding factors that contribute to falls risk and previous falls such as physical activity levels and medications affecting balance. In addition, a simple question construct was used to ascertain falls, and it is possible that a more detailed questioning within the framework of a research protocol might have extracted more accurate information [55]. However, in the context of risk assessment undertaken in the clinic, optimised repeatability and simplicity are likely to be worth a modest sacrifice in accuracy. Finally, not all cohorts used a dose-responsive question construct on number of previous falls.

In summary, a uniform question construct regarding previous falls is associated with incident fracture risk, independent of BMD. Moreover, fracture risk increases with each additional fall in women and men. These data provide further support to incorporate previous falls into future iterations of FRAX to guide clinical management of those individuals at highest risk of fracture.

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**Compliance with ethical standards**

All individual cohorts with candidate risk factors available have been approved by their local ethics committees and informed consent has been obtained from all study participants. General ethics approval for the use of these cohorts is also given by the University of Sheffield.

*Conflict of interest*   
JA Kanis led the team that developed FRAX as director of the WHO Collaborating Centre for Metabolic Bone Diseases; he is a director of Osteopoorosis Research Ltd that maintains FRAX. EV McCloskey, WD Leslie, M Lorentzon, NC Harvey, M Schini, E Liu, L Vandenput and H Johansson are members of the FRAX team. JA Kanis, NC Harvey, and EV McCloskey are members of the advisory body to the National Osteoporosis Guideline Group.

KE Åkesson has no financial interest related to FRAX; chaired the National SALAR Group for Person-Centered Care Pathway Osteoporosis.

FA Anderson led the team that developed GLOW, while director of the Center for Outcomes Research at the University of Massachusetts Medical School; he has no financial interest in FRAX.

R Azagra has received funding for research from Instituto Carlos III of Spanish Ministry of Health, IDIAP Jordi Gol of Catalan Government and from Scientific Societies SEMFYC and SEIOMM.

CL Bager is employed at Nordic Bioscience and owns stock in Nordic Bioscience. She declares no competing interests in relation to this work.

HA Bischoff-Ferrari has no financial interest in FRAX. For the DO-HEALTH trial cohort, Prof. Bischoff-Ferrari reports independent and investigator-initiated grants from European Commission Framework 7 Research Program, from the University of Zurich, from NESTEC, from Pfizer Consumer Healthcare, from Streuli Pharma, plus non-financial support from DNP. For the study cohort extension, she reports independent and investigator-initiated grants from Pfizer and from Vifor. Further, Prof. Bischoff-Ferrari reports non-financial support from Roche Diagnostics and personal fees from Wild, Sandoz, Pfizer, Vifor, Mylan, Roche, Meda Pharma, outside the submitted work with regard to speaker fees and travel fees.

JR Center has received honoraria for speaking at educational meetings and for advisory boards from Amgen and honoraria for an advisory board from Bayer, all unrelated to this work.

R Chapurlat has no financial interest in FRAX. He has received grant funding from Amgen, UCB, Chugai, MSD, Mylan and Medac. He has received honoraria from Amgen, UCB, Chugai, Galapagos, Biocon, Abbvie, Haoma Medica, Pfizer, Amolyt, MSD, Lilly, BMS, Novartis, Arrow, PKMed, Kyowa-Kirin, and Sanofi.

C Christiansen owns stock in Nordic Bioscience. He declares no competing interests in relation to this work.

C Cooper reports personal fees from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB.

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C Ohlsson is listed as a coinventor on two patent applications regarding probiotics in osteoporosis treatment.

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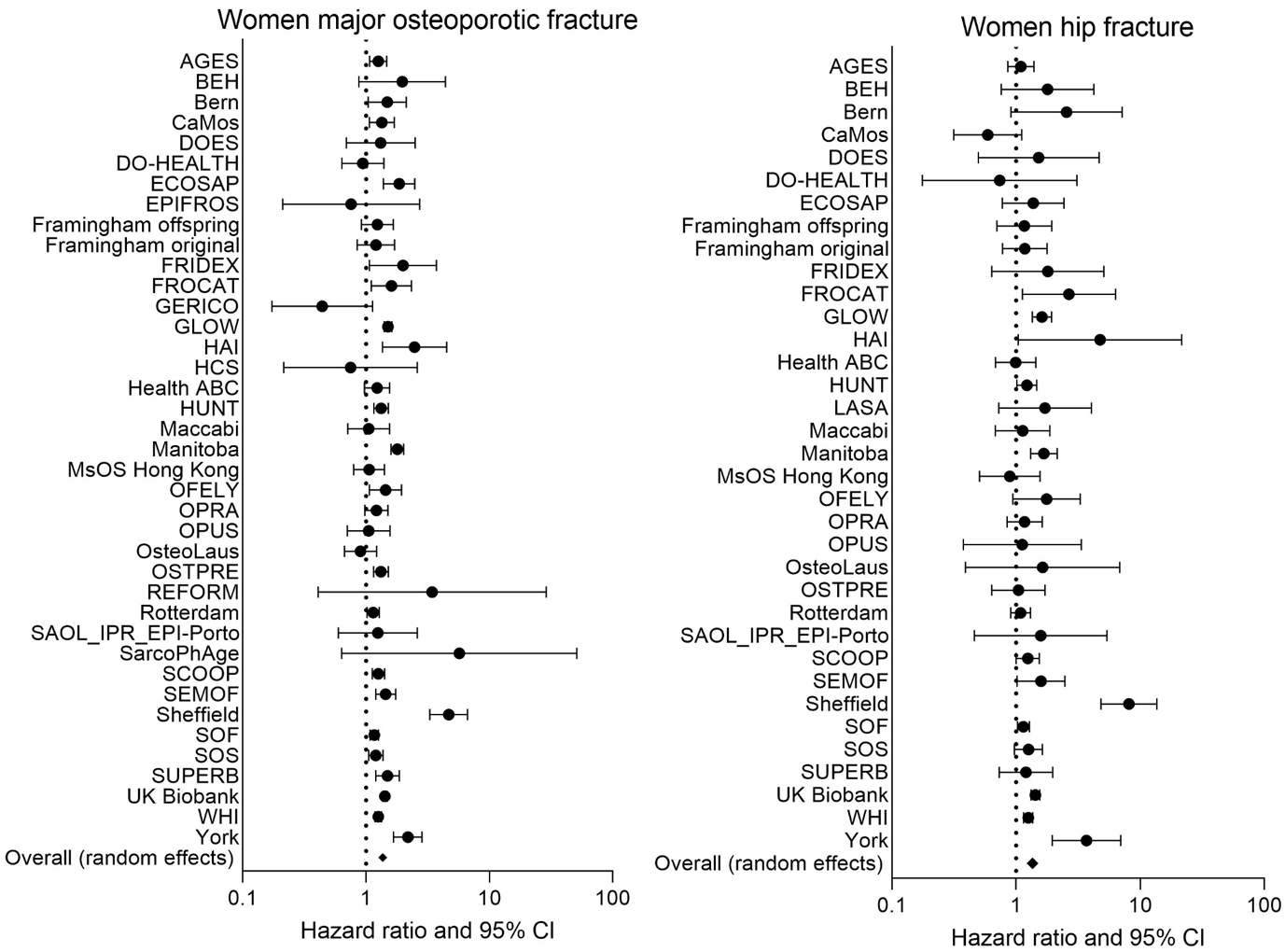
*Human and animal rights*   
This study does not contain any original studies with human participants or animals performed by any of the authors.

*Ethics*All individual cohorts with candidate risk factors available have been approved by their local ethics committees and informed consent has been obtained from all study participants. General ethics approval for the use of these cohorts is also given by the University of Sheffield. Participant data will be stored in coded, de-identified form. Only summary statistics and aggregate data is published, not allowing for identification of individual study participants.

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A comparison of a number of patients with osteoporotic injuries

Description automatically generated

**Fig 1** Forest plots of the association of previous falls with subsequent risk of a major osteoporotic fractures or a hip fracture in women (upper panels) and men (lower panels). Effect estimates (hazard ratios) are shown for fracture (circles), adjusted for age and duration of follow-up. The horizontal lines represent 95% confidence intervals.



**Fig 2** Interaction between one or more falls in the year prior to baseline and age at baseline in the association with subsequent risk of a hip fracture in women (left panel) and men (right panel). Hazard ratios (HR), adjusted for duration of follow-up, and 95% confidence interval are shown. P values are for the interaction term with age at baseline

**Table 1.** Description of cohort characteristics, previous falls, and incident fracture outcomes

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cohort** | **n** | **Person-years** | **Age (years)** | | | **Women**  **(%)** | **Previous fall (%)** | **Number of falls** | **FN BMD (n)** | **Number of incident fractures** | | | |
| **Mean** | **Min** | **Max** | **Any** | **Ost** | **MOF** | **Hip** |
| AGES | 5637 | 45188 | 76.9 | 66.0 | 96.0 | 57.5 | 18.6 | 1: 694  2 or 3: 210  4 or 5: 38  6 or more: 35 | 4772 | 1600 | 1378 | 1120 | 525 |
| BEH | 2299 | 10196 | 69.3 | 60.0 | 96.0 | 51.4 | 10.7 | - | 2291 | 98 | 76 | 46 | 40 |
| Berna | 3690 | 13840 | 59.9 | 20.1 | 94.3 | 77.6 | 12.2 | 2 or more: 452 | 3642 | 475 | 339 | 237 | 23 |
| CaMosb | 9423 | 121634 | 62.1 | 25.0 | 103.0 | 69.4 | 6.7 | - | 8290 | 2435 | 1753 | 1188 | 340 |
| DOES | 2086 | 19341 | 70.1 | 47.0 | 94.0 | 60.7 | 30.0 | 1: 447  2: 121  3: 46  4: 38 | 2057 | 480 | 404 | 299 | 95 |
| DO-HEALTH | 2156 | 5956 | 74.9 | 70.0 | 95.0 | 61.7 | 42.0 | 1: 658  2: 148  3: 48  4: 21  5: 6  6 or more: 8 | 1451 | 267 | 192 | 119 | 10 |
| ECOSAP | 5146 | 16857 | 72.3 | 65.0 | 100.0 | 100.0 | 26.7 | - | - | 311 | 259 | 188 | 52 |
| EPIFROS | 284 | 2826 | 61.6 | 40.0 | 96.0 | 54.6 | 18.3 | 1: 34  2: 9  3: 3  4: 2  5: 1  12: 1 | 12 | 27 | 20 | 16 | 3 |
| FORMEN | 1886 | 16265 | 72.5 | 65.0 | 93.0 | 0.0 | 16.3 | - | 1882 | 90 | 90 | 58 | 10 |
| Framingham\_offspring | 3491 | 47178 | 61.4 | 33.0 | 88.0 | 54.1 | 20.0 | 1: 488  2: 121  3: 36  4: 11  5: 8  6 or more: 15 | 2908 | 677 | 524 | 271 | 88 |
| Framingham\_original | 1094 | 9390 | 79.5 | 72.0 | 101.0 | 64.7 | 29.9 | 1: 184  2: 80  3: 29  4: 7  5: 3  6 or more: 13 | 884 | 261 | 234 | 166 | 113 |
| FRIDEX | 815 | 8077 | 56.8 | 40.0 | 84.0 | 100.0 | 24.4 | 1: 128  2: 31  3: 25  4: 5  5: 4  6 or more: 6 | 815 | 112 | 56 | 41 | 15 |
| FROCAT | 1930 | 19174 | 69.3 | 32.0 | 111.0 | 55.5 | 25.9 | 1: 257  2: 104  3: 59  4: 22  5: 11  6 or more: 12 | 233 | 228 | 182 | 159 | 33 |
| GERICO | 758 | 2742 | 67.9 | 64.6 | 71.8 | 79.4 | 47.4 | 1: 218  2: 67  3: 34  4: 13  5: 1  6 or more: 26 | 744 | 71 | 51 | 26 | 2 |
| GLOW | 53673 | 214575 | 68.2 | 55.0 | 108.0 | 100.0 | 37.6 | 1: 12200  2 or more: 7968 | - | 5628 | 4233 | 2804 | 480 |
| HAI | 3515 | 9291 | 70.5 | 69.2 | 72.0 | 50.4 | 11.1 | - | 3436 | 125 | 113 | 77 | 10 |
| HCS | 251 | 2009 | 66.0 | 61.3 | 70.9 | 96.8 | 19.9 | 1: 39  2: 9  3: 1  4: 1 | 250 | 33 | 24 | 17 | 0 |
| Health ABC | 3064 | 36348 | 73.6 | 68.0 | 80.0 | 51.5 | 21.3 | - | 3032 | 699 | 595 | 520 | 235 |
| HUNT | 6803 | 69261 | 77.1 | 70.0 | 96.9 | 55.0 | 20.3 | - | 1859 | 2290 | 1998 | 1445 | 843 |
| LASA | 1472 | 7568 | 75.7 | 64.8 | 88.7 | 51.5 | 32.3 | 1: 249  2: 116  3: 37  4: 24  5: 17  6 or more: 29 | 519 | 132 | 96 | - | 39 |
| Maccabi | 83577 | 757792 | 65.4 | 37 | 91 | 64.8 | 5.0 | - | 7678 | 19335 | 19248 | 18408 | 5780 |
| Manitoba | 37246 | 105145 | 66.6 | 20.0 | 104.3 | 89.0 | 20.9 | 1: 4654  2: 1641  3: 670  4: 270  5: 307  6 or more: 259 | 37246 | 2064 | 1936 | 1437 | 342 |
| MINOS | 681 | 6152 | 65.2 | 50.0 | 86.0 | 0.0 | 24.1 | 1: 100  2 or more: 64 | 672 | 63 | 56 | 25 | 3 |
| MrOS Hong Kong | 2000 | 19744 | 72.4 | 65.0 | 92.0 | 0.0 | 15.4 | 1: 234  2 or 3: 63  4 or 5: 7  6 or more: 3 | 2000 | 231 | 201 | 148 | 63 |
| MrOS Sweden | 3001 | 34078 | 74.9 | 69.0 | 81.0 | 0.0 | 16.5 | - | 2809 | 964 | 869 | 724 | 338 |
| MrOS USA | 5994 | 75015 | 73.7 | 64.0 | 100.0 | 0.0 | 21.2 | 1: 722  2 or 3: 448  4 or 5: 67  6 or more: 31 | 5993 | 1394 | 1082 | 814 | 330 |
| MsOS Hong Kong | 2000 | 17528 | 72.6 | 65.0 | 98.0 | 100.0 | 24.1 | 1: 320  2 or 3: 137  4 or 5: 22  6 or more: 3 | 2000 | 338 | 298 | 247 | 69 |
| OFELY | 867 | 15136 | 58.8 | 40.0 | 89.0 | 100.0 | 30.8 | 1: 157  2: 68  3: 22  4: 8  5: 5  6 or more: 7 | 861 | 245 | 207 | 180 | 40 |
| OPRA | 914 | 10664 | 75.2 | 75.0 | 76.0 | 100.0 | 28.4 | 1: 126  2: 65  3: 40  4: 11  5: 10  7 or more: 8 | 825 | 457 | 413 | 398 | 173 |
| OPUS | 1978 | 12135 | 62.0 | 20.2 | 80.0 | 100.0 | 29.0 | 1: 304  2: 120  3: 73 | 1970 | 234 | 146 | 112 | 14 |
| OsteoLaus | 1475 | 6726 | 64.5 | 50.2 | 81.5 | 100.0 | 25.4 | - | 1457 | 307 | 245 | 226 | 8 |
| OSTPRE | 9998 | 97799 | 57.3 | 52.4 | 62.7 | 100.0 | 36.0 | 1: 1675  2: 1014  3: 429  4: 151  5: 147  6 or more: 187 | 2460 | 1635 | 1123 | 824 | 68 |
| REFORM | 1003 | 1482 | 77.9 | 65.0 | 99.0 | 60.5 | 65.2 | 1: 314  2: 186  3: 83  4: 33  5: 10  6 or more: 24 | - | 30 | 17 | 12 | 4 |
| Rotterdam | 10382 | 133691 | 68.7 | 55.0 | 106.2 | 59.0 | 18.7 | - | 7786 | 2885 | 2580 | 2103 | 790 |
| SAOL-IPR-EPIPorto | 916 | 11139 | 55.9 | 40.0 | 89.0 | 77.6 | 22.8 | 1: 111  2: 42  3: 33  4: 4  5: 5  6 or more: 12 | 914 | 104 | - | 41 | 12 |
| SarcoPhAge | 228 | 440 | 75.9 | 68.2 | 93.4 | 57.0 | 37.3 | - | 217 | 13 | 8 | 5 | 1 |
| SCOOP | 12368 | 58845 | 75.6 | 70.0 | 86.0 | 100.0 | 27.8 | - | 2790 | 1932 | 1630 | 1288 | 375 |
| SEMOF | 7131 | 20625 | 75.2 | 70.0 | 91.3 | 100.0 | 31.4 | - | 919 | 683 | 596 | 464 | 80 |
| Sheffieldc | 2175 | 7441 | 80.0 | 74.3 | 100.9 | 100.0 | 6.0 | 2 or more: 131 | 2154 | 289 | 234 | 191 | 67 |
| SOF | 9654 | 135907 | 71.6 | 65.0 | 89.0 | 100.0 | 30.0 | 1: 1875  2 or 3: 867  4 or 5: 127  6 or more: 32 | 7760 | 4346 | 3462 | 2801 | 1411 |
| SOS | 16441 | 61467 | 74.2 | 60.8 | 92.5 | 100.0 | 27.5 | 1: 2336  2: 1243  3: 537  4 or more: 401 | 4071 | 1365 | 1306 | 978 | 253 |
| STRAMBO | 821 | 7564 | 72.2 | 51.0 | 88.4 | 0.0 | 20.7 | - | 803 | 117 | 86 | 42 | 17 |
| SUPERB | 3025 | 10752 | 77.8 | 74.7 | 81.0 | 100.0 | 29.6 | - | 3012 | 463 | 421 | 341 | 70 |
| UK Biobank | 499867 | 5735643 | 56.5 | 38.0 | 73.0 | 54.4 | 19.8 | 1: 65958  2 or more: 33141 | 19530 | 25049 | 19977 | 12044 | 3925 |
| WHI | 78612 | 1072537 | 64.4 | 49.0 | 79.0 | 100.0 | 32.3 | 1: 15680  2: 6508  3 or more: 3232 | 5576 | 6377 | 5020 | 4392 | 2278 |
| York | 4532 | 9044 | 77.1 | 47.6 | 98.9 | 100.0 | 30.1 | 1: 699  2: 356 | - | 393 | 310 | 223 | 42 |
| Overall (total/mean) | 906359 | 9102207 | 61.6 | 20.0 | 111.0 | 66.9 | 21.4 |  | 160580 | 87352 | 74088 | 57265 | 19509 |

FN BMD, femoral neck bone mineral density; OST, osteoporotic fracture; MOF, major osteoporotic fracture; AGES, Age, Gene/Environment Susceptibility‐Reykjavik Study; BEH, Bushehr Elderly Health; CaMos, Canadian Multicentre Osteoporosis Study; DOES, Dubbo Osteoporosis Epidemiology Study; DO-HEALTH, VitaminD3-Omega3-Home Exercise-Healthy Aging and Longevity Trial; ECOSAP, Ecografía Osea en Atención Primaria; EPIFROS**,** EPIdemiology and Fracture Risk factors for Osteoporosis in Spain; FORMEN, Fujiwara-kyo Osteoporosis Risk in Men; FRIDEX, Fracture RIsk factors and bone DEnsitometry type central dual X-ray; FROCAT, Fracture Risk factors for Osteoporosis in CATalonia; GERICO, Geneva Retirees Cohort; GLOW, Global Longitudinal Study of Osteoporosis in Women; HAI, Healthy Ageing Initiative; HCS, Hertfordshire Cohort Study; Health ABC, Health, Aging and Body Composition; HUNT, Trøndelag Health Study; LASA, Longitudinal Aging Study Amsterdam; MINOS, Montceau les MINes OSteoporosis; MrOS, Osteoporotic Fractures in Men; MsOS, Osteoporotic Fractures in Women; OFELY, Os des Femmes de Lyon; OPRA, Osteoporosis Prospective Risk Assessment; OPUS, Osteoporosis and Ultrasound Study; OSTPRE, Kuopio OSTeoporosis risk factor and PREvention study; REFORM, REducing Falls with ORthoses and a Multifaceted podiatry intervention; SAOL-IPR-EPIPorto, Santo António dos Olivais, Instituto Português de Reumatologia and EPIPorto; SarcoPhAge, Sarcopenia and Physical Impairment with advancing Age; SCOOP, screening for prevention of fractures in older women; SEMOF, Swiss Evaluation of the Methods of Measurement of Osteoporotic Fracture risk; SOF, Study of Osteoporotic Fractures; SOS, SALT Osteoporosis Study; STRAMBO, Structure of the Aging Men’s Bone; SUPERB, Sahlgrenska University hospital Prospective Evaluation of Risk of Bone fractures; WHI, Women’s Health Initiative.

a, 2 or more falls in the last 12 months; b, falls in the last month; c, 2 or more falls within the previous months; all other cohorts, “fallen during the last year/12months”

**Table 2.** Association of previous falls with subsequent fracture risk at the sites indicated in women and men

|  |  |  |  |
| --- | --- | --- | --- |
| Outcome  fracture | Number  of  cohorts | I2  (%) | HR (95% CI) |
| ***Women*** |  |  |  |
| Any | 40 | 85 | 1.42 (1.33-1.51) |
| Hip | 35 | 69 | 1.36 (1.23-1.50) |
| MOF | 39 | 78 | 1.37 (1.28-1.46) |
| Ost | 39 | 84 | 1.41 (1.32-1.51) |
| ***Men*** |  |  |  |
| Any | 27 | 51 | 1.53 (1.41-1.67) |
| Hip | 20 | 39 | 1.59 (1.38-1.84) |
| MOF | 25 | 59 | 1.50 (1.32-1.70) |
| Ost | 25 | 54 | 1.59 (1.44-1.76) |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age and duration of follow-up.

BMD, bone mineral density; MOF, major osteoporotic fracture; Ost, osteoporotic fracture; I2, heterogeneity statistic

**Table 3.** Interaction between previous falls and sex in the association with subsequent fracture risk at the sites indicated in women and men

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome**  **fracture** | **Number of**  **cohorts** | **Women** | **Men** | **P value**  **for interaction** |
| **HR (95% CI)** | **HR (95% CI)** |
| Any | 21 | 1.34 (1.23-1.46) | 1.51 (1.32-1.73) | <0.001 |
| Hip | 15 | 1.28 (1.13-1.44) | 1.57 (1.24-1.98) | 0.017 |
| MOF | 19 | 1.32 (1.20-1.45) | 1.53 (1.27-1.84) | 0.013 |
| Ost | 19 | 1.35 (1.22-1.48) | 1.58 (1.35-1.85) | <0.001 |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age and duration of follow-up.  
MOF, major osteoporotic fracture; Ost, osteoporotic fracture

**Table 4.** Interaction between previous falls and age at baseline in the association with subsequent fracture risk at the sites indicated in women and men

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Outcome  fracture | Number  of cohorts | Age (years) | | | | | | P value\* |
| 40 | 50 | 60 | 70 | 80 | 90 |
| HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| ***Women*** |  |  |  |  |  |  |  |  |
| Any | 39 | 1.75 (1.53-2.01) | 1.65 (1.47-1.84) | 1.55 (1.42-1.68) | 1.45 (1.36-1.54) | 1.36 (1.31-1.41) | 1.28 (1.25-1.30) | <0.001 |
| Hip | 32 | 2.63 (1.85-3.76) | 2.21 (1.68-2.90) | 1.85 (1.53-2.25) | 1.55 (1.38-1.74) | 1.30 (1.23-1.38) | 1.09 (1.00-1.19) | <0.001 |
| MOF | 36 | 1.73 (1.44-2.08) | 1.61 (1.39-1.87) | 1.50 (1.34-1.68) | 1.40 (1.29-1.51) | 1.30 (1.24-1.36) | 1.21 (1.17-1.25) | <0.001 |
| Ost | 37 | 1.66 (1.41-1.96) | 1.56 (1.35-1.79) | 1.46 (1.30-1.63) | 1.37 (1.25-1.49) | 1.28 (1.20-1.36) | 1.20 (1.15-1.25) | <0.001 |
| ***Men*** |  |  |  |  |  |  |  |  |
| Any | 25 | 1.96 (1.47-2.62) | 1.83 (1.47-2.27) | 1.70 (1.47-1.96) | 1.58 (1.46-1.72) | 1.47 (1.38-1.58) | 1.37 (1.22-1.55) | 0.068 |
| Hip | 17 | 2.21 (1.05-4.63) | 2.03 (1.10-3.75) | 1.87 (1.15-3.04) | 1.72 (1.20-2.47) | 1.58 (1.25-2.01) | 1.46 (1.27-1.67) | 0.21 |
| MOF | 23 | 2.05 (1.32-3.20) | 1.90 (1.35-2.66) | 1.75 (1.38-2.22) | 1.62 (1.41-1.86) | 1.50 (1.37-1.63) | 1.38 (1.21-1.59) | 0.15 |
| Ost | 23 | 2.02 (1.40-2.91) | 1.89 (1.43-2.50) | 1.77 (1.46-2.14) | 1.65 (1.47-1.85) | 1.54 (1.45-1.65) | 1.44 (1.30-1.60) | 0.13 |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for duration of follow-up.

MOF, major osteoporotic fracture; Ost, osteoporotic fracture; \*P value for the interaction term with age at baseline

**Table 5.** Interaction between previous falls and duration of follow-up in the association with subsequent fracture risk at the sites indicated in women and men.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Outcome  fracture | Number  of cohorts | Duration of follow-up (years) | | | | | | P value\* |
| 0 | 2 | 4 | 6 | 8 | 10 |
| HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| ***Women*** |  |  |  |  |  |  |  |  |
| Any | 39 | 1.49 (1.38-1.62) | 1.44 (1.35-1.53) | 1.39 (1.33-1.46) | 1.34 (1.29-1.40) | 1.30 (1.23-1.36) | 1.25 (1.17-1.34) | 0.0041 |
| Hip | 34 | 1.54 (1.36-1.74) | 1.48 (1.33-1.65) | 1.42 (1.29-1.55) | 1.36 (1.25-1.47) | 1.30 (1.22-1.40) | 1.25 (1.17-1.33) | <0.001 |
| MOF | 38 | 1.46 (1.34-1.59) | 1.40 (1.31-1.50) | 1.35 (1.29-1.42) | 1.30 (1.25-1.36) | 1.26 (1.19-1.32) | 1.21 (1.13-1.30) | 0.0036 |
| Ost | 38 | 1.52 (1.40-1.65) | 1.45 (1.36-1.55) | 1.39 (1.32-1.46) | 1.33 (1.28-1.39) | 1.28 (1.21-1.34) | 1.22 (1.15-1.30) | <0.001 |
| ***Men*** |  |  |  |  |  |  |  |  |
| Any | 26 | 1.84 (1.65-2.05) | 1.72 (1.61-1.84) | 1.61 (1.52-1.71) | 1.51 (1.37-1.66) | 1.42 (1.22-1.64) | 1.33 (1.09-1.62) | 0.023 |
| Hip | 19 | 1.74 (1.32-2.28) | 1.69 (1.36-2.10) | 1.65 (1.40-1.95) | 1.61 (1.41-1.85) | 1.57 (1.37-1.80) | 1.53 (1.30-1.81) | 0.48 |
| MOF | 24 | 1.84 (1.66-2.03) | 1.76 (1.67-1.86) | 1.68 (1.56-1.82) | 1.61 (1.41-1.85) | 1.55 (1.26-1.90) | 1.48 (1.12-1.96) | 0.24 |
| Ost | 24 | 1.86 (1.70-2.04) | 1.75 (1.66-1.84) | 1.64 (1.53-1.76) | 1.54 (1.36-1.73) | 1.44 (1.21-1.72) | 1.35 (1.07-1.72) | 0.042 |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age.

MOF, major osteoporotic fracture; Ost, osteoporotic fracture; \*P value for the interaction term with duration of follow-up

**Table 6.** Interaction between previous falls and femoral neck T-score in the association with subsequent fracture risk at the sites indicated in women and men

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Femoral neck T-score** | **Outcome fracture** | | | |
| Any | Hip | MOF | Ost |
| HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| ***Women*** |  |  |  |  |
| -4 | 1.29 (1.18-1.41) | 1.40 (1.05-1.87) | 1.27 (1.11-1.46) | 1.24 (1.10-1.40) |
| -3 | 1.33 (1.25-1.42) | 1.44 (1.20-1.72) | 1.31 (1.20-1.43) | 1.31 (1.21-1.41) |
| -2 | 1.38 (1.30-1.46) | 1.48 (1.28-1.71) | 1.36 (1.26-1.46) | 1.38 (1.29-1.47) |
| -1 | 1.42 (1.31-1.55) | 1.52 (1.21-1.91) | 1.40 (1.27-1.55) | 1.45 (1.32-1.59) |
| 0 | 1.47 (1.30-1.65) | 1.56 (1.10-2.22) | 1.45 (1.24-1.68) | 1.52 (1.33-1.75) |
| 1 | 1.52 (1.29-1.78) | 1.61 (0.99-2.60) | 1.49 (1.21-1.84) | 1.61 (1.33-1.94) |
| 2 | 1.56 (1.28-1.91) | 1.65 (0.89-3.07) | 1.54 (1.18-2.02) | 1.69 (1.33-2.15) |
| 3 | 1.61 (1.27-2.06) | 1.70 (0.80-3.62) | 1.59 (1.14-2.22) | 1.78 (1.32-2.39) |
| 4 | 1.67 (1.25-2.22) | 1.75 (0.71-4.28) | 1.64 (1.11-2.43) | 1.87 (1.32-2.66) |
| Number of cohorts | 35 | 32 | 34 | 34 |
| P value**\*** | 0.15 | 0.70 | 0.32 | 0.072 |
| ***Men*** |  |  |  |  |
| -4 | 1.71 (1.34-2.20) | 0.88 (0.49-1.61) | 1.24 (0.82-1.87) | 1.58 (1.20-2.09) |
| -3 | 1.66 (1.40-1.97) | 1.06 (0.70-1.60) | 1.31 (0.98-1.75) | 1.58 (1.31-1.91) |
| -2 | 1.61 (1.45-1.78) | 1.27 (1.00-1.60) | 1.39 (1.17-1.64) | 1.58 (1.41-1.77) |
| -1 | 1.55 (1.44-1.68) | 1.52 (1.31-1.75) | 1.47 (1.34-1.60) | 1.57 (1.45-1.71) |
| 0 | 1.50 (1.33-1.70) | 1.81 (1.41-2.33) | 1.55 (1.34-1.79) | 1.57 (1.38-1.79) |
| 1 | 1.46 (1.20-1.76) | 2.17 (1.42-3.32) | 1.64 (1.27-2.12) | 1.57 (1.27-1.94) |
| 2 | 1.41 (1.07-1.84) | 2.60 (1.41-4.79) | 1.73 (1.18-2.53) | 1.56 (1.16-2.11) |
| 3 | 1.36 (0.96-1.93) | 3.11 (1.39-6.95) | 1.83 (1.10-3.04) | 1.56 (1.06-2.30) |
| 4 | 1.32 (0.86-2.03) | 3.72 (1.37-10.09) | 1.94 (1.03-3.64) | 1.55 (0.96-2.51) |
| Number of cohorts | 24 | 18 | 23 | 23 |
| P value**\*** | 0.44 | 0.073 | 0.40 | 0.96 |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age and duration of follow-up.

MOF, major osteoporotic fracture; Ost, osteoporotic fracture; \*P value for the interaction term with femoral neck T-score

**Table7.** Association between number of previous falls and subsequent fracture risk at the sites indicated in women and men

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome**  **fracture** |  | **1 fall vs none** | | **2 falls vs none** | | **≥ 3 falls vs none** | |
| Number of cohorts | HR (95% CI) | Number of cohorts | HR (95% CI) | Number of cohorts | HR (95% CI) |
| ***Women*** |  |  |  |  |  |  |  |
| Any |  | 25 | 1.32 (1.24-1.41) | 27 | 1.55 (1.38-1.74) | 22 | 1.73 (1.55-1.93) |
| Hip |  | 21 | 1.28 (1.16-1.41) | 21 | 1.57 (1.27-1.95) | 17 | 1.73 (1.49-2.02) |
| MOF |  | 24 | 1.27 (1.19-1.36) | 23 | 1.48 (1.30-1.68) | 20 | 1.68 (1.51-1.87) |
| Ost |  | 24 | 1.32 (1.22-1.42) | 25 | 1.53 (1.35-1.73) | 20 | 1.74 (1.55-1.96) |
| ***Men*** |  |  |  |  |  |  |  |
| Any |  | 15 | 1.46 (1.38-1.54) | 15 | 2.03 (1.71-2.42) | 12 | 2.27 (1.72-3.00) |
| Hip |  | 10 | 1.58 (1.39-1.79) | 8 | 2.43 (1.80-3.28) | 8 | 4.00 (2.51-6.37) |
| MOF |  | 13 | 1.48 (1.30-1.69) | 13 | 2.13 (1.69-2.68) | 9 | 2.45 (1.65-3.63) |
| Ost |  | 14 | 1.50 (1.41-1.60) | 13 | 2.12 (1.72-2.61) | 12 | 2.53 (1.78-3.59) |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age and duration of follow-up.

MOF, major osteoporotic fracture; Ost, osteoporotic fracture; BMD, bone mineral density

**Appendix**

**Appendix Table 1.** Description of cohort characteristics, previous falls, and incident fracture outcomes in women

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cohort** | **n** | **Person-years** | **Age (years)** | | | **Previous**  **fall (%)** | **FN BMD**  **(n)** | **Number of incident fractures** | | | |
| **Mean** | **Min** | **Max** | **Any** | **Ost** | **MOF** | **Hip** |
| AGES | 3243 | 26843 | 76.9 | 66.0 | 96.0 | 21.1 | 2673 | 1141 | 1011 | 839 | 368 |
| BEH | 1182 | 5269 | 69.2 | 60.0 | 94.0 | 14.4 | 1176 | 72 | 51 | 33 | 28 |
| Bern | 2863 | 10783 | 60.9 | 20.1 | 94.3 | 12.5 | 2827 | 396 | 287 | 205 | 18 |
| CaMos | 6539 | 86156 | 63.0 | 25.0 | 103.0 | 6.6 | 5712 | 1910 | 1384 | 981 | 270 |
| DOES | 1267 | 11926 | 70.3 | 47.0 | 94.0 | 35.4 | 1256 | 349 | 296 | 233 | 73 |
| DO-HEALTH | 1331 | 3670 | 74.8 | 70.0 | 93.0 | 46.4 | 923 | 202 | 150 | 101 | 8 |
| ECOSAP | 5146 | 16857 | 72.3 | 65.0 | 100.0 | 26.7 | - | 311 | 259 | 188 | 52 |
| EPIFROS | 155 | 1536 | 62.0 | 40.0 | 90.0 | 21.3 | 12 | 21 | 18 | 14 | 3 |
| Framingham\_offspring | 1888 | 26120 | 61.4 | 33.0 | 88.0 | 22.0 | 1620 | 474 | 359 | 194 | 66 |
| Framingham\_original | 708 | 6324 | 80.0 | 72.0 | 101.0 | 29.4 | 554 | 208 | 188 | 141 | 95 |
| FRIDEX | 815 | 8077 | 56.8 | 40.0 | 84.0 | 24.4 | 815 | 112 | 56 | 41 | 15 |
| FROCAT | 1071 | 10607 | 69.7 | 32.0 | 100.0 | 30.8 | 219 | 168 | 130 | 116 | 24 |
| GERICO | 602 | 2187 | 67.9 | 64.6 | 71.8 | 45.8 | 590 | 62 | 43 | 22 | 2 |
| GLOW | 53673 | 214575 | 68.2 | 55.0 | 108.0 | 37.6 | - | 5628 | 4233 | 2804 | 480 |
| HAI | 1770 | 4619 | 70.5 | 69.2 | 72.0 | 13.4 | 1719 | 83 | 75 | 55 | 7 |
| HCS | 243 | 1940 | 66.0 | 61.3 | 70.9 | 19.8 | 242 | 33 | 24 | 17 | 0 |
| Health ABC | 1578 | 19838 | 73.5 | 68.0 | 80.0 | 24.1 | 1564 | 463 | 397 | 355 | 150 |
| HUNT | 3743 | 39848 | 77.3 | 70.0 | 96.8 | 22.5 | 1310 | 1599 | 1452 | 1060 | 592 |
| LASA | 758 | 4076 | 75.7 | 64.8 | 88.6 | 34.2 | 260 | 81 | 60 | 0 | 21 |
| Maccabi | 54175 | 497082 | 65.5 | 37.0 | 91.0 | 5.1 | 6665 | 14294 | 14236 | 13579 | 4071 |
| Manitoba | 33136 | 94303 | 66.9 | 20.0 | 104.3 | 20.5 | 33136 | 1839 | 1718 | 1283 | 298 |
| MsOS Hong Kong | 2000 | 17528 | 72.6 | 65.0 | 98.0 | 24.1 | 2000 | 338 | 298 | 247 | 69 |
| OFELY | 867 | 15136 | 58.8 | 40.0 | 89.0 | 30.8 | 861 | 245 | 207 | 180 | 40 |
| OPRA | 914 | 10664 | 75.2 | 75.0 | 76.0 | 28.4 | 825 | 457 | 413 | 398 | 173 |
| OPUS | 1978 | 12135 | 62.0 | 20.2 | 80.0 | 29.0 | 1970 | 234 | 146 | 112 | 14 |
| OsteoLaus | 1475 | 6726 | 64.5 | 50.2 | 81.5 | 25.4 | 1457 | 307 | 245 | 226 | 8 |
| OSTPRE | 9998 | 97799 | 57.3 | 52.4 | 62.7 | 36.0 | 2460 | 1635 | 1123 | 824 | 68 |
| REFORM | 607 | 899 | 77.6 | 65.0 | 99.0 | 63.9 | - | 23 | 12 | 7 | 2 |
| Rotterdam | 6125 | 81489 | 69.5 | 55.0 | 106.2 | 23.3 | 4409 | 2155 | 1959 | 1645 | 613 |
| SAOL-IPR\_EPIPorto | 711 | 8715 | 55.2 | 40.0 | 85.0 | 25.2 | 709 | 93 | 0 | 34 | 11 |
| SarcoPhAge | 130 | 251 | 75.7 | 68.2 | 93.4 | 41.5 | 124 | 12 | 8 | 5 | 1 |
| SCOOP | 12368 | 58845 | 75.6 | 70.0 | 86.0 | 27.8 | 2790 | 1932 | 1630 | 1288 | 375 |
| SEMOF | 7131 | 20625 | 75.2 | 70.0 | 91.3 | 31.4 | 919 | 683 | 596 | 464 | 80 |
| Sheffield | 2175 | 7441 | 80.0 | 74.3 | 100.9 | 6.0 | 2154 | 289 | 234 | 191 | 67 |
| SOF | 9654 | 135907 | 71.6 | 65.0 | 89.0 | 30.0 | 7760 | 4346 | 3462 | 2801 | 1411 |
| SOS | 16441 | 61467 | 74.2 | 60.8 | 92.5 | 27.5 | 4071 | 1365 | 1306 | 978 | 253 |
| SUPERB | 3025 | 10752 | 77.8 | 74.7 | 81.0 | 29.6 | 3012 | 463 | 421 | 341 | 70 |
| UK Biobank | 272086 | 3143813 | 56.4 | 39.0 | 71.0 | 23.1 | 9969 | 16515 | 14558 | 8913 | 2613 |
| WHI | 78612 | 1072537 | 64.4 | 49.0 | 79.0 | 32.3 | 5576 | 6377 | 5020 | 4392 | 2278 |
| YORK | 4532 | 9044 | 77.1 | 47.6 | 98.9 | 30.1 | - | 393 | 310 | 223 | 42 |
| Overall (total/mean) | 606715 | 5864409 | 62.6 | 20.0 | 108.0 | 24.5 | 114339 | 67308 | 58375 | 45530 | 14829 |

FN BMD, femoral neck bone mineral density; OST, osteoporotic fracture; MOF, major osteoporotic fracture

**Appendix Table 2.** Description of cohort characteristics, previous falls, and incident fracture outcomes in men

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cohort** | **n** | **Person-years** | **Age (years)** | | | **Previous**  **fall (%)** | **FN BMD**  **(n)** | **Number of incident fractures** | | | |
| **Mean** | **Min** | **Max** | **Any** | **Ost** | **MOF** | **Hip** |
| AGES | 2394 | 18345 | 77.0 | 67.0 | 96.0 | 15.2 | 2099 | 459 | 367 | 281 | 157 |
| BEH | 1117 | 4926 | 69.5 | 61.0 | 96.0 | 6.7 | 1115 | 26 | 25 | 13 | 12 |
| Bern | 827 | 3057 | 56.2 | 20.1 | 91.1 | 11.5 | 815 | 79 | 52 | 32 | 5 |
| CaMos | 2884 | 35478 | 59.9 | 25.0 | 97.0 | 6.7 | 2578 | 525 | 369 | 207 | 70 |
| DOES | 819 | 7415 | 69.7 | 59.0 | 92.0 | 21.6 | 801 | 131 | 108 | 66 | 22 |
| DO-HEALTH | 825 | 2287 | 75.2 | 70.0 | 95.0 | 34.8 | 528 | 65 | 42 | 18 | 2 |
| EPIFROS | 129 | 1290 | 61.1 | 40.0 | 96.0 | 14.7 | - | 6 | 2 | 2 | 0 |
| FORMEN | 1886 | 16265 | 72.5 | 65.0 | 93.0 | 16.3 | 1882 | 90 | 90 | 58 | 10 |
| Framingham\_offspring | 1603 | 21057 | 61.4 | 37.0 | 88.0 | 17.5 | 1288 | 203 | 165 | 77 | 22 |
| Framingham\_original | 386 | 3065 | 78.7 | 72.0 | 99.0 | 30.8 | 330 | 53 | 46 | 25 | 18 |
| FROCAT | 859 | 8566 | 68.7 | 41.0 | 111.0 | 19.7 | 14 | 60 | 52 | 43 | 9 |
| GERICO | 156 | 555 | 68.1 | 65.5 | 71.8 | 53.2 | 154 | 9 | 8 | 4 | 0 |
| HAI | 1745 | 4671 | 70.5 | 69.9 | 71.7 | 8.8 | 1717 | 42 | 38 | 22 | 3 |
| HCS | 8 | 69 | 66.3 | 64.6 | 69.1 | 25.0 | 8 | 0 | 0 | 0 | 0 |
| Health ABC | 1486 | 16510 | 73.8 | 69.0 | 80.0 | 18.3 | 1468 | 236 | 198 | 165 | 85 |
| HUNT | 3060 | 29413 | 76.8 | 70.0 | 96.9 | 17.7 | 549 | 691 | 546 | 385 | 251 |
| LASA | 714 | 3492 | 75.7 | 64.8 | 88.7 | 30.3 | 259 | 51 | 36 | 0 | 18 |
| Maccabi | 29402 | 260710 | 65.0 | 40.0 | 91.0 | 5.0 | 1013 | 5041 | 5012 | 4829 | 1709 |
| Manitoba | 4110 | 10862 | 64.7 | 20.0 | 101.2 | 24.3 | 4110 | 225 | 218 | 154 | 44 |
| MINOS | 681 | 6152 | 65.2 | 50.0 | 86.0 | 24.1 | 672 | 63 | 56 | 25 | 3 |
| MrOS Hong Kong | 2000 | 19744 | 72.4 | 65.0 | 92.0 | 15.4 | 2000 | 231 | 201 | 148 | 63 |
| MrOS Sweden | 3001 | 34078 | 74.9 | 69.0 | 81.0 | 16.5 | 2809 | 964 | 869 | 724 | 338 |
| MrOS USA | 5994 | 75015 | 73.7 | 64.0 | 100.0 | 21.2 | 5993 | 1394 | 1082 | 814 | 330 |
| REFORM | 396 | 584 | 78.3 | 65.0 | 99.0 | 67.2 | - | 7 | 5 | 5 | 2 |
| Rotterdam | 4257 | 52202 | 67.5 | 55.0 | 97.6 | 11.9 | 3377 | 730 | 621 | 458 | 177 |
| SAOL-IPR-EPIPorto | 205 | 2424 | 58.1 | 40.0 | 89.0 | 14.6 | 205 | 11 | 0 | 7 | 1 |
| SarcoPhAge | 98 | 189 | 76.2 | 68.5 | 89.4 | 31.6 | 93 | 1 | 0 | 0 | 0 |
| STRAMBO | 821 | 7564 | 72.2 | 51.0 | 88.4 | 20.7 | 803 | 117 | 86 | 42 | 17 |
| UK Biobank | 227781 | 2591829 | 56.8 | 38.0 | 73.0 | 15.9 | 9561 | 8534 | 5419 | 3131 | 1312 |
| Overall (total/mean) | 299644 | 3237814 | 59.5 | 20.0 | 111.0 | 15.1 | 46241 | 20044 | 15713 | 11735 | 4680 |

FN BMD, femoral neck bone mineral density; OST, osteoporotic fracture; MOF, major osteoporotic fracture

**Appendix Table 3.** Association of previous falls with subsequent fracture risk at the sites indicated in women and men adjusted for age and duration of follow-up and additionally adjusted for BMD. Analysis includes only cohorts with femoral neck BMD

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | Cohorts with BMD |  | Adjusted for BMD |
| Outcome  fracture | Number of  cohorts | I2 (%) | HR (95% CI) | I2 (%) | HR (95% CI) |
| ***Women*** |  |  |  |  |  |
| Any | 35 | 80 | 1.37 (1.27-1.47) | 76 | 1.37 (1.26-1.49) |
| Hip | 32 | 68 | 1.34 (1.18-1.53) | 59 | 1.36 (1.18-1.56) |
| MOF | 34 | 77 | 1.33 (1.22-1.44) | 72 | 1.33 (1.21-1.46) |
| Ost | 34 | 80 | 1.35 (1.25-1.47) | 76 | 1.36 (1.24-1.49) |
| ***Men*** |  |  |  |  |  |
| Any | 24 | 54 | 1.49 (1.36-1.63) | 0 | 1.51 (1.42-1.62) |
| Hip | 19 | 36 | 1.55 (1.35-1.79) | 0 | 1.55 (1.36-1.77) |
| MOF | 23 | 61 | 1.46 (1.29-1.67) | 0 | 1.47 (1.35-1.60) |
| Ost | 23 | 54 | 1.53 (1.38-1.69) | 0 | 1.51 (1.40-1.62) |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age and duration of follow-up.

BMD, bone mineral density; MOF, major osteoporotic fracture; Ost, osteoporotic fracture; I2, heterogeneity statistic

**Appendix Table 4**. Association of previous falls with subsequent fracture risk at the sites indicated in those cohorts with a uniform question construct.

|  |  |  |  |
| --- | --- | --- | --- |
| Outcome  fracture | Number  of  cohorts | I2  (%) | HR (95% CI) |
| *Women* |  |  |  |
| Any | 36 | 86 | 1.37 (1.29-1.45) |
| Hip | 31 | 47 | 1.28 (1.19-1.37) |
| MOF | 35 | 78 | 1.31 (1.23-1.40) |
| Ost | 35 | 84 | 1.35 (1.27-1.44) |
| *Men* |  |  |  |
| Any | 24 | 92 | 1.53 (1.32-1.77) |
| Hip | 18 | 85 | 1.61 (1.29-2.01) |
| MOF | 22 | 91 | 1.48 (1.24-1.77) |
| Ost | 22 | 77 | 1.57 (1.39-1.77) |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age and duration of follow-up.

MOF, major osteoporotic fracture; Ost, osteoporotic fracture; I2, heterogeneity statistic

**Appendix Table 5**. Association of previous falls with subsequent fracture risk at the sites indicated in women and men combined according to race/ethnicity.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome**  **fracture** | **Number**  **of cohorts** | **HR (95% CI)** | **HR (95% CI)** | **P value**  **for interaction** |
| ***Asian vs Caucasian*** | | Caucasian | Asian |  |
| Any | 4 | 1.15 (0.64-2.08) | 0.86 (0.37-2.01) | 0.40 |
| Hip | 3 | 1.08 (0.58-2.01) | 0.68 (0.14-3.38) | 0.55 |
| MOF | 4 | 1.13 (0.63-2.02) | 0.92 (0.37-2.27) | 0.60 |
| ***Black vs Caucasian*** | | Caucasian | Black |  |
| Any | 5 | 1.15 (0.68-1.94) | 1.15 (0.53-2.50) | 0.99 |
| Hip | 5 | 1.17 (0.73-1.88) | 1.05 (0.48-2.31) | 0.77 |
| MOF | 5 | 1.16 (0.69-1.93) | 1.16 (0.53-2.54) | 0.99 |
| ***Hispanic vs Caucasian*** | | Caucasian | Hispanic |  |
| Any | 2 | 1.30 (1.19-1.41) | 0.95 (0.69-1.32) | 0.063 |
| Hip | 2 | 1.32 (1.12-1.56) | 1.58 (0.05-45.67) | 0.92 |
| MOF | 2 | 1.24 (1.17-1.32) | 1.28 (0.47-3.52) | 0.95 |
| ***Other than Caucasian vs Caucasian*** | | Caucasian | Other than Caucasian |  |
| Any | 7 | 1.17 (0.79-1.74) | 0.93 (0.50-1.73) | 0.43 |
| Hip | 6 | 1.17 (0.80-1.70) | 0.90 (0.45-1.82) | 0.46 |
| MOF | 7 | 1.19 (0.80-1.75) | 1.05 (0.57-1.91) | 0.66 |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age, sex, and duration of follow-up.  
MOF, major osteoporotic fracture

**Appendix Table 6**. Association of previous falls with subsequent fracture risk at the sites indicated in women and men according to quality score of the cohorts

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Quality score 0-1** | | | **Quality score 2-3** | | | **Quality score 4** | | |
| Outcome  fracture | Number  of  cohorts | Person years | HR (95% CI) | Number  of  cohorts | Person years | HR (95% CI) | Number  of  cohorts | Person years | HR (95% CI) |
| ***Women*** |  |  |  |  |  |  |  |  |  |
| Any | 3 | 3216 | 1.79 (0.59-5.44) | 22 | 4753408 | 1.50 (1.38-1.64)b | 15 | 771719 | 1.27 (1.20-1.34) |
| Hip | 0 | 0 | - | 21 | 4938300 | 1.54 (1.33-1.77)c | 14 | 872607 | 1.16 (1.07-1.27) |
| MOF | 3 | 3288 | 1.64 (0.28-9.72) | 22 | 4856680 | 1.45 (1.32-1.59)b | 14 | 796066 | 1.25 (1.18-1.32) |
| Ost | 3 | 3253 | 1.38 (0.50-3.80) | 21 | 4799082 | 1.50 (1.37-1.64)b | 15 | 785274 | 1.27 (1.20-1.34) |
| ***Men*** |  |  |  |  |  |  |  |  |  |
| Any | 2 | 1119 | 1.62 (0.41-6.39) | 10 | 2601682 | 1.77 (1.56-2.01)b | 15 | 541337 | 1.44 (1.34-1.53) |
| Hip | 0 | 0 | - | 5 | 2624302 | 2.01 (1.79-2.26)c | 15 | 581155 | 1.46 (1.29-1.67) |
| MOF | 2 | 1130 | 1.48 (0.36-6.12) | 9 | 2631427 | 1.71 (1.37-2.13) | 14 | 553866 | 1.41 (1.28-1.55) |
| Ost | 2 | 1122 | 1.81 (0.54-6.04) | 8 | 2617095 | 1.86 (1.73-2.01)c | 15 | 549659 | 1.47 (1.36-1.60) |

Values are hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age and duration of follow-up.  
MOF, major osteoporotic fracture; Ost, osteoporotic fracture

a, P<0.05; b, P<0.01; c, P<0.001; comparison with high quality (quality score 4)