

## Original Full Length Article

Ten-year risk of second hip fracture. A NOREPOS study<sup>☆</sup>

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## ABSTRACT

**Background:** Second hip fracture risk is elevated after the first, however whether risk differs with age, by sex or over time is not well known.

**Objective:** To examine the risk of second hip fracture by sex, age and time after first hip fracture.

**Design:** Data on all hip fractures in subjects 50 years and older and treated in Norwegian hospitals during 1999–2008 were retrieved. Surgical procedure codes and additional diagnosis codes were used to define incident fractures. Survival analyses with and without adjustment for competing risk of death were used to estimate the risk of second hip fracture.

**Results:** Among the 81,867 persons who sustained a first hip fracture, 6161 women and 1782 men suffered a second hip fracture during follow-up. The overall age-adjusted hazard ratio (HR) of a second hip fracture did not differ between the sexes (women versus men, HR = 1.03; 95% confidence interval (CI): 0.98–1.09). Taking competing risk of death into account, the corresponding age-adjusted HR of a second hip fracture was 1.40 (95% CI: 1.33–1.47) in women compared to men. The greater risk in women was due to a higher mortality in men. Based on competing risk analyses, we estimate that 15% of women and 11% of men will have suffered a second hip fracture within 10 years after the first hip fracture. The ten-year cumulative incidence was above 10% in all age-groups, except in men 90 years and older.

**Conclusion:** Fracture preventive strategies have a large potential in both women and men who suffer their first hip fracture due to the high risk of another hip fracture.

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## Introduction

Osteoporotic fractures constitute a major public health problem [1]. Associated with excess mortality, hip fractures are the most serious ones [2,3]. After any osteoporotic fracture, there is an increased risk

of a subsequent fracture [4–6]. A second hip fracture is associated with reduced mobility and social independence [7], and increased mortality compared to the risk following a first hip fracture [8,9]. The absolute risk of a second hip fracture in different studies varies from 2% to 20%, depending upon length of follow-up and whether competing risk of death has been taken into account or not [10–17].

Increased risk of subsequent hip fractures has been reported in studies including only women [10–12] and in studies with both women and men [11,13,18]. There is consensus that subsequent fracture risk is highest the first month after an initial fracture and decreases thereafter [11,14], but the length of time after initial fracture that the increased risk persists is still unclear [14,19]. Results from some studies indicate that the risk of a second hip fracture is higher in women than in men [8,13,14,20], whereas other studies found no such sex differences [16,17,21].

**Abbreviations:** HR, Hazard ratio; ICD, International Classification of Diseases; NOREPOS, The NORwegian EPidemiologic Osteoporosis Studies.

<sup>☆</sup> NOREPOS (The NORwegian EPidemiologic Osteoporosis Studies) is a collaboration between epidemiologic osteoporosis studies, which are sub-studies within large population-based surveys in four districts of Norway (Tromsø, Nord-Trøndelag, Hordaland, and Oslo). The NOREPOS Hip Fracture Database includes all hospitalizations for hip fracture in Norway.

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Studying incidence of second hip fracture in different subgroups might help identify high-risk groups and determine appropriate timing of secondary fracture interventions. However, most studies of second hip fracture are not large enough or do not have long enough follow-up time to be able to examine whether there are sex-specific differences in risk of second hip fracture and whether these differences vary according to age at first hip fracture [10–13,15–17]. The only study that was large enough to examine this issue did not account for the high mortality after an incident hip fracture [14]. Therefore, the aim of the present population study was to examine cumulative incidences of second hip fractures by sex, age and time after first hip fracture, taking competing risk of death into account.

## Methods

### Hip fracture registration

Data on hip fractures treated in Norwegian hospitals from 1 January 1994 to 31 December 2008 were retrieved through a system developed by the Norwegian Knowledge Centre for the Health Services. In short, the patient administrative systems in all 48 hospitals/health trusts in Norway treating hip fracture patients provided information on the discharge diagnosis. Hip fractures were identified according to the International Classification of Diseases, Ninth Revision (ICD-9): 820–820.9 and Tenth Revision (ICD-10): S72.0–S72.2 including cervical, trochanteric and sub-trochanteric hip fractures. The unique 11-digit personal identification number assigned to every permanent resident in Norway was used to identify hospitalizations for hip fracture and enabled identification of first and second hip fracture during the period. All data were encrypted before use.

Death and emigration dates of the hip fracture patients were obtained from the National Population Register. To assure that the index fracture was indeed the first, only patients listed with a first fracture between 1 January 1999 and 31 December 2008 were included ( $n = 81,891$ ), as the probability of recurrent fracture is highest the first few years following an initial fracture [19].

Additional diagnosis codes and surgical procedure codes (also obtained from the patient administrative systems) were used to identify which hospital stays represented an incident hip fracture. A more detailed description of the data collection and the definition of incident fractures in the NOREPOS Hip Fracture Database (NORHip) were available as supplemental material to the original paper by Omsland et al. [22].

The validity of the second hip fractures in NORHip was tested against local x-ray or journal verified fracture registers in Tromsø and Oslo (among 58,773 participants in the Oslo Health and the Tromsø Health Study). Cohen's kappa for the agreement between NORHip and local fracture registers was 0.76, and the NORHip database underestimated the number of second hip fractures by approximately 10%.

### Statistics

A competing risk is defined as an event that precludes or alters the probability of a main event under examination. With the common Kaplan–Meier approach, patients who die are considered censored, and if the death rate is high, the risk of a second hip fracture will be overestimated [23]. Cumulative incidence is the appropriate estimate of failure probabilities when competing risks are present. Cumulative incidence estimates the probability that a second hip fracture occurs before a given time, taking the competing risk of death into account.

Initially, Cox's proportional hazard regression was used to analyze the risk of subsequent hip fracture in women and men. Additional analyses adjusting for the competing risk of death were also performed and repeated in 10-year age-groups using age at first fracture. The STATA command 'stcomp' was used in the competing risk analyses. Based

on the competing risk of death analysis, cumulative incidence of second hip fracture was tabulated and plotted.

In all analyses, subjects who had sustained a first hip fracture after 1 January 1999 were included. Time from first to second hip fracture, end of follow-up, or death, was calculated. All analyses were adjusted for age at first fracture. Proportionality was tested on the basis of Schoenfeld residuals and the criteria of proportional hazards (by gender) were fulfilled. Estimates obtained from Cox's regression are called hazard ratio (HR), and estimates obtained from competing risk of death regression analyses are called sub-hazard ratio. For simplicity, we refer to both estimates as hazard ratios (HR).

Mortality following the first hip fracture was analyzed using Cox's regression adjusted for age. Trends in total mortality by time after first hip fracture were calculated as rates and percentage of initial number with a first hip fracture, separately for men and women.

### Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics, the Norwegian Data Inspectorate, the Directorate of Health, and Statistics Norway.

## Results

A total of 81,867 subjects were identified with a first hip fracture after 1 January 1999. Among these, 7943 also had a second hip fracture (6161 women and 1782 men). Median time between first and second hip fracture was 1.5 (interquartile range: 0.5–3.2) years in women and 1.2 (interquartile range: 0.4–2.7) years in men.

The crude incidence of second hip fracture per 10,000 person years was 379 (95% confidence interval – CI: 370, 389) in women and 333 (95% CI: 318–349) in men. Using standard Cox's proportional hazards regression analyses, the age-adjusted risk of a second fracture during the 10-year period was not higher in women compared to men (HR = 1.03; 95% CI: 0.98–1.09).

The age-adjusted overall mortality after hip fracture was 77% higher in men versus women (95% CI: 73–80), and the higher mortality in men was most prominent during the first year after fracture (Table 1).

When taking competing risk of death into account, the age-adjusted HR of second hip fracture was 1.40 (95% CI: 1.33–1.47) in women compared to men, and the cumulative incidence of second hip fracture was 4.4% in women and 3.2% in men during the first year after the first hip fracture (Table 2 and Fig. 1). After 10 years, the cumulative incidence of second hip fracture was 15.1% in women and 11.0% in men (Table 2 and Fig. 1). In a sensitivity analysis only patients with surgical procedure codes for the second hip fracture were included ( $n = 5465$  second hip fractures in analysis), and the age-adjusted HR of second hip fracture in women compared to men was almost unchanged (HR = 1.42; 95% CI: 1.33–1.52).

The steepest rise in cumulative incidence was observed during the first years after the initial hip fracture in both sexes (Table 2 and Fig. 1). Furthermore, considering time after initial fracture and adjusting

**Table 1**

Total crude mortality after first hip fracture. The NOREPOS hip fracture database 1999–2008.

Time (years) <sup>a</sup>	Mortality per 10,000 person years	
	Women	Men
0–1	2478	4423
1–2	1312	1889
2–3	1443	1770
3–4	1493	1675
4–5	1484	1672
5–10	1514	1547

<sup>a</sup> Time after first hip fracture.

**Table 2**

Cumulative incidence of second hip fracture tabulated by time after first hip fracture and hazard ratios (95% confidence intervals) for second hip fractures in women versus men. The NOREPOS hip fracture database 1999–2008.

Time	Total no. second hip fractures	Cumulative incidence of second hip fracture <sup>a</sup>		HR <sup>a</sup> in women compared to men
		Women	Men	
		%	%	
3 months	1114	1.4	1.4	0.98 (0.86–1.12)
6 months	1988	2.7	1.9	1.06 (0.96–1.17)
1 year	3175	4.4	3.2	1.16 (1.07–1.26)
2 years	4805	6.9	5.0	1.24 (1.16–1.32)
3 years	5898	8.8	6.4	1.30 (1.22–1.38)
4 years	6620	10.3	7.5	1.33 (1.26–1.41)
5 years	7130	11.5	8.3	1.35 (1.28–1.43)
10 years	7943	15.1	11.0	1.40 (1.33–1.48)

HR = hazard ratio.

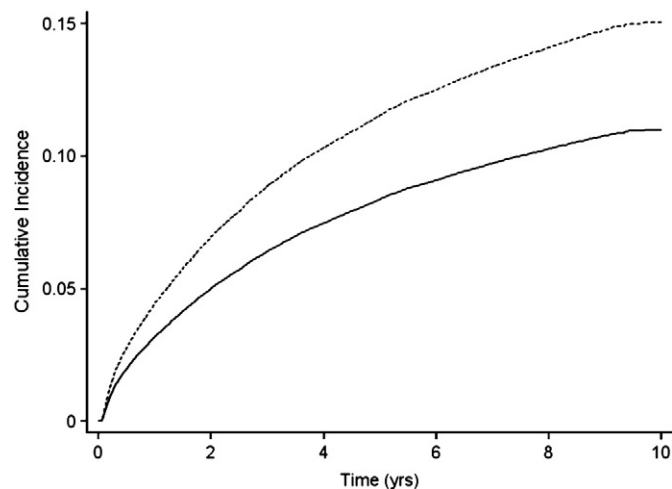
<sup>a</sup> Estimates are from competing risk of death regression model, adjusted for age at first fracture.

for age, there was no significant difference between women and men 3 months (HR = 0.98; 95% CI: 0.86–1.12) and 6 months (HR = 1.06; 95% CI: 0.96–1.17) after the initial fracture. However, after one year and thereafter, the age-adjusted risk was higher in women than in men (HR = 1.16; 95% CI: 1.07–1.26).

Taking competing risk of death into account, the 10-year cumulative incidence of hip fracture of approximately 11–12% was fairly stable across age-groups in men, except in the oldest age-group (>90 years) where the cumulative 10-year incidence was approximately 6% (Table 3). In women the risk of a second hip fracture increased with advancing age, except in the oldest age-group in which the incidence was approximately 10%. In the age-groups above 70 years, women had a higher risk of sustaining a second fracture than men, and the same pattern was marginally significant in the age-group 60–69 years (Table 3). The highest cumulative incidence in women was observed in the age-span between 70 and 89 years; 16.5% after 10 years (Fig. 2).

## Discussion

In the present study, including more than 80,000 hip fractures sustained during 1999–2008 in the Norwegian population, we estimated that 15% of women and 11% of men with an initial hip fracture would suffer a second hip fracture during the subsequent 10 years. The higher cumulative incidence in women was explained by a lower



**Fig. 1.** Cumulative incidence of second hip fracture in women (dashed line) and men (solid line) with a first hip fracture. Results were obtained from competing risk of death regression model with adjustment for age at first hip fracture. The NOREPOS Hip Fracture Database 1999–2008.

**Table 3**

Ten-year cumulative incidence and hazard ratio (95% confidence interval) for second hip fracture in women versus men by age at first hip fracture. The NOREPOS hip fracture database 1999–2008.

Age-category	Women	Men	Hazard ratio <sup>a</sup>
50–59	10.0	11.3	0.88 (0.6–1.16)
60–69	12.6	10.8	1.18 (0.99–1.41)
70–79	16.5	12.6	1.33 (1.21–1.47)
80–89	16.4	11.4	1.48 (1.37–1.60)
90+	10.2	6.4	1.63 (1.36–1.95)

<sup>a</sup> Estimates are from competing risk of death regression model, adjusted for age at first fracture.

mortality. Except among those over 90 years, the 10-year cumulative incidence of a second hip fracture increased by increasing age in women, but was stable in men.

## Incidence of second hip fracture

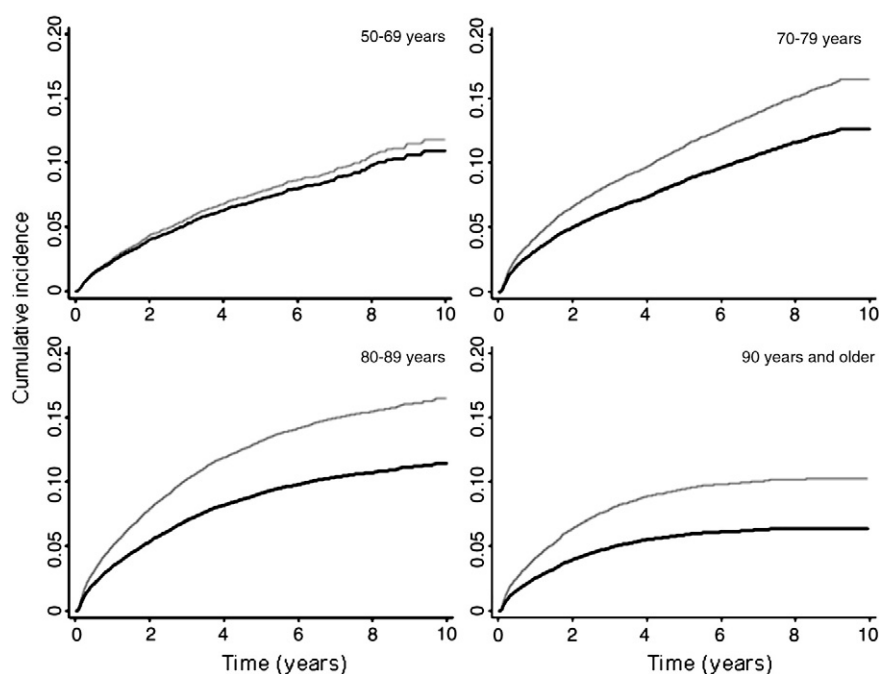
The mortality is high after a hip fracture [24]. As a result, the risk of a second hip fracture is overestimated when persons who die are censored as in standard survival and Kaplan–Meier analyses. When competing risk of death is taken into account [23], the calculated cumulative incidence incorporates the fact that subjects who die are no longer at risk of fracture. In a nationwide population-based cohort study from Denmark, the fracture registration was similar to our study [14]. However, the reported incidence of second hip fracture of 9% after one year and 20% after 5 years was based on Kaplan–Meier estimates and is therefore higher than in our study using competing risk analyses. Similarly, in a Finish study using the Kaplan–Meier method, the estimates of 5% and 8% within one and two years, respectively, after the first hip fracture were higher than ours [16]. If using the Kaplan–Meier method in the present study, approximately 27% of women and 23% of men sustained a second hip fracture within ten years after the first hip fracture.

Death was considered as a competing risk of second hip fracture in two American studies. In the Framingham study 95 men and 386 women with an initial hip fracture were followed until a second hip fracture, death, drop-out or study completion [13]. The cumulative incidence in this study was 2.5% at one year, 8.2% at five years, and 12.2% at 10 years. The corresponding numbers for women and men combined in the present study were 4.0%, 11.0% and 13.9%, respectively. In Olmsted County, Minnesota, all hip fracture events were identified between 1980 and 2006, and in 2752 patients with hip fractures 311 new fractures occurred [20]. The cumulative incidence of second hip fracture after 10 years was 11% in women and 6% in men [20]. Compared to these results, a higher proportion of Norwegians sustain a second fracture compared to Americans. However, fracture registration methods were different making direct comparisons difficult. For more accurate comparisons on the risk of subsequent fracture between studies, larger cohorts, comparable fracture registration and statistical analyses are warranted, and the competing risk of death in hip fracture patients should be taken into account.

Using standard Cox's analyses in the present study, the age-adjusted risk of a second fracture was not significantly different between women and men. However, the ten-year risk of a second fracture was 40% higher in women compared to men after adjustment for competing risk of death. In other words, women and men have the same risk of a second hip fracture per se, but in general women with prior fracture have a higher risk of a second hip fracture because they live longer.

## Clinical implications of results

Several studies have reported that the risk of a subsequent fracture is highest the first period after an initial fracture [19,25]. With



**Fig. 2.** Cumulative incidence of second hip fracture by age in women (thin line) and men (thick line) with a prior hip fracture. Competing risk of death regression model, adjusted for age at first hip fracture. The NOREPOS Hip Fracture Database 1999–2008.

the steepest rise in cumulative incidence during the first couple of years after the initial fracture, the present study supports these observations, and documents a need for an immediate attention in both women and men who sustain their first hip fracture.

In all age-groups the cumulative incidence of a second hip fracture was 10% or higher, except for men 90 years or older. Thus, the potential to prevent a second hip fracture is substantial. To put this in perspective, in 100,000 women aged 70–89 years with a first hip fracture (with 16,500 expected second fractures), 6600 second hip fractures can theoretically be prevented by anti-osteoporotic drugs if all incident cases received treatment (assuming a treatment efficacy of 40% [26,27]). Despite the large potential for second fracture prevention, it is not common to begin therapy in patients with a recent hip fracture. Roerholt et al. showed that only 9% of women and only 4% of men in Denmark began therapy following hip fracture in 2004 [28]. Moreover, data from Norway show that only 15% of women and 4% of men who sustained a hip fracture in 2003 or 2004 received anti-osteoporosis drugs in 2005 [29].

However, optimal care and fracture prevention cannot be achieved by medication use alone. Patients at risk of a second hip fracture often have co-morbidities, they are underweight, and use multiple drugs, all of which can contribute to increased risk of fracture. Another important issue is prevention of falls, and use of hip protectors should be considered in this high risk group [30]. Moreover, it takes time before osteoporosis drugs are effective in reducing fracture risk, and there is a need for multidisciplinary fall prevention strategies instantly after a hip fracture. Studies investigating such possible strategies are warranted.

#### Strengths and limitations

One of the strengths of this study is that it covers an entire country's population, unlike most previous studies which have had selected samples. Personal identifiable data on all hip fractures in Norway between 1994 and 2008 were available and the number of initial and second hip fractures is substantial. It is possible however, that some hip fracture patients may have died before being hospitalized,

or were treated abroad, and were thus not registered in the patient administrative systems, however these numbers are most likely very small. Surgical procedure codes and ICD codes were used to exclude admissions due to rehospitalization for previous fractures [22], and the validity of the second hip fractures was acceptable although the NORHip database tended to underestimate the number of second hip fractures (confer [Methods](#) section). Unfortunately, data on fractures sustained before 1994 were not available. However, the probability of misclassifying second hip fractures after a first fracture decreases with time after known first fracture, and to minimize such misclassification subjects registered with a first hip fracture during 1994–1998 were excluded.

#### Conclusion

Despite similar incidence rates of second hip fracture in women and men, the 10-year risk of a second hip fracture was 40% higher in women compared to men, and the difference was explained by a higher mortality in men. Ten-year cumulative incidence of second hip fracture was above 10% in all age-groups, except in men aged 90 years and older. Due to the high risk of another hip fracture there is a large potential in second hip fracture prevention strategies, including anti-osteoporotic drugs.

#### Disclosure statement

All authors state they have no conflict of interest.

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