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Falls Explain Between-Center Differences in the Incidence of Limb Fracture across Europe

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There is important geographic variation in the occurrence of the major osteoporotic fractures across Europe. The aim of this study was to determine whether between-center variation in limb fracture rates across Europe could be explained by variation in the incidence of falls. Men and women, aged 50–79 years, were recruited from population-based registers in 30 European centers. Subjects were followed by postal questionnaire to ascertain the occurrence of incident fractures, and were also asked about the occurrence and number of recent falls. Self-reported fractures were confirmed, where possible, by review of the radiographs, medical record, or subject interview. The age- and gender-adjusted incidence of falls was calculated by center using Poisson regression. Poisson regression was also used to assess the extent to which between-center differences in the incidence of limb fractures could be explained by differences in the age- and gender-adjusted incidence of falls at those centers. In all, 6302 men (mean age 63.9 years) and 6761 women (mean age 63.1 years) completed at least one questionnaire concerning fractures and falls. During a median follow-up time of 3 years, 3647 falls were reported by men and 4783 by women. After adjusting for age and gender, there was evidence of significant between-center differences in the occurrence of falls. There was also between-center variation in the occurrence of upper limb, lower limb, and distal forearm fractures. Variation in the age- and gender-adjusted center-specific fall rates explained 24%, 14%, and 6% of the between-center variation in incidence of distal forearm and upper and lower limb fractures, respectively. Given the constraints inherent in such an analysis, in men and women aged 50–79 years, variation in fall rates could explain a significant proportion of the between-center variation in the incidence of limb fracture across Europe. (Bone 31:712–717; 2002)

Key Words: Falls; Prospective study; Epidemiology; Osteoporosis; Incident limb fractures.

Introduction

There is an important geographic variation in the occurrence of major osteoporotic fractures both within and between different regions and populations of the world.[12,13] Across Europe, the incidence of hip fracture varies by a factor of 11-fold in women and 4–7-fold in men,[6,8] whereas, using data from single-center studies, the incidence of distal forearm fracture varies by a factor of about 3-fold.[13] Such variation may be explained on the basis of variation in the level of bone strength, trauma (and in particular falls), or both. Bone mass is the major determinant of bone strength; however, it seems unlikely that differences in level of bone mass between communities could explain the observed spread of fracture risk.[9,10] There is some evidence that falls may play a role in explaining differences in fracture risk. Thus, the lower incidence of hip fracture in Asians compared with whites has been thought in part due to the lower risk of falls in that population.[1,2,5,19]

We hypothesized that the incidence of falls would vary across Europe and that the variation in the occurrence of falls would explain some of the observed variation in the incidence of limb fracture. Using data from the European Prospective Osteoporosis Study, we first aimed to determine whether there was evidence of variation in the incidence of falls across Europe and, second, to what extent, if any, variation in the occurrence of falls could explain between-center variation in the occurrence of limb fractures in the populations studied.

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Subjects and Methods

Subjects

The subjects included in this analysis were recruited for participation in the European Vertebral Osteoporosis Study (EVOS). The detailed methods of this study have been reported elsewhere.[17,18] In brief, men and women, aged ≥50 years, were recruited from population registers in 36 European centers. Stratified sampling was used with the aim of recruiting equal numbers of men and women in each of six 5 year age bands: 50–54 years; 55–59 years; 60–64 years; 65–69 years; 70–74 years; and ≥75 years. Those who took part had an interviewer-administered questionnaire and lateral spine radiographs performed.

Subjects recruited at 32 centers were followed prospectively by annual postal questionnaire. Subjects were asked to record the occurrence of any incident fractures and the occurrence and number of falls since the baseline survey or the previous postal contact. Self-reported fractures were confirmed where possible by review of radiograph, medical record, or subject interview. The validity of this approach for fracture definition has been reported elsewhere.[7] One center was not included in the analysis because of a low follow-up rate and another because of incomplete data concerning falls.

Analysis

The incidence of falls was determined by dividing the total number of falls experienced by all subjects by the person-years at risk. Because individuals who experienced a fracture may have been more likely to recall a fall than individuals who did not experience a fracture, we repeated the analysis using “fracture-free” falls, which we defined as falls that occurred without causing a fracture. The fracture-free fall rate was calculated by subtracting the number of fractures from the number of falls an individual experienced, and dividing by the person-years at risk. The incidence of falls (“all” and “fracture-free” falls) were calculated by age group and gender. The age-standardized incidence of falls in men and women was calculated at each center using a standard European population.[23] Spearman’s correlation coefficient (r) was used to determine the association between the age-standardized incidence of falls in men and women by center. Age- and gender-adjusted fall rates were calculated using Poisson regression.

Fractures were classified using the ninth edition of the International Classification of Diseases,[25] and analyses were undertaken using the following categories of limb fracture: upper limb (including the distal forearm); lower limb; and distal forearm alone. To model statistically the incidence of these fractures, subjects contributed follow-up time (person-years) from the date of the baseline survey until the first occurrence of the individual limb fracture type, death, or the end of the study.

Poisson regression was then used to assess for any between-center differences in the age- and gender-adjusted incidence of limb fractures. Subsequently, Poisson regression was used to determine the contribution of falls — both “all falls” and “fracture-free” falls (using the age- and gender-adjusted incidence of falls at each center) to the observed between-center variation in age- and gender-adjusted incidence of the limb fracture types. This was formally assessed by looking at the proportion of the between-center deviance in fracture rate (degrees of freedom [df] = 29) due to falls (df = 1). Poisson regression was used because it allows modeling of multiple (fracture) events. Analyses were performed using STATA, version 6 (Stata Corp., College Station, TX).[21]

Results

Subjects

In the 30 centers that contributed data to this analysis, 6302 men, mean age 63.9 (SD = 8.0) years, and 6761 women, mean age

Table 1. Incidence of falls and fracture-free falls by age group and gender

Age group (years)	Men					
	N	Number of falls	Person-years of follow-up	Incidence of falls/100 person-years (95% CI)	Number of fracture-free falls	Incidence of fracture-free falls/100 person-years (95% CI)
50–54	1091	819	3382	24.2 (22.6, 25.9)	785	23.2 (21.6, 24.9)
55–59	1223	667	3764	17.7 (16.4, 19.1)	650	17.3 (16.0, 18.6)
60–64	1220	522	3741	14.0 (12.8, 15.2)	500	13.4 (12.2, 14.6)
65–69	1122	692	3408	20.3 (18.8, 21.9)	668	19.6 (18.1, 21.1)
70–74	987	524	2894	18.1 (16.6, 19.7)	496	17.1 (15.7, 18.7)
75–79	659	423	1900	22.3 (20.2, 24.5)	402	21.2 (19.1, 23.3)

Age group (years)	Women					
	N	Number of falls	Person-years of follow-up	Incidence of falls/100 person-years (95% CI)	Number of fracture-free falls	Incidence of fracture-free falls/100 person-years (95% CI)
50–54	1306	757	4046	18.7 (17.4, 20.1)	711	17.6 (16.3, 18.9)
55–59	1419	874	4406	19.8 (18.5, 21.2)	812	18.4 (17.2, 19.7)
60–64	1309	934	4006	23.3 (21.8, 24.9)	865	21.6 (20.2, 23.1)
65–69	1156	874	3528	24.8 (23.2, 26.5)	799	22.6 (21.1, 24.3)
70–74	971	738	2861	25.8 (24.0, 27.7)	685	23.9 (22.2, 25.8)
75–79	600	606	1716	35.3 (32.6, 38.3)	554	32.3 (29.7, 35.1)

63.1 (SD = 7.9) years, were followed for a median of 3 years (range 0.4–5.7 years).

Incidence of Falls

During the follow-up period, 3647 falls were reported by men and 4783 by women. The median number of falls per center was 221 (interquartile range 123–339). The overall crude incidence of falls was 19 per 100 person-years in men and 23 per 100 person-years in women. The incidence of falls by age and gender is shown in **Table 1**. In women, incidence rose gradually with age from 19 per 100 person-years at age 50–54 years to 35 per 100 person-years at age 75–79 years. In men, incidence rose with age from 60–64 years. There was a relatively high incidence at age 50–54 years, the reason for which is unclear.

Excluding falls that resulted in fractures, there were 3501 falls in men and 4426 in women. The overall crude incidence was 18 per 100 person-years in men and 22 per 100 person-years in women. The incidence of fracture-free falls by age and gender is shown in Table 1. The pattern of incidence by age and gender was similar to that observed for all falls.

The age-standardized incidence of falls, by center, in men and women, is shown in **Table 2**. For most centers, the incidence of falls was greater in women than men. There was a significant correlation, by center, between the incidence of falls in men and women ($r = 0.81$, $p < 0.05$). Using Poisson regression there was statistically significant between-center variation in the incidence of falls in both men and women.

Incidence of Fractures

In total, 94% of upper limb, 89% of lower limb, and 92% of distal forearm fractures were confirmed by review of the radiograph or medical record or by subject review. The crude incidence of fractures among women was: upper limb, 1.1 per 100 person-years; lower limb, 0.78 per 100 person-years; and distal forearm, 0.74 per 100 person-years. For men, the crude incidence was: upper limb, 0.33 per 100 person-years; lower limb, 0.35 per 100 person-years; and distal forearm, 0.17 per 100 person-years. For fractures of the upper limb, lower limb, and distal forearm, there was evidence of significant between-center variation in occurrence (all sites; $p < 0.05$).

Relationship Between Falls and Fractures

The relationship between the age-adjusted incidence of falls and the age-adjusted incidence of upper limb, lower limb, and distal forearm fractures (by center) in men and women are shown in **Figures 1, 2**, and **3**, respectively. There was a significant correlation between the incidence of falls and the incidence of upper limb fracture: men, $r = 0.51$; women, $r = 0.42$. Also, there was a correlation between the incidence of falls and incidence of distal forearm fracture: men, $r = 0.60$; women, $r = 0.48$. For lower limb fractures, the correlation coefficients were weaker but remained significant: men, $r = 0.34$; women, $r = 0.30$. Similar findings were observed for the association between the incidence of fracture-free falls and fracture.

Table 2. Age-standardized incidence of falls by center and gender

	Men		Women	
Center	Number of falls	Incidence[a] (95% CI)	Number of falls	Incidence[a] (95% CI)
Aberdeen (UK)	164	23.2 (19.6, 26.9)	120	16.5 (13.5, 19.4)
Athens (Greece)	4	3.1 (0.0, 6.3)	40	7.4 (5.1, 9.7)
Bath (UK)	50	17.0 (12.3, 21.8)	93	31.6 (25.1, 38.2)
Berlin-Charite (Germany)	97	13.8 (11.0, 16.6)	109	15.9 (12.9, 18.8)
Berlin-Potsdam (Germany)	74	12.5 (9.6, 15.4)	89	16.8 (13.1, 20.4)
Berlin-Steglitz (Germany)	82	12.0 (9.4, 14.6)	139	16.5 (13.7, 19.3)
Bochum (Germany)	137	15.7 (13.1, 18.4)	102	15.9 (12.7, 19.0)
Budapest (Hungary)	211	29.8 (25.8, 33.9)	419	47.6 (43.0, 52.1)
Cambridge (UK)	28	10.0 (6.0, 14.0)	95	15.7 (12.4, 19.0)
Erfurt (Germany)	91	11.0 (8.7, 13.2)	116	13.1 (10.6, 15.6)
Graz (Austria)	364	33.0 (29.6, 36.4)	473	38.0 (34.5, 41.5)
Harrow (UK)	49	17.5 (12.6, 22.4)	119	21.7 (17.8, 25.6)
Heidelberg (Germany)	83	8.4 (6.5, 10.4)	97	10.0 (7.9, 12.0)
Istanbul (Turkey)	22	6.4 (3.7, 9.1)	60	11.6 (8.6, 14.5)
Jena (Germany)	113	12.8 (10.3, 15.3)	226	26.9 (23.2, 30.5)
Lubeck (Germany)	114	15.5 (12.5, 18.4)	103	18.0 (14.1, 21.1)
Madrid (Spain)	16	3.7 (1.9, 5.5)	29	5.6 (3.5, 7.7)
Malmo (Sweden)	114	9.5 (7.6, 11.3)	173	14.6 (12.3, 16.9)
Montceau-les-Mines (France)	35	5.2 (3.5, 7.0)	87	16.2 (12.7, 19.6)
Moscow (Russia)	38	7.2 (4.8, 9.6)	207	22.7 (19.6, 25.8)
Oporto (Portugal)	13	11.3 (4.8, 18.0)	51	44.0 (31.8, 56.2)
Oslo (Norway)	514	75.1 (68.4, 81.7)	389	52.5 (47.1, 57.9)
Oviedo (Spain)	102	13.2 (10.6, 15.8)	187	23.0 (19.7, 26.4)
Pellenberg (Belgium)	25	7.6 (4.0, 9.2)	69	14.5 (10.9, 18.1)
Piestany (Slovakia)	312	34.7 (30.9, 38.6)	263	32.8 (28.8, 36.8)
Prague (Czech Republic)	309	43.4 (38.3, 48.4)	182	34.4 (28.6, 40.2)
Rotterdam (Holland)	11	1.7 (0.7, 2.6)	20	3.0 (1.7, 4.4)
Siena (Italy)	29	4.6 (2.9, 6.4)	67	12.3 (9.3, 15.3)
Truro (UK)	128	20.5 (16.8, 24.2)	208	42.6 (36.6, 48.6)
Warsaw (Poland)	318	29.8 (26.5, 33.1)	451	38.9 (35.2, 42.5)

[a]Age standardized to European population (50–79 years)/100 person-years.

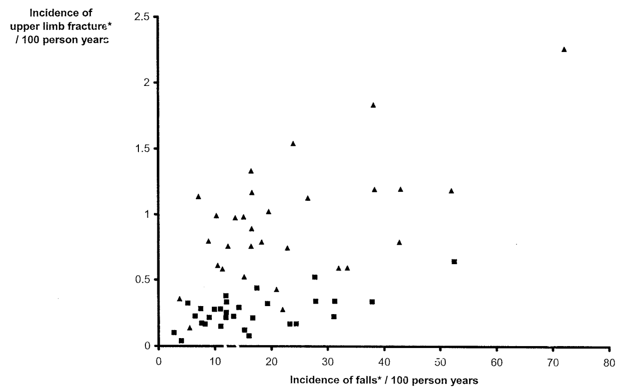

Figure 1. Incidence of falls and upper limb fracture by center in men and women. Asterisk: adjusted to age 50–54 years. Squares: men; triangles: women.

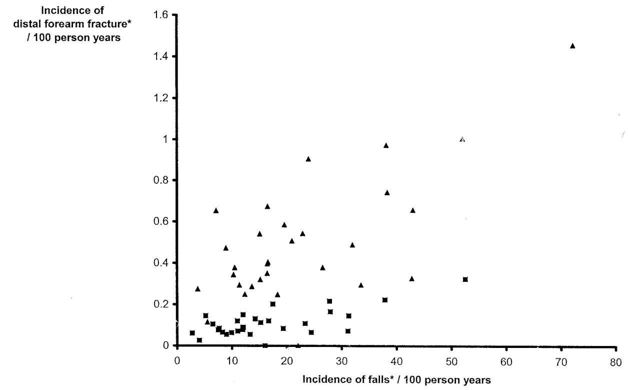

Figure 3. Incidence of falls and distal forearm fracture by center in men and women. Asterisk: adjusted to age 50–54 years. Squares: men; triangles: women.

The risk of upper, lower, and distal forearm fracture, adjusted for age, gender, and center, increased with an increasing incidence of falls in the upper limb (relative risk [RR] = 5.1 per fall per person-years, 95% confidence interval [CI] 2.6–10.1), lower limb (RR = 2.7, 95% CI 1.2–6.3), and distal forearm fracture (RR = 9.4, 95% CI 4.1–20.3). There was no evidence of an interaction with age for any of the three fracture types ($p = 0.26$, 0.56, and 0.24 for upper limb, lower limb, and distal forearm fracture, respectively).

We looked next at the proportion of the between-center variation in the incidence of the different limb fracture types explained by falls. We undertook this analysis after exclusion of a consistent outlier value (see Figures 1–3, Norwegian women). The results of this analysis are presented in **Table 3**. Difference in the incidence of all falls explained 14% of the between-center deviation in upper limb fracture, 6% in lower limb fractures, and 24% for distal forearm fracture. For fracture-free falls the corresponding data were 13%, 5%, and 22%. Including the outlier value, the proportions of the between-center variation in the incidence of different limb fracture types explained by falls were, (all falls): upper limb (35%); lower limb (9%); and distal forearm 44%. For fracture-free falls, the corresponding data were 33%, 8%, and 42%, respectively.

Discussion

In this multicenter study, there was evidence of geographic variation in the incidence of falls across Europe. Such variation explained part of the between-center differences in the occurrence of limb fractures. The contribution of falls to the between-center variation in fracture incidence was greater for upper than for lower limb fractures.

This study had several advantages. It was prospective, population-based, and used standard methods in both design and analysis. There are, however, a number of limitations to be considered in interpreting the data. In EPOS, limb fractures were ascertained using a postal questionnaire with subsequent validation of positive self-reports at each of the investigating centers. Not all individuals who experienced fractures will have reported them, most likely due to poor recall. In a small validation study, however, the proportion of individuals with a known history of fracture in the previous 18 months who did not report this was relatively small (7%).[7] Furthermore, we can think of no reason why underreporting would differ to any important degree in the different participating centers, and therefore would not have influenced our findings.

Information concerning the occurrence of falls was obtained using an annual postal questionnaire. Due to practical constraints, it was not possible to contact individual subjects as frequently as has been done in other studies of fall occurrence (every 4 months or less), and some degree of underreporting due to poor recall is likely.[4,11,16]. In one study investigating the recall of falls, 13% of individuals who reported a fall during weekly questioning did not report having a fall at the end of a 12 month period.[4]

It is possible that individuals may have been selectively more likely to recall a fall if they had experienced a fracture as a result of that fall. If true, such recall bias may have influenced the study

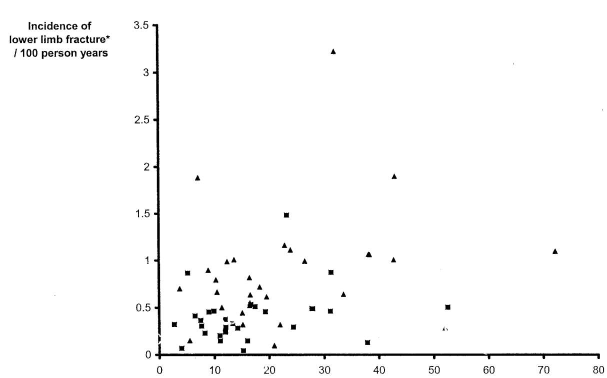

Figure 2. Incidence of falls and lower limb fracture by center in men and women. Asterisk: adjusted to age 50–54 years. Squares: men; triangles: women.

Table 3. Contribution of "study center" to deviation in fracture rates (using Poisson model) and the proportion of the between-center deviance due to falls

Fracture type	Overall deviation explained by center[a] (chi-square, 29 *df*)	Between-center deviation explained by: All falls (%)	Between-center deviation explained by: Fracture-free falls (%)
Upper limb	44.0[b]	14.3[b]	13.1[b]
Lower limb	60.3[b]	6.2	5.2
Wrist	43.6[b]	24.0[b]	22.3[b]

df, degrees of freedom.
[a]Excluding Norwegian women.
[b]$p < 0.05$.

findings, because those centers with high fracture rates may, consequently, also have had a higher frequency of reported falls. In our study, however, when the analysis was repeated looking only at falls that did not result in a fracture (fracture-free falls), the results were broadly similar, providing some reassurance that the main findings were not a consequence of recall bias.

Our data are consistent with previous studies having shown a greater fall rate among women as well as an increase in incidence with age that is more marked in women.[20,24] To our knowledge, this is the first study that has examined the influence of falls in explaining between-community differences in fracture rates. Data from single-center studies suggest that differences in hip fracture rates in Japanese Asians and American whites may be explained by differences in falls.[1,2,5,19] Our data confirm the importance of falls in explaining differences in fracture risk and suggest that differences in the incidence of falls explains up to 25% of the between-center differences in the incidence of distal forearm fracture, 14% of the between-center difference in upper limb fracture, and 6% of the between-center difference in lower limb fracture.

There was wide variation in the age-standardized incidence of falls by center, although excluding the centers with highest and lowest incidence of falls did significantly reduce this (in men from 1.7 to 75.1/100 person-years to 3.1 to 43.4/100 person-years). Such variation in the reporting of falls may be real — due to true center variation or artifactual and, consequently, methodological factors. To minimize differences in meaning/interpretation of the fall question and therefore the reporting of falls, the postal questionnaires (containing the fall questions) were standardized and translated back into the relevant European languages. It remains possible, however, that differences in interpretation/meaning may have contributed to the between-center variation in reporting of falls. Differential response bias is possible, although follow-up rates at all centers were relatively high (>80%).

What is the cause of any true center variation in the incidence of falls? The causes of falls are complex. Both intrinsic (host) and environmental factors influence the risk of falling.[15,22] Variation in the level of any of these factors in the different participating centers may in part explain the between-center differences in incidence of falls. Further research is required to better understand the causes of the center differences in incidence of falls and such knowledge may help in the development of targeted prevention programs to reduce the risk of falls.

In our analysis, falls explained a greater proportion of the between-center difference in the incidence of upper limb fractures, particularly distal forearm fractures, more so than lower limb fractures. The reason for this is unclear.

The data suggest that, in the age groups studied herein, non-fall factors may play a relatively more important role in explaining between-center variation in the occurrence of lower limb fractures than upper limb fractures. Such factors may include differences in bone mass and other skeletal parameters that influence strength such as geometry, bone quality, or microarchitecture. There is some evidence that bone mass varies in different European populations.[10] Furthermore, we have recently shown that there are significant geographic differences in femoral neck geometry across Europe, which may contribute to the variation in hip fracture risk.[3] Another possible explanation for the findings relates to the mechanism or type of fall. Type of fall is an important determinant of the site of fracture, with falls to the hip being more likely to lead to a fracture of the hip, whereas falls to the hand are more likely to lead in fractures of the wrist.[14] It is possible that variation in the relative types of fall, with perhaps greater between-center variability in falls to the upper limb (compared with the lower limb) may explain the greater contribution of falls in explaining upper limb rather than lower limb fractures. We did not, however, in EPOS seek information about the type of fall and can therefore neither confirm nor refute this. Another consideration is age — subjects in our study were relatively young (mean age for women 63.1 years) and were therefore at low risk of hip fracture. It may be that, in older age groups, among whom the incidence of hip fracture is greater, the contribution of falls in explaining between-center variation in lower limb fractures is higher.

In summary, we have shown that differences in center-specific fall rates play a role in explaining differences in fracture rates in different European centers. Understanding the causes of the variation in fall rates may help provide clues to pathogenesis and help in developing targeted prevention programs with the ultimate goal of reducing the occurrence of fracture.

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