Risk Factors for Fragility Fracture in Middle Age. A prospective population-based study of 33 000 men and women.

Anna H Holmberg[1], Olof Johnell[1], Peter M Nilsson[2], Jan-Åke Nilsson[1], Göran Berglund[2] and Kristina Åkesson[1].

Clinical and Molecular Research Unit[1)] and Internal Medicine Research Unit[2)],

Department of Clinical Sciences Malmö, Lund University, Malmö University Hospital, SE-205 02 Malmö, Sweden.

Correspondence to:

Kristina Åkesson
Dept. of Orthopaedics,
Malmö University Hospital,
20502 Malmö, Sweden.
Phone: +46-40-336123
Fax: +46 40–33 62 00
E-Mail: kristina.akesson@med.lu.se

Abstract

Background: The incidence of fragility fractures begins to increase in middle age. We investigated prospectively risk factors for low-energy fractures in men and women, and specifically for forearm, proximal humerus, vertebral and ankle fractures.

Methods: The population-based Malmö Preventive Project consists of 22444 men and 10902 women, mean age 44 and 50 years at inclusion. Baseline assessment included multiple examinations and lifestyle information. Mean follow-up: 16 and 11 years for men and women, respectively, regarding incident fractures. Fractures were ascertained from radiographic files.

Results: At least one low-energy fracture occurred in 1262 men and 1257 women. In men, the risk factors most strongly associated with low-energy fractures were diabetes (RR 2.38, CI 95% 1.65-3.42) and hospitalization for mental health problems (RR 1.92, CI 95 % 1.47-2.51). Factors associated with mental health and lifestyle significantly increased the fracture risk in most of the specific fracture groups; hospitalizations for mental health problems (RR 2.28 to 3.38), poor appetite (RR 3.05 to 3.43), sleep disturbances (RR 1.72 to 2.95), poor, self-rated health (RR 1.80 to 1.83) and smoking (RR 1.70 to 2.72).
In women, the risk factors most strongly associated with low-energy fractures were diabetes (RR 1.87, CI 95 % 1.26-2.79) and previous fracture (RR 2.00, CI 95 % 1.56-2.58). High body mass index significantly increased the risk of proximal humerus and ankle fractures (RR 1.21 to 1.33), while, by contrast lowering the risk of forearm fractures (RR 0.88, CI 95 % 0.81-0.96).

Conclusion: Risk factors for fracture in middle-aged men and women are similar, but with gender differences, for forearm, vertebral, proximal humerus and hip fracture, whereas risk factors for ankle fractures differ to a certain extent. The risk factor pattern indicates a generally impaired health status with mental health problems as a major contributor to fracture risk, particularly in men.

Key words: Fragility fractures, risk factors, diabetes, mental health

Introduction

Over recent decades the incidence of fractures has increased substantially, especially among the elderly [1, 2]. Different fracture types dominate at different ages and the fracture pattern varies between women and men [1]. In middle age, forearm and ankle fractures are the most frequent fractures, whereas in the elderly hip fractures become the predominating problem. Fracture incidence is usually greater among men than women before the age of 50 years, but at higher ages women suffer more fractures [3]. In general, 75 percent of all fractures among men occur before the age of 45, whereas in women 75 percent of all fractures occur after the age of 45 [4].

Although the consequences of a limb fracture are usually not as devastating as those of a hip fracture, the suffering, inconvenience and the temporary or sometimes permanent disability of the individual are strong enough reasons to motivate a closer epidemiological investigation of these fractures. The fracture-related costs to the society are substantial; the cost for the direct medical care of osteoporotic fractures other than hip fractures in the USA was 5.1 billion dollars in 1995 [5]. Prevention of these fractures would free resources for other areas of health care and avoid unnecessary suffering.

Having a history of a previous fracture is a known risk factor predisposing for future fractures in the elderly [6-8]. The identification of factors associated with fracture risk already in middle age, when a fracture is still a rare event, has not been extensively investigated. Increased knowledge in this area would ultimately enable us to initiate preventive measures when most appropriate.

 The primary objective of this study was to investigate the risk factor pattern for fractures commonly occurring in women and men in middle age, 48-68 years. A secondary objective was to identify differences in risk between men and women.

Material and methods

The Malmö Preventive Project is a prospective, population-based, cardiovascular screening study consisting of 33 346 probands, 22 444 men and 10 902 women, representing 72% of the invited population [9]. Mean age at the baseline investigation was 44 (range 27-61) years for men and 50(range 28-58) years for women. The inclusion period for men was 1974 to 1984 (10 years) and for women from 1977 to 1992 (15 years). The primary objective of the Malmö Preventive Project was to describe cardiovascular risk factors and related conditions in a middle-aged population and to improve the scientific basis for cardiovascular disease prevention. Over and above this, the study provides data for evaluation of other common public health conditions such as fracture and diabetes. The probands were followed prospectively till the end of 1999, with a mean follow-up of 19 years (range 7-25 years) for men and 15 years (7-22 years) for women for incident fractures and mortality.

Physical examination
The baseline physical investigation included height and body weight measurement as well as triceps skinfold thickness. Blood pressure and pulse rate were measured twice after a 10-minute rest and the mean was recorded. Simple spirometry (Spirotron[®], Drägerwerke, Germany) was performed and pulmonary function parameters were calculated.

In a subgroup of the women, bone mineral density of the distal radius was measured and has been reported previously [10].

Questionnaire
At baseline the participants in the study completed a questionnaire regarding health-related and lifestyle issues, previously described in detail [11]. During the extended inclusion period certain questions were added while others were withdrawn. The total number of questions used in the questionnaire were 417, 78 of which were core questions asked throughout the

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inclusion period. The mean response rate was for the women about 98 % and for the men 72 % for the core questions. In the early period of this study (the beginning of the seventies) the computer technique was still young, and due to computer problems some of the questionnaire results were lost for 6368 men. The response rate was 99% for the remaining results. Questions that were added during the inclusion period had a response rate of almost 100 % for those who had the opportunity to respond.

The amount of data is extensive, thus only variables of biological interest and with possible impact on fracture risk were selected for this report.

Laboratory investigation
Morning blood samples were collected from the participants after an over-night fast. The following analyses were performed and used in this substudy; haematoglobin, erythrocyte sedimentation rate (ESR), serum creatinine, fasting blood glucose, serum γ -glutamyl transferase, serum triglycerides, serum total cholesterol, serum uric acid and serum phosphate. Due to skewed distribution of serum γ -glutamyl transferase, data were logarithmically transformed when used in the analyses.

Fracture identification
The fracture data were obtained by linking the probands included in the Malmö Preventive Project with the register at the Department of Diagnostic Radiology at Malmö University Hospital. In the city of Malmö all emergency radiographic examinations are performed at the Department of Diagnostic Radiology at Malmö University Hospital, the fractures are recorded and the films are stored and saved permanently. The unique 10-digit personal identification number, based on birth date and issued to every Swedish citizen, makes identification of cases easy and precise. The fractures identified were confirmed through manual search of the medical and radiological files. Previous studies have shown that at least 97 % of all fractures

experienced by citizens of Malmö can be identified this way [12]. The fractures registered were classified under the following categories, namely, forearm, vertebral, proximal humerus and ankle fractures (Table 1). Data on hip fractures, previously reported [11], are included for comparison. Regarding vertebral fractures, only those coming to clinical attention and described in radiographic reports, or accidentally found on chest or abdominal x-rays for other causes and described in the radiographic report were included. The degree of deformity was not quantified.

The fractures were classified as high or low-energy trauma depending on the cause of fracture. Fractures caused by falling from standing height or less were classified as low-energy fractures and those caused by high-energy trauma as high-energy fractures. The classification was based on information given in the radiographic reports. Of all fractures, 4098 (97.7 %) were described with adequate information about the degree of trauma in the radiology reports. The 98 fractures with insufficient information concerning trauma were classified as low-energy fractures, based on the experience that it is highly unlikely that information about high-energy accidents is not reported.

Fractures caused by high-energy trauma were excluded from the analyses, as were pathological fractures caused by cancer or other bone diseases.

Statistics

For this substudy, relevant data were extracted from the Malmö Preventive Project main database. The population was divided into those with and those without fracture. Individuals suffering exclusively fractures caused by high-energy were excluded from the fracture population and included in the non-fracture population. Individuals with at least one low-energy incident fracture were classified into the low-energy fracture group, even if a previous or subsequent high-energy fracture was recorded during the study period. The first fracture of each fracture type was the one included in the calculation, even if the individual had suffered more than one fracture of the same type. If an individual suffered more than one type of fracture, the individual was included in the calculations for each fracture type, albeit under different dates for the fracture incident. Fracture incidence was calculated as the number of fractures per 1000 person years.

Baseline descriptive data of the whole cohort and the fracture subgroups were presented as percentages, means and standard deviations (SD). Due to the skewed distribution of serum γ - glutamyl transferase it was logarithmically transformed when used in the analyses. Variables of biological interest were chosen from the database. Z-scores were calculated for the continuous variables, to permit comparison of different variables. The variables were analyzed, one by one, in an age-adjusted Cox proportional hazard model. To reduce the risk of mass significance through multiple testing we chose a p-value of <0.01 as the level of significance. A final multiple regression model was constructed consisting of 11 (women) and 10 (men) variables. The variables were selected from the age-adjusted Cox proportional hazard model based on the strength of their association with the different fracture types. Among variables with possible interdependence we chose the one with the strongest association and highest response rate. Two questions; one regarding previous fracture history

and another regarding hormone replacement therapy, were not included throughout the study, thus generating an incomplete data set. Despite their significant impact on fracture risk we chose to exclude these questions from the final Cox analysis.

 The statistics program used was SPSS 12.0 for Windows (Statistics package for Social Sciences, Chicago, Illinois, USA).

Results

Descriptives

Women
During the 15-year follow-up, 1878 incident fractures were registered affecting 1292 women,

i.e. 12 % of the female study population. Of these, 1257 women (97%) were classified as

suffering low-energy fractures. The number of women with only one low-energy fracture was

894, representing 71 % of the women with low-energy fractures. Of the total number of 1805

low-energy fractures recorded, 662 were forearm fractures, 155 proximal humerus, 160

vertebral, 223 ankle, and 141 hip fractures (Table 1). Fracture incidence rates for each type of

fracture are reported in figure 1. The age effect is most pronounced in women.

Baseline characteristics are reported for the entire cohort and for the major fracture types

(Table 2). The women suffering fractures were slightly older at study start than the non-

fracture population, with the exception of women with ankle fractures. Mean body weight was

3.5 kg greater at inclusion in women with ankle and proximal humerus fractures compared to

the non-fracture population, and 2.5 kg less in women with a hip fracture. The prevalence of

diabetes seemed higher in women with ankle, vertebral and hip fractures. Women with

vertebral and hip fractures also appeared to suffer from more comorbidities than the non-

fracture population.

Men
During the 19-year follow-up 2422 incident fractures were registered affecting 1505 men, i.e.

6.7% of the male study population. Of these, 1262 men (84%) were classified as suffering

low-energy fractures. The number of men with only one low-energy fracture was 822,

representing 65% of the men with low-energy fractures. Of the total number of 1975 low-

energy fractures recorded, 330 were forearm fractures, 123 proximal humerus, 168 vertebral,

259 ankle, and 174 hip fractures (Table 1). The fracture incidence rates were half of those in women and the age effect was seen only in the highest age group (Fig1).

Men with fractures were slightly older at the start of the study than the non-fracture population, which was especially apparent in men with a hip fracture (Table 2). Mean body weight and BMI were slightly lower in all separate fracture groups except for ankle fractures, where it was slightly higher. Smoking was more common among men suffering from vertebral, proximal humerus and hip fractures.

Risk factors for low-energy fractures overall and for specified types of fracture, for women and for men, are reported separately. The factors evaluated are presented as means and standard deviations in Table 3a and b. In the following we will highlight the results for women and men in the uni- and multivariate models presented in Table 4 -7.

Risk factors in women

Low energy fractures

The risk factor with the largest impact on low energy fractures in general was a history of previous fracture, doubling the fracture risk (RR 2.00, CI 95 % 1.56-2.58, p=0.001) Diabetes was associated with a similar risk increase (RR 1.95, 1.33-2.86, p=0.001), while high serum γ -glutamyl transferase and poor, self-rated health gave smaller risk increases. A relative risk decrease was seen for those using Hormone Replacement Therapy (HRT). In the final Cox model, diabetes remained a significant risk factor of low energy fractures. (Tables 4 and 6)

Forearm fractures

The risk factor with the largest impact on forearm fractures was a history of previous fracture, doubling the risk (RR 2.00, 1.40-2.85, p=0.001), whereas diabetes was not associated with an

increased risk of forearm fracture. High BMI was associated with decreased risk of forearm fracture.

Vertebral fractures

Diabetes was the risk factor with the largest impact on vertebral fractures, increasing the fracture risk more than three times (RR 3.56, 1.75-7.23, p=0.001). A history of previous fracture (RR 3.13, 1.67-5.85, p=0.001) also increased the fracture risk, as did high serum γ - glutamyl transferase, smoking and decreased lung capacity (FVC) but to a lesser extent. ESR as an indicator of inflammation was also associated with a small risk increase (RR 1.16, 1.04-1 29, p=0.009).

Proximal humerus fractures

In contrast to most of the other fracture groups the risk of proximal humerus fracture was not affected by previous fracture history, diabetes, smoking or high serum γ -glutamyl transferase. The factor most strongly associated with proximal humerus fracture was being in the higher age segment of the study population, with RR 2.27 (1.76-2.93, p=0.001). High body weight, high BMI and poor, self-rated health also increased the fracture risk.

Ankle fractures

A history of previous fracture doubled the risk of ankle fracture (RR 2.11, 1.17-3.80, p=0.001), whereas the variable most strongly associated with ankle fractures was diabetes (RR 3.36, 1.58-7.15, p=0.002). High serum γ -glutamyl transferase as well as high body weight and BMI increased the risk of ankle fracture.

Risk factors in men

Low energy fractures

The factor associated with the strongest risk effect on low energy fractures in general was suffering from diabetes, which more than doubled the fracture risk (RR 2.50, 1.75-3.57, p=0.001). A history of hospitalization for mental disorders (RR 1.92, 1.47-2.51, p=0.001) and having a poor appetite (RR 1.72, 127-2.32, p=0.001) also increased the low energy fracture risk. Smoking and a high serum γ-glutamyl transferase, an indirect measure of an alcohol effect, were associated with moderately increased risks of fracture. High BMI was associated with a decreased risk of low energy fractures in men, it is a protective attribute. In the final Cox model the associations remained chiefly the same. (Tables 5 and 7)

Forearm fractures

The factor associated with the strongest risk effect on forearm fractures was hospitalization for mental disorders (RR 2.28, 1.37-3.78, p=0.001). The only other factor significantly associated with forearm fractures in men was high BMI (RR 0.85, 0.75-0.96, p=0.007), which decreased the risk of fracture.

Vertebral fractures

A history of hospitalization for mental disorders increased the fracture risk significantly (RR 2.34, 1.36-4.03, p=0.002). Other strong risk factors for men with vertebral fractures were having a poor appetite (RR 3.05, 1.80-5.17, p=0.001) and being on sick leave at the time of the baseline investigation (RR 2.98, 1.83-4.85, p=0.001). Smoking and a high serum γ-glutamyl transferase were also associated with increased risks of vertebral fracture.

Proximal humerus fractures

For proximal humerus fractures several factors related to mental health were significant contributors to fracture risk, each increasing the fracture risk three-fold; prior hospitalization for mental disorders, poor appetite and premature awakening. Smoking and high serum γ -glutamyl transferase were also associated with increased risks of proximal humerus fracture. In men a high BMI decreased the risk of proximal humerus fracture.

In the final Cox model a high level of serum triglycerides was associated with a decreased risk of proximal humerus fractures.

Ankle fractures

The significant risk factors for ankle fractures were to some extent similar to other peripheral fractures in men but with a lower impact; prior hospitalization for mental disorders (RR 2.74, 1.62-4.66, p=0.002), premature awakening and high serum γ -glutamyl transferase.

In the final Cox model only the association between high serum γ -glutamyl transferase and ankle fracture remained.

Discussion

The aetiology of fractures is multi-facetted and complex, making fracture studies and reporting difficult and never complete. Our aim has been to determine and examine a range of factors that affect fracture risk in middle age, low energy fractures in general, and in more detail fractures of the forearm, vertebrae, proximal humerus and ankle. Low energy fractures in general were, in women, strongly associated with diabetes and previous fracture history, and in men with diabetes and mental health problems. For the specified fracture groups, the risk factor pattern was to some extent different, but certain factors affected almost all the subgroups; in women being in the higher age segment of the study population, a history of previous fracture and diabetes. In men being in the higher age segment of the study population, low BMI, high serum γ -glutamyl transferase, smoking, sleep disturbances and hospitalization for mental disorders were all factors identified as significant contributors to risk in most of the fracture subgroups. Our findings suggest that individuals in middle age with impaired physical and mental health are at high risk of experiencing peripheral and vertebral fractures.

Fracture incidences were calculated for the specified fracture groups. The results are similar to those of a study of the Geelong population in Australia, except for forearm fractures [13]. The discrepancies may be attributable to the low number of fractures in some categories. Our incidence curves are similar to the results of a register study by Kanis and co-workers performed on the total population of Malmö through fracture registers, although our incidence rates are lower [14]. However, our incidence rates are similar to earlier clinical studies in Malmö [1] but as previously recognised, the rates for some of the fractures, forearm fractures in particular, are higher than in other, large epidemiological studies [15]. It cannot be excluded that this study, as well as other population-based cohort studies, attract a somewhat

more health-conscious segment of the population, who thus sustain fewer fractures, in contrast to a register study that includes all citizens.

In both men and women, high body weight and BMI lowered the risk of forearm and hip fractures, in men also of proximal humerus fractures. In contrast, in women high body weight and BMI increased the risk of proximal humerus and ankle fractures. This further elicits the complexity of fracture aetiology, when both being overweight and being thin affects fracture risk, albeit different types of fracture. One could speculate that there is an association between poor nutrition and poor bone quality, as well as between high body weight and clumsiness, with an increased tendency to fall and a higher impact of a fall even from standing height. These findings suggest two different types of individuals, both prone to fracture but with different risk factors predominating. A case-control study of 448 men and women over 45-years of age found that high BMI as well as frequent falling were risk factors for proximal humerus fracture [16]. This is consistent with our findings in women. Proximal humerus fractures, at least in elderly subjects, have been associated with low bone mineral density [17] and considered a type fracture of osteoporosis. A study by Olsson and co-workers of both middle-aged and elderly subjects showed associations between humerus fractures and previous fracture history as well as increased risk of future fracture [18]. This further supports our hypothesis about subgroups within the fracture population.

 High body weight and BMI increased the risk of ankle fractures in women but decreased the risk of forearm and hip fractures. In the age-adjusted Cox model we found other risk factors common to these fracture types, but in the final Cox model only BMI remained a significant risk factor for ankle fractures and a factor decreasing risk of hip fractures. The age effect was no longer significant for ankle fractures, in contrast to the other fracture types. This is

consistent with previous reports [10, 19-22] suggesting that risk factors for ankle fractures are related to lifestyle including a physically active life, whereas the risk associated with forearm fractures is more dependent on bone density. Our results indicate that ankle fractures differ in risk factor profile compared to fractures commonly associated with poor bone quality, and it is thus questionable to include these in an analysis of osteoporotic fractures, a point which is further supported by a report by Kanis and co-workers [4].

Diabetes, in both men and women, was strongly associated with an increased relative risk of low energy fractures and hip fractures, in women also of vertebral and ankle fractures, a result consistent with previous studies [23-27]. In the multivariate analysis the association between ankle fractures and diabetes in women disappeared. This is probably due to the small number of cases of diabetes found in each specific fracture group, and not to a lack of impact from diabetes on ankle fractures. Where diabetes is of long duration, multiple organ systems of the body are affected, leading to angiopathy, neuropathy and nephropathy, with effects on bone mass and on the tendency to fall. In a previous study [11] we have shown that diabetes has a large impact on hip fracture risk already in middle-age, suggesting more fragile bone structure in individuals suffering from diabetes.

Blood lipids have in recent studies been associated with BMD, reporting a positive correlation between serum-triglycerides and BMD and a negative correlation between serum-cholesterol and BMD [28, 29]. In this study we have found that in both men and women of middle age, high levels of serum-triglycerides are associated with a decreased risk of some peripheral fracture types. A high level of blood lipids may possibly represent a good status concerning nutrition and a good health, protecting the individual from fracture. The true correlation between blood lipids and fracture risk remains to be explored.

Elevated levels of serum γ -glutamyl transferase may be an indicator of alcohol over-consumption [30-32]. Also in the population studied alcohol over-consumption has been shown to be the main cause of elevated levels of γ -glutamyl transferase [33]. However, indicators of the metabolic syndrome, including liver derived serum lipids, may influence the levels of γ -glutamyl transferase, and the likelihood of interaction is high. Nevertheless alcohol was still a major contributor [34]. In this study elevated serum γ-glutamyl transferase was associated with an increased risk of low energy fractures in general in both men and women for most of the specified fracture subtypes. Studies have shown that alcohol over-consumption increases the risk of fracture through metabolic effects as well as alcohol-related falls and a more hazardous life style in general [35-37]. The fracture pattern of the men in this study, with a high proportion of high-energy fractures as well as hand and skull fractures, may indicate an unsafe life style, possibly in connection with alcohol abuse. In women elevated serum γ-glutamyl transferase levels were associated with an increased risk of vertebral and ankle fractures. One could speculate that the effect on ankle fractures may be a result of acute alcohol intoxication, since ankle fractures seem to be more associated with lifestyle factors than poor bone quality, and the effect on vertebral fractures seem more related to long-term effects of alcohol consumption. Unfortunately the study did not include specific questions on alcohol consumption, thus we rely on this indirect but nevertheless objective measure.

In many previous reports smoking has been found to be a risk factor for fractures in general and hip fractures in particular [38-40] with a negative effect on BMD[41, 42]. In this study smoking was associated with increased risk of vertebral fractures in women, and in men with low energy fractures in general and with vertebral, proximal humerus and hip fractures.

Several variables regarding psychological well-being are recorded, allowing us to evaluate the impact on fracture risk. In men one variable was a significant risk factor for all types of fracture, namely previous hospitalization for mental health problems. When we compared the individuals reporting mental health problems with the non-fracture population, these individuals appeared to suffer from more comorbidities than the non-fracture population. A study from Tromsö, Norway reported psychiatric disease in men as a risk factor for all fracture types and especially for forearm and proximal humerus fractures, in agreement with our findings [43]. Individuals with mental health problems may lead a more irregular life, with possible alcohol and drug abuse affecting their health, creating a frailer body constitution and also with an increased risk of falling. Similar reasoning may be applicable regarding the increased risk of vertebral fractures in those currently on sick leave, assuming that sick leave is a sign of co-morbidity.

This study has some limitations. Since the original study was not designed to investigate fractures and fracture risk and because of computer error, certain data sets are incomplete and information is accessible only for the major parts of the study population. Nevertheless, the overall response rate is excellent. BMD measurements were performed only on a small part of the population [10], thus the level of prevalent osteoporosis cannot be determined.

A strength of this study is that, to our knowledge, this is one of the first prospective studies evaluating a broader range of risk factors of common fracture types in middle age in both men and women. Furthermore, we have been able to evaluate factors that are not commonly studied, which should be regarded as a strength. The study is large and with a long follow-up, which makes the results more reliable.

This study has identified and described many risk factors for low-energy fractures in middle age, and their impact on different fracture types. This confirms the multitude and complexity of factors affecting fracture risk. The study indicates similarities in the risk factor patterns between forearm, vertebral, proximal humerus and hip fractures, whereas the study indicates that ankle fractures to a certain extent have a different risk profile. A middle-aged person of generally impaired physical and mental health status with subsequent impaired bone strength as a possible background factor is, according to this study, at high risk of a peripheral fracture. Identification of risk factors in younger age groups gives us a unique opportunity to implement preventive strategies at a time when intervention may still prevent irreversible bone loss.

Acknowledgements

Tables

Table 1

Distribution of all fractures in 33 346 women and men from inclusion date until final follow-up, December 31, 1999. The mean follow-up time was 11 years for women and 16 years for men. Reported in order of frequency in women.

Fracture type	Women			Men		
	Number of fractures	Number of low energy fractures	% of all low energy fractures	Number of fractures	Number of low energy fractures	% of all low energy fractures
Forearm	666	662	36.7	379	330	16.7
Ankle	231	223	12.4	292	259	13.1
Vertebral	166	160	8.9	219	168	8.5
Proximal humerus	158	158	8.8	133	123	6.2
Hand and foot	150	144	8.0	466	354	17.9
Hip	143	141	7.8	192	174	8.8
Patella	49	47	2.6	79	70	3.5
Tibial condyle	49	45	2.5	56	35	1.8
Elbow	40	35	1.9	42	33	1.7
Pelvis	41	31	1.7	57	37	1.9
Rib cage	25	22	1.2	129	106	5.4
Clavicle and scapula	30	20	1.1	89	74	3.7
Femoral fracture below hip	20	17	0.9	43	31	1.6
Diaphyseal tibia and lower leg	16	13	0.7	40	21	1.1
Radius and ulna	14	12	0.7	17	11	0.6
Diaphyseal humerus	12	12	0.7	22	15	0.8
Scull and face	12	11	0.6	68	53	2.7
Other	56	52	2.9	99	81	4.1
Total	1878	1805	100	2422	1975	100

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Table 2

Baseline data for a population, both **female** and **male**, without fracture, with low energy fracture of any type and the fracture group subdivided according to type of fracture; forearm, vertebral, proximal humerus, ankle and hip fracture. Percentages of prevalent conditions at baseline are included.

Variable (unit)	No fracture n= 9645		Any low energy fracture n=1257		Forearm fracture n=600		Vertebral fracture n=138		Proximal humerus fracture n=146		Ankle fracture n=217		Hip fracture n=135	
WOMEN	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (yrs)	49.5	7.5	51.1	6.0	51.8	5.4	52.0	4.8	52.5	4.3	49.9	7.1	51.7	5.14
Body height (cm)	164	6.1	164	6.2	164	6.3	164	6.6	164	6.6	164	6.2	164	5.75
Body weight (kg)	65.3	11.5	65.8	11.9	64.7	11.0	65.3	11.5	68.7	14.3	68.8	12.7	62.7	11.3
Body mass index (kg/m²)	24.4	4.2	24.6	4.3	24.2	4.0	24.2	3.6	25.7	5.1	25.7	4.6	23.2	3.93
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Diabetes	105	1.1	27	2.2	9	1.5	8	3.8	4	2.7	7	3.3	6	4.4
Smoking	3357	37.0	451	37.3	204	35.4	101	49.5	50	35.0	74	36.2	57	42.2
Hypertension	833	8.7	93	7.4	38	6.3	17	8.0	15	10.3	22	10.2	13	9.6
Angina	189	2.0	31	2.5	12	2.0	6	2.8	2	1.4	6	2.8	3	2.2
Joint pain	2291	24.0	304	24.4	145	24.3	67	31.8	31	21.3	50	23.4	30	22.2
Back pain	5114	53.3	660	52.7	300	50.0	127	60.2	75	51.4	124	57.7	76	56.3
Cancer	400	4.2	61	4.9	30	5.0	21	10.0	9	6.2	11	5.1	7	5.2

Variable (unit)	No fracture n= 20939		Any low energy fracture n=1278		Forearm fracture n=315		Vertebral fracture n=156		Proximal humerus fracture n=115		Ankle fracture n=250		Hip fracture n=163	
MEN	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (yrs)	43.7	6.6	45.1	6.9	44.4	7.0	46.9	7.1	45.8	6.2	43.9	6.2	48.1	6.5
Body height (cm)	177	6.7	177	7.2	177	7.2	177	7.0	177	7.0	176	6.6	178	7.7
Body weight (kg)	77.4	11.5	76.8	12.1	76.2	11.8	76.1	12.3	75.5	12.1	78.0	12.2	74.7	12.8
Body mass index (kg/m²)	24.7	3.3	24.4	3.4	24.2	3.2	24.3	3.3	24.0	3.7	25.0	3.5	23.7	3.5
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Diabetes	218	1.0	31	2.4	6	1.9	3	1.2	2	1.7	3	1.2	13	8.0
Smoking	10343	48.9	698	54.6	164	52.1	156	63.7	69	60.0	133	53.2	114	69.9
Hypertension	833	3.9	61	4.8	12	3.8	8	3.3	7	6.1	12	4.8	15	9.2
Angina	288	1.9	34	3.5	8	3.4	10	5.1	0	-	3	1.6	6	3.7
Joint pain	2008	13.3	168	17.5	35	14.9	46	23.6	12	13.0	25	13.4	38	23.3
Back pain	7316	48.4	495	51.4	122	51.9	106	54.4	46	50.0	97	51.9	75	46.0
Cancer	121	0.8	7	0.7	1	0.4	0	-	2	2.2	0	-	1	0.6

Table 3a

Means, standard deviation and percentages (%) of biological and medical history variables included in this study for **women**.

Variable (unit)	No fracture n=9645		Any low energy fracture n=1257		Forearm fracture n=600		Vertebral fracture n=138		Proximal humerus fracture n=146		Ankle fracture n=217		Hip fracture n=135	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Skinfold	223	18.9	223	18.9	224	17.1	222	22.6	227	15.7	227	21.1	220	21.2
Forced vital capacity, FVC (L)	3.3	0.7	3.2	0.7	3.2	0.7	3.0	0.7	3.1	0.7	3.3	0.6	3.1	0.7
Systolic blood pressure (mmHg)	125	17	125	17	125	17	128	18	130	19	127	16	126	18
Diastolic blood pressure (mmHg)	82	9	82	9	82	8	83	9	85	10	83	9	83	10
Resting pulse (beats/minute)	68	9	69	9	68	9	69	9	68	8	70	10	70	9
Serum-triglycerides (mmol/L)	1.11	0.60	1.14	0.64	1.05	0.50	1.19	0.78	1.18	0.67	1.25	0.79	1.19	0.74
Serum-cholesterol (mmol/L)	5.80	1.11	5.92	1.12	5.90	1.06	5.88	1.07	6.05	1.12	5.95	1.23	5.75	1.15
γ-glutamyl transferase (mmol/L)	0.31	0.55	0.34	0.52	0.33	0.53	0.34	0.45	0.35	0.49	0.37	0.48	0.36	0.45
Serum-phosphate (mmol/L)	1.05	0.16	1.06	0.16	1.07	0.15	1.06	0.17	1.04	0.16	1.04	0.18	1.08	0.14
Serum-creatinine (mmol/L)	76	12	76	12	76	12	75	11	76	11	76	11	75	11
Serum-uric acid (mmol/L)	254	57	255	61	251	58	257	61	267	66	263	60	248	58
Blood-haemoglobin (mmol/L)	134	9	134	10	133	10	135	11	133	10	135	10	134	11
Sedimentation rate, ESR (mm/hour)	10	8	10	8	10	8	11	10	12	8	11	8	10	8
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
>10 kg weight gain since age 30	3030	31.4	427	34.0	196	32.7	44	31.9	58	39.7	88	40.6	35	25.9
Sick leave at present	653	6.8	83	6.6	37	6.2	12	8.7	10	6.8	15	6.9	11	8.1
Pressure in the chest	2826	29.3	383	30.5	174	29.0	44	31.9	42	28.8	63	29.0	44	32.6
Poor self-rated health	2933	30.4	443	35.2	198	33.0	48	34.8	61	41.8	75	34.6	62	45.9
Poor appetite	213	2.2	31	2.5	10	1.7	3	2.2	5	3.4	4	1.8	4	3.0
Premature awakening	2179	22.6	302	24.0	143	23.8	50	36.2	35	24.0	46	21.2	43	31.9
Hospitalization for mental a disorder	383	4.0	61	4.9	23	3.8	10	7.2	4	2.7	13	6.0	12	8.9
Physical activity	7476	77.5	939	74.7	452	75.3	101	73.2	105	71.9	165	76.0	99	73.3
Hormone replacement therapy	889	9.2	83	6.6	39	6.5	8	5.8	13	8.9	15	6.9	7	5.2
History of previous fracture	250	2.6	65	5.2	33	5.5	11	8.0	6	4.1	12	5.5	15	11.1

2006-08-03

Table 3b

Means, standard deviations and percentages (%) of biological and medical history variables included in this study for **men**.

Variable (unit)	No fracture n= 20939		Any low energy fracture n=1278		Forearm fracture n=315		Vertebral fracture n=156		Proximal humerus fracture n=115		Ankle fracture n=250		Hip fracture n=163	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Skinfold	191	20.9	190	21.5	191	19.6	187	21.5	192	23.1	190	20.9	189	22.8
Forced vital capacity, FVC (L)	4.5	0.9	4.4	1.0	4.4	0.9	4.3	0.9	4.3	1.1	4.5	0.9	4.2	1.0
Systolic blood pressure (mmHg)	127	15	129	16	127	14	129	16	130	16	129	16	130	18
Diastolic blood pressure (mmHg)	85	9.6	86	10	86	10	87	10	87	10	87	10	88	11
Resting pulse (beats/minute)	67	11	68	10	67	9	68	11	70	10	67	10	71	10
Serum-triglycerides (mmol/L)	1.51	1.02	1.50	1.50	1.54	1.21	1.51	1.54	1.31	0.76	1.52	1.09	1.75	3.04
Serum-cholesterol (mmol/L)	5.61	1.09	5.60	1.12	5.56	1.06	5.49	1.06	5.52	1.05	5.70	1.07	5.71	1.40
γ -glutamyl transferase (mmol/L)	0.52	0.54	0.60	0.49	0.55	0.53	0.69	0.44	0.68	0.47	0.65	0.49	0.72	0.41
Serum-phosphate (mmol/L)	0.98	0.16	1.00	0.17	1.00	0.17	1.03	0.18	1.01	0.15	1.02	0.17	0.99	0.20
Serum-creatinine (mmol/L)	93	19	93	23	92	13	93	12	94	13	97	44	93	13
Serum-uric acid (mmol/L)	324	63	324	64	324	63	324	69	327	58	323	65	326	66
Blood-haemoglobin (mmol/L)	148	10	148	10	148	9	149	10	147	10	148	11	148	9
Sedimentation rate, ESR (mm/hour)	6	6	6	6	6	5	6	6	6	6	6	6	7	6
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
>10 kg weight gain since age 30	4043	19.1	254	19.9	65	20.6	28	17.9	17	14.8	50	20.0	43	26.4
Sick leave at present	545	2.6	39	3.1	9	2.9	12	7.7	5	4.3	7	2.8	9	5.5
Pressure in the chest	4276	20.2	286	22.4	76	24.1	47	30.1	27	23.5	62	24.8	42	25.8
Poor self-rated health	5651	26.7	396	31.0	91	28.9	64	41.0	36	31.3	74	29.6	66	40.5
Poor appetite	446	2.1	45	3.5	8	2.5	9	5.8	8	7.0	9	3.6	8	4.9
Premature awakening	2088	9.9	188	14.7	39	12.4	35	22.4	30	26.1	39	15.6	34	20.9
Hospitalization for a mental disorder	508	2.4	57	4.5	16	5.1	12	7.7	9	7.8	15	6.0	12	7.4
Physical activity	16318	77.1	999	78.2	234	74.2	125	80.1	91	79.1	194	77.6	126	77.3

Table 4

Relative risk (RR) for low-energy fractures in **women,** with each variable analysed in an age-adjusted regression analysis using z-scores with 1 SD change as the unit for the continuous variables and yes versus no for the categorical variables.

Variable	Low energy fracture n=1257			Forearm fracture n=600			Vertebral fracture n=138			Proximal humerus fracture n=146			Ankle fracture n=217			Hip fracture n=135		
	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p
Age	1.55	1.45-1.67	**0.001**	1.81	1.62-2.03	**0.001**	1.94	1.60-2.35	**0.001**	2.27	1.76-2.93	**0.001**	1.30	1.12-1.51	**0.001**	2.21	1.71-2.86	**0.001**
Body height	1.04	0.98-1.10	0.22	1.02	0.94-1.10	0.68	1.06	0.93-1.22	0.39	1.06	0.89-1.25	0.51	0.98	0.86-1.12	0.80	1.18	0.99-1.40	0.06
Body weight	1.01	0.95-1.07	0.76	0.89	0.82-0.97	**0.01**	0.97	0.85-1.12	0.68	1.22	1.06-1.41	**0.001**	1.31	1.17-1.47	**0.001**	0.72	0.59-0.88	**0.001**
Body mass index, BMI	0.99	0.94-1.05	0.81	0.88	0.81-0.96	**0.005**	0.92	0.80-1.07	0.28	1.21	1.04-1.40	**0.01**	1.33	1.18-1.49	**0.001**	0.63	0.51-0.78	**0.001**
>10 kg weight gain since age 30	0.98	0.87-1.10	0.73	1.09	0.92-1.30	0.32	1.13	0.79-1.63	0.50	1.22	0.58-1.14	0.24	1.54	1.17-2.04	**0.002**	0.67	0.45-0.99	0.04
Skinfold	1.01	0.95-1.07	0.82	1.00	0.92-1.09	0.95	0.92	0.81-1.04	0.18	1.18	0.97-1.44	0.09	1.33	1.12-1.57	**0.001**	0.83	0.73-0.94	**0.004**
Forced vital capacity, FVC	0.94	0.88-1.01	0.09	0.93	0.85-1.03	0.18	0.77	0.66-0.91	**0.002**	0.86	0.70-1.05	0.13	0.97	0.82-1.15	0.72	0.90	0.74-1.10	0.31
Systolic blood pressure	0.99	0.93-1.04	0.63	0.93	0.86-1.01	0.08	1.06	0.93-1.21	0.38	1.17	1.00-1.36	0.04	1.12	0.98-1.27	0.10	0.96	0.81-1.15	0.68
Diastolic blood pressure	1.02	0.96-1.07	0.60	0.92	0.84-1.00	0.04	1.10	0.96-1.26	0.17	1.25	1.06-1.47	**0.006**	1.16	1.01-1.32	0.03	1.11	0.93-1.31	0.25
Resting pulse	1.05	0.99-1.11	0.09	0.99	0.92-1.08	0.86	1.13	1.00-1.29	0.06	0.99	0.84-1.17	0.94	1.18	1.04-1.34	**0.009**	1.22	1.05-1.43	**0.01**
Diabetes	1.95	1.33-2.86	**0.001**	0.73	0.38-1.41	0.35	3.56	1.75-7.23	**0.001**	0.40	0.15-1.09	0.07	3.36	1.58-7.15	**0.002**	4.07	1.79-9.26	**0.001**
Serum-triglycerides	1.03	0.97-1.08	0.32	0.87	0.79-0.96	**0.005**	1.10	0.99-1.23	0.07	1.08	0.94-1.25	0.25	1.16	1.06-1.28	**0.001**	1.09	0.94-1.26	0.26
Serum-cholesterol	1.02	0.96-1.09	0.43	0.96	0.88-1.05	0.42	0.98	0.84-1.13	0.74	1.07	0.90-1.27	0.43	1.15	1.00-1.32	0.05	0.82	0.67-0.99	0.04
γ-glutamyl transferase	1.10	1.04-1.16	**0.001**	1.00	0.92-1.08	0.93	1.24	1.10-1.39	**0.001**	1.15	0.99-1.33	0.07	1.25	1.11-1.40	**0.001**	1.18	1.01-1.38	0.04
Serum-phosphate	1.06	0.97-1.16	0.23	1.08	0.95-1.24	0.25	0.98	0.80-1.20	0.86	0.85	0.63-1.15	0.29	0.96	0.77-1.19	0.70	1.13	0.86-1.48	0.40
Serum-creatinine	0.94	0.88-1.00	0.03	0.93	0.85-1.01	0.09	0.91	0.78-1.05	0.20	0.97	0.81-1.15	0.70	0.95	0.83-1.10	0.53	0.90	.075-1.09	0.29
Serum-uric acid	0.98	0.93-1.04	0.47	0.89	0.82-0.97	**0.006**	0.96	0.84-1.10	0.57	1.15	0.98-1.34	0.08	1.17	1.02-1.33	0.02	0.85	0.71-1.01	0.07
Blood-haemoglobin	1.00	0.94-1.05	0.88	1.09	1.01-1.18	0.04	1.10	0.96-1.26	0.18	1.05	0.89-1.23	0.52	1.14	0.99-1.30	0.06	1.05	0.89-1.25	0.57
Sedimentation rate, ESR	1.06	1.01-1.12	0.03	1.02	0.95-1.11	0.56	1.16	1.04-1.29	**0.009**	1.18	1.04-1.34	**0.01**	1.15	1.03-1.28	**0.01**	1.02	0.86-1.20	0.82
Smoking	1.11	0.99-1.25	0.07	0.95	0.80-1.13	0.58	1.88	1.42-2.47	**0.001**	0.94	0.67-1.33	0.75	0.97	0.73-1.30	0.86	1.47	1.04-2.08	0.03
Sick leave at present	1.01	0.81-1.26	0.93	1.10	0.79-1.54	0.57	0.72	0.45-1.16	0.18	1.01	0.53-1.92	0.98	0.88	0.52-1.49	0.64	0.77	0.41-1.42	0.40
Pressure in the chest	1.04	0.92-1.18	0.50	1.05	0.88-1.25	0.58	0.88	0.66-1.17	0.38	1.08	0.76-1.55	0.67	0.99	0.74-1.33	0.93	0.87	0.61-1.25	0.46
Poor self-rated health	1.19	1.06-1.34	**0.004**	1.06	0.90-1.26	0.48	1.08	0.81-1.44	0.60	1.52	1.09-2.12	**0.01**	1.22	0.92-1.62	0.17	1.82	1.30-2.56	**0.001**
Poor appetite	1.25	0.88-1.79	0.21	1.17	0.63-2.19	0.62	0.68	0.30-1.54	0.36	0.56	0.23-1.37	0.20	1.12	0.42-3.02	0.82	0.63	0.23-1.72	0.37
Premature awakening	1.02	0.89-1.16	0.80	1.03	0.85-1.24	0.77	1.52	1.14-2.03	**0.004**	1.06	0.72-1.55	0.78	1.09	0.78-1.51	0.63	0.68	0.47-0.98	0.04
Hospitalization, mental disorder	1.18	0.91-1.53	0.20	1.09	0.72-1.66	0.68	1.87	1.12-3.12	0.03	1.61	0.60-4.36	0.35	0.66	0.37-1.15	0.14	2.17	1.19-3.85	**0.01**
Physical activity	0.87	0.76-0.98	0.03	0.88	0.76-1.03	0.11	0.80	0.55-1.16	0.24	0.77	0.54-1.11	0.17	0.90	0.66-1.23	0.50	1.13	0.93-1.37	0.21
Hormone replacement therapy	0.68	0.54-0.85	**0.001**	0.64	0.46-0.89	**0.008**	0.68	0.39-1.18	0.17	0.83	0.47-1.49	0.53	0.75	0.44-1.28	0.29	0.55	0.26-1.19	0.13
History of previous fracture	2.00	1.56-2.58	**0.001**	2.00	1.40-2.85	**0.001**	3.13	1.67-5.85	**0.001**	1.32	0.58-3.01	0.50	2.11	1.17-3.80	**0.001**	4.76	2.74-8.26	**0.001**

Note to the reviewer: This table may be appendixed.

Table 5

Relative risk (RR) for low-energy fractures in **men,** with each variable analysed in an age-adjusted regression analysis using z-scores with 1 SD change as the unit for the continuous variables and yes versus no for the categorical variables.

Variable	Low energy fracture n=1278			Forearm fracture n=315			Vertebral fracture n=156			Proximal humerus fracture n=115			Ankle fracture n=250			Hip fracture n=163		
	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p
Age	1.19	1.13-1.26	**0.001**	1.14	1.02-1.28	0.02	1.70	1.49-1.92	**0.001**	1.42	1.17-1.72	**0.001**	1.06	0.93-1.20	0.37	2.08	1.77-2.43	**0.001**
Body height	1.04	0.99-1.10	0.14	1.05	0.94-1.18	0.37	0.99	0.87-1.13	0.94	1.08	0.90-1.30	0.41	0.92	0.81-1.04	0.19	1.20	1.02-1.40	0.03
Body weight	0.95	0.90-1.00	0.06	0.90	080-1.01	0.06	0.89	0.78-1.01	0.07	0.82	0.68-1.00	0.06	1.06	0.94-1.20	0.34	0.75	0.64-0.89	**0.001**
Body mass index, BMI	0.91	0.86-0.97	**0.002**	0.85	0.75-0.96	**0.007**	0.86	0.75-0.98	0.03	0.77	0.63-0.94	**0.01**	1.12	0.99-1.26	0.07	0.63	0.53-0.76	**0.001**
>10 kg weight gain since age 30	1.04	0.90-1.20	0.57	1.03	0.73-1.29	0.84	1.39	0.92-2.12	0.12	1.68	0.99-2.85	0.06	1.02	0.70-1.35	0.88	0.96	0.67-1.37	0.82
Skinfold	0.91	0.86-0.96	**0.001**	0.95	0.85-1.07	0.40	0.79	0.70-0.90	**0.001**	0.97	0.80-1.17	0.75	0.91	0.80-1.03	0.14	0.86	0.74-1.00	0.05
Forced vital capacity, FVC	0.92	0.86-0.98	**0.006**	0.90	0.80-1.02	0.10	0.85	0.74-0.97	0.02	0.81	0.66-0.99	0.04	0.92	0.81-1.06	0.24	0.82	0.69-0.97	0.02
Systolic blood pressure	1.08	1.02-1.14	**0.005**	1.00	0.90-1.12	0.94	1.08	0.96-1.21	0.22	1.11	0.93-1.32	0.25	1.14	1.01-1.29	0.03	1.07	0.93-1.24	0.33
Diastolic blood pressure	1.06	1.00-1.12	0.04	0.99	0.89-1.11	0.92	1.10	0.98-1.25	0.11	1.09	0.91-1.31	0.33	1.13	1.00-1.28	0.05	1.18	1.02-1.36	0.03
Resting pulse	1.07	1.01-1.13	**0.01**	1.03	0.93-1.15	0.56	1.08	0.95-1.22	0.23	1.23	1.04-1.46	**0.01**	0.96	0.84-1.09	0.50	1.34	1.17-1.53	**0.001**
Diabetes	2.50	1.75-3.57	**0.001**	0.46	0.21-1.04	0.06	0.85	0.27-2.65	0.78	0.53	0.13-2.13	0.37	0.73	0.23-2.29	0.59	7.75	4.37-13.7	**0.001**
Serum-triglycerides	0.98	0.93-1.04	0.61	1.03	0.93-1.14	0.61	1.01	0.89-1.14	0.87	0.71	0.53-0.95	0.02	1.02	0.90-1.14	0.79	1.13	1.05-1.21	**0.001**
Serum-cholesterol	0.96	0.91-1.02	0.21	0.93	0.82-1.05	0.23	0.82	0.72-0.95	**0.007**	0.85	0.69-1.04	0.11	1.09	0.97-1.23	0.16	1.01	0.86-1.19	0.87
γ-glutamyl transferase	1.21	1.15-1.27	**0.001**	1.09	0.98-1.22	0.11	1.39	1.25-1.54	**0.001**	1.39	1.19-1.63	**0.001**	1.35	1.22-1.50	**0.001**	1.45	1.28-1.65	**0.001**
Serum-phosphate	1.16	1.08-1.25	**0.001**	1.15	1.00-1.34	0.06	1.43	1.22-1.68	**0.001**	1.32	1.04-1.67	0.02	1.31	1.12-1.53	**0.001**	1.20	0.97-1.48	0.09
Serum-creatinine	1.01	0.96-1.06	0.64	0.89	0.76-1.04	0.15	0.95	0.81-1.12	0.56	1.03	0.90-1.17	0.69	1.07	1.02-1.11	**0.006**	0.89	0.72-1.11	0.30
Serum-uric acid	1.00	0.95-1.06	0.96	1.00	0.89-1.12	0.99	0.99	0.87-1.12	0.87	1.05	0.88-1.26	0.58	0.99	0.87-1.12	0.87	1.03	0.89-1.20	0.70
Blood-haemoglobin	0.99	0.94-1.04	0.71	0.98	0.88-1.09	0.68	1.02	0.90-1.16	0.77	0.90	0.75-1.07	0.24	1.01	0.89-1.14	0.87	1.00	0.86-1.16	0.99
Sedimentation rate, ESR	1.04	0.99-1.09	0.09	1.00	0.90-1.12	1.00	0.99	0.87-1.12	0.84	1.03	0.87-1.21	0.74	1.05	0.94-1.16	0.41	1.11	1.00-1.23	0.05
Smoking	1.31	1.17-1.46	**0.001**	1.18	0.94-1.47	0.14	1.98	1.53-2.58	**0.001**	1.70	1.17-2.48	**0.006**	1.23	0.96-1.59	0.10	2.72	1.94-3.80	**0.001**
Sick leave at present	0.79	0.91-1.74	0.16	1.20	0.62-2.32	0.58	2.98	1.83-4.85	**0.001**	1.79	0.73-4.35	0.20	1.16	0.55-2.50	0.70	1.99	1.01-3.91	0.05
Pressure in the chest	1.09	0.95-1.25	0.24	1.23	0.93-1.61	0.14	1.46	1.09-1.96	**0.01**	1.09	0.69-1.69	0.71	1.28	0.94-1.72	0.11	0.96	0.67-1.38	0.83
Poor self-rated health	1.25	1.11-1.41	**0.001**	1.14	0.89-1.46	0.29	1.80	1.39-2.32	**0.001**	1.28	0.86-1.90	0.22	1.19	0.91-1.56	0.21	1.83	1.33-2.50	**0.001**
Poor appetite	1.72	1.27-2.32	**0.001**	1.23	0.61-2.50	0.55	3.05	1.80-5.17	**0.001**	3.43	1.66-7.10	**0.001**	1.75	0.90-3.45	0.10	2.10	1.03-4.27	0.04
Premature awakening	1.53	1.31-1.80	**0.001**	1.28	0.90-1.79	0.17	2.17	1.57-2.98	**0.001**	2.95	1.90-4.59	**0.001**	1.72	1.21-2.45	**0.003**	1.84	1.25-2.70	**0.002**
Hospitalization, mental disorder	1.92	1.47-2.51	**0.001**	2.28	1.37-3.78	**0.001**	2.34	1.36-4.03	**0.002**	3.38	1.70-6.73	**0.001**	2.74	1.62-4.66	**0.002**	2.64	1.46-4.76	**0.001**
Physical activity	0.98	0.86-1.12	0.78	0.80	0.62-1.03	0.08	1.00	0.67-1.49	1.00	0.96	0.61-1.61	0.85	0.99	0.73-1.33	0.94	0.78	0.54-1.12	0.18

Note to the reviewer: This table may be appendixed.

Table 6

Final Cox model with risk factors for any low energy fracture and for specified fracture types in **women,** where a selection of the variables is included. Risk ratios are calculated using z-scores with 1 SD change as the unit for the continuous variables and yes versus no for the categorical variables.

| Variable	Low energy fracture n=1257			Forearm fracture n=600			Vertebral fracture n=138			Proximal humerus fracture n=146			Ankle fracture n=217			Hip fracture n=135		
	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p
Age	1.56	1.45-1.68	**0.001**	1.86	1.66-2.09	**0.001**	1.97	1.61-2.40	**0.001**	2.01	1.55-2.61	**0.001**	1.19	1.01-1.39	0.03	2.48	1.90-3.25	**0.001**
Body mass index	0.96	0.90-1.03	0.24	0.90	0.83-1.00	0.05	0.89	0.76-1.04	0.14	1.09	0.92-1.29	0.31	1.21	1.06-1.38	**0.006**	0.57	0.46-0.72	**0.001**
Diastolic blood pressure	1.01	0.95-1.08	0.70	0.94	0.86-1.03	0.19	1.14	0.98-1.32	0.09	1.24	1.04-1.48	0.02	1.09	0.94-1.26	0.26	1.18	0.98-1.42	0.08
Resting pulse	1.04	0.98-1.10	0.18	1.02	0.93-1.11	0.69	1.10	0.96-1.26	0.19	0.91	0.76-1.08	0.29	1.12	0.98-1.28	0.11	1.17	0.99-1.38	0.07
Diabetes	1.87	1.26-2.79	**0.002**	1.47	0.73-2.99	0.28	2.89	1.32-6.29	**0.008**	2.14	0.77-5.95	0.15	2.40	1.08-5.35	0.03	4.02	1.72-9.35	**0.001**
Serum-triglycerides	0.97	0.91-1.03	0.30	0.86	0.77-0.96	**0.005**	0.97	0.85-1.12	0.70	0.95	0.80-1.13	0.58	1.03	0.92-1.16	0.63	1.03	0.87-1.21	0.76
γ-glutamyl transferase	1.07	1.01-1.14	0.02	1.03	0.95-1.12	0.49	1.19	1.04-1.36	**0.009**	1.08	0.92-1.27	0.33	1.14	0.99-1.30	0.06	1.14	0.96-1.35	0.13
Sedimentation rate	1.03	0.98-1.09	0.07	1.03	0.95-1.12	0.48	1.10	0.97-1.24	0.13	1.14	1.00-1.31	0.05	1.04	0.91-1.19	0.54	1.01	0.86-1.19	0.89
Smoking	1.12	0.99-1.27	0.07	1.04	0.87-1.25	0.67	1.96	1.47-2.64	**0.001**	1.14	0.79-1.64	0.48	1.12	0.83-1.51	0.48	1.40	0.97-2.02	0.07
Poor, self-rated health	1.16	1.02-1.31	0.02	1.03	0.94-1.13	0.48	1.01	0.75-1.37	0.92	1.19	1.01-1.41	0.05	1.03	0.89-1.20	0.65	1.34	1.12-1.60	**0.001**

Table 7

Final Cox model with risk factors for any low energy fracture and different fracture types in **men,** where a selection of the variables is included. Risk ratios are calculated using z-scores with 1 SD change as the unit for the continuous variables and yes versus no for the categorical variables.

Variable	Low energy fracture n=1278			Forearm fracture n=315			Vertebral fracture n=156			Proximal humerus fracture n=115			Ankle fracture n=250			Hip fracture n=163		
	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p	RR	CI 95 %	p
Age	1.19	1.12-1.26	**0.001**	1.19	1.05-1.33	**0.004**	1.75	1.54-2.00	**0.001**	1.45	1.19-1.77	**0.001**	1.02	0.89-1.17	0.76	2.18	1.84-2.57	**0.001**
Body mass index	0.88	0.83-0.94	**0.001**	0.81	0.71-0.92	**0.001**	0.89	0.77-1.03	0.11	0.80	0.65-0.99	0.04	1.05	0.92-1.21	0.43	0.58	0.49-0.69	**0.001**
Resting pulse	1.05	0.99-1.11	0.10	1.02	0.92-1.15	0.68	1.04	0.92-1.19	0.50	1.21	1.02-1.44	0.03	0.90	0.79-1.03	0.12	1.24	1.08-1.43	**0.002**
Diabetes	2.38	1.65-3.42	**0.001**	2.15	0.95-4.83	0.07	1.11	0.35-3.50	0.85	1.09	0.15-7.87	0.93	1.42	0.45-4.46	0.55	6.37	3.42-11.76	**0.001**
Serum-triglycerides	0.93	0.86-0.99	0.04	1.06	0.96-1.17	0.27	0.78	0.64-0.95	**0.01**	0.60	0.43-0.84	**0.003**	0.87	0.73-1.02	0.09	1.04	0.96-1.13	0.34
Serum-cholesterol	0.95	0.89-1.01	0.08	0.91	0.80-1.03	0.14	0.79	0.68-0.91	**0.002**	0.85	0.68-1.05	0.14	1.04	0.91-1.19	0.53	0.94	0.79-1.11	0.48
γ-glutamyl transferase	1.24	1.18-1.31	**0.001**	1.13	1.01-1.27	0.04	1.43	1.28-1.60	**0.001**	1.54	1.32-1.80	**0.001**	1.38	1.23-1.55	**0.001**	1.44	1.27-1.63	**0.001**
Serum-creatinine	1.01	0.97-1.06	0.60	0.89	0.76-1.04	0.15	0.96	0.82-1.13	0.64	1.03	0.92-1.16	0.61	1.07	1.02-1.12	0.004	0.93	0.76-1.14	0.49
Smoking	1.25	1.11-1.39	**0.001**	1.12	0.89-1.40	0.33	1.85	1.41-2.42	**0.001**	1.58	1.08-2.33	0.02	1.18	0.91-1.52	0.21	2.14	1.51-3.01	**0.001**
Poor, self-rated health	1.19	1.06-1.35	**0.004**	1.07	0.84-1.38	0.58	1.61	1.24-2.10	**0.001**	1.18	0.79-1.76	0.43	1.10	0.83-1.45	0.51	1.62	1.17-2.23	**0.003**

Figure 1

Incidence per 1000 person years for each type of fracture in women and men, based on a population sample of 10 902 women and 22 444 men.
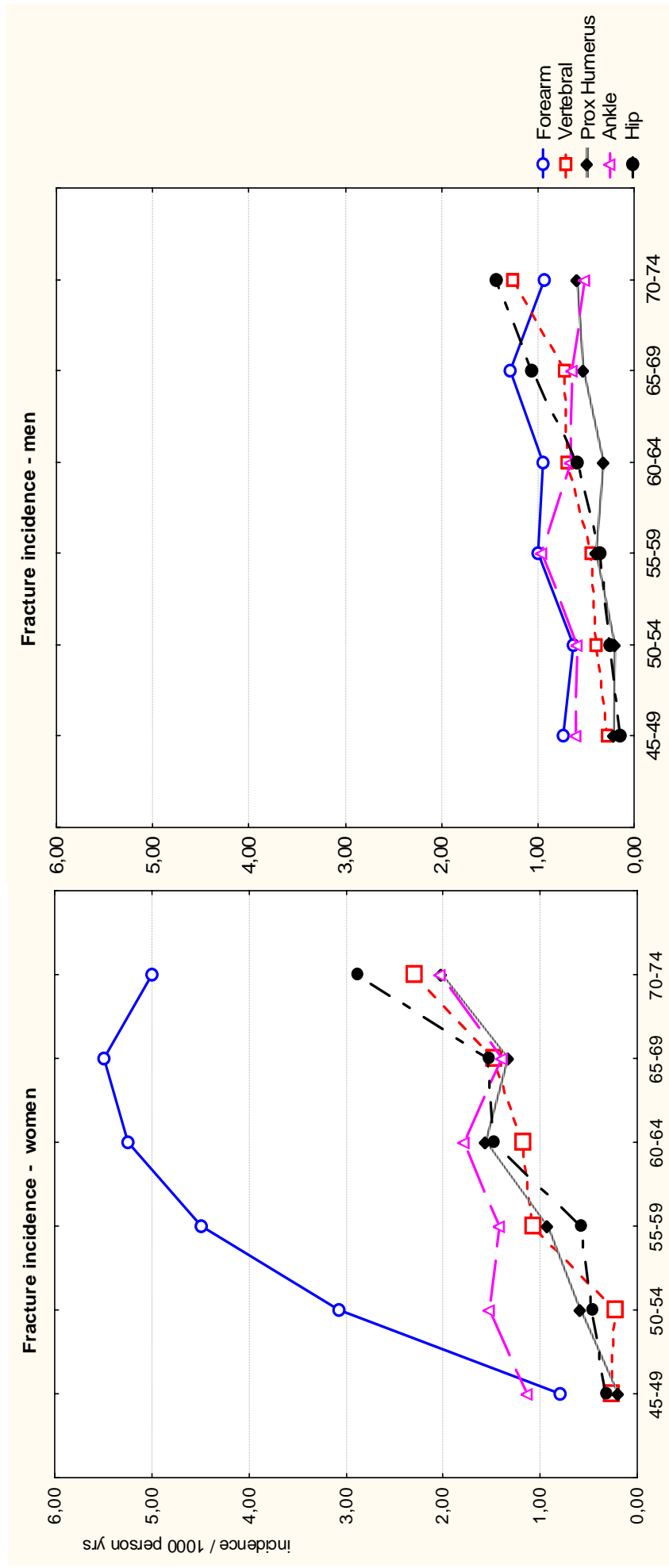
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