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# Mortality in British hip fracture patients, 2000–2010: A population-based retrospective cohort study

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ABSTRACT

*Background:* Data on recent trends in mortality after hip fracture are scarce. Aims were therefore to examine secular trends in all-cause and cause-specific mortality post hip fracture and to compare this to the general population from 2000 to 2010.
*Methods:* Population-based cohort study within the United Kingdom Clinical Practice Research Datalink and linked to cause of death data for 57.7% of patients. Patients with a first hip fracture (n = 31,495) were matched to up to four controls by age, sex, index date, and practice. All subjects were followed for death, and lifestyle, disease and medication history adjusted hazard ratios (HRs) were calculated.
*Results:* One-year all-cause mortality after hip fracture declined from 2009 and was 14% lower after, compared with before 2009 (22.3% to 20.5%, adj. HR 0.86, 95% CI: 0.81–0.92). The decline was observed for males (≥75 years) and females (≥85 years). Significant contributors to the decline in mortality post hip fracture were respiratory infections in females as were malignant diseases in males. However, one-year all-cause mortality remained unaltered over the decade when compared to controls with a 3.5-fold and 2.4-fold increased risk in males and females respectively. No significant changes were observed in the relative risks for one-year cause-specific mortality for both genders.
*Conclusions:* One-year mortality after hip fracture has declined over the last decade in the UK. However, the difference in one-year mortality between hip fracture patients and the general population remained unaltered. These observations highlight the need for the continued implementation of evidence-based standards for good hip fracture care.



## Introduction

Hip fractures are a major public health concern in terms of morbidity, healthcare costs and mortality. A large meta-analysis showed that mortality in the year post hip fracture ranges from 20% to 26% amongst elderly females and males respectively. When compared to patients without hip fracture, mortality is 2 -to 4-fold higher in the subsequent year, and is higher for men than for women at any given age. This excess mortality persists even for ten years following the fracture [1]. Although there is little change in age-standardised hip fracture rates in the United Kingdom, the absolute number of hip fractures will continue to rise due to the ageing of the population [2].

Despite the advances in the surgical and medical management of hip fracture data on recent trends in mortality are scarce. Secular trends for mortality after hip fracture have been reported from 1968 through 1998 in the United Kingdom. Between 1968–73 and 1979–83 there was a significant decline in one-year mortality and this stabilised in the period thereafter [3]. A US study that used 20% of all Medicare claims found no reduction in one-year mortality from 1995 to 2005 [4]. Conversely, a study in Texas reported a significant decrease in hip fracture-related

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mortality by 0.8% per year between 1990 and 2007 in males but not in females [5].

However, it remains unknown whether the difference in mortality between hip fracture patients and the general population has changed over the last decade. In addition, cause-specific trends for mortality after hip fracture remain to be determined. Therefore, the aims of this study were [1] to describe all-cause and cause-specific one-year mortality following a hip fracture between the years 2000 and 2010 and [2] to determine, over the last decade, the relative difference in (all-cause and cause-specific) mortality between individuals with a hip fracture and controls.

## Methods

### *Study population*

A cohort study was conducted within the Clinical Practice Research Datalink (CPRD) (formerly known as the General Practitioner Research Database, www.cprd.com). This database contains computerised medical records of 625 primary care practices in the United Kingdom, representing 8% of the total population. Data recorded in the CPRD includes demographic information, laboratory tests, specialist referrals, hospital admissions, prescription details, and lifestyle variables such as body mass index (BMI), smoking status, and alcohol consumption. Previous studies have shown a high validity of hip fracture registration (>90% of fractures were confirmed) [6], and high degrees of accuracy and completeness of these data have been shown for other diagnoses [7–9]. In addition, a high level of sensitivity (98%) and specificity (99%) for mortality recording has been observed [10]. Linkage of CPRD data to the Office for National Statistics (ONS) was possible for 57.7% of the population captured within the CPRD, which are all residing in England and Wales. The ONS provides data for the cause(s) of death and the exact date of death as recorded on death certificates by a registered medical practitioner who has attended the patient during their last period. Death certificates are divided into part I (the primary cause of death) and part II (conditions that may have contributed significantly to the death). The all-cause mortality analysis was performed from January 1st 2000 up to December 31st 2011 with unlinked CPRD data. For analyses concerning cause-specific mortality, CPRD data was linked to death registration data (ONS) from January 1st 2001 up to December 31st 2011.

The study population consisted of all patients aged ≥18 years with a CPRD read code for their first hip fracture between January 1st 2000 and December 31st 2010. The index date was defined as the first record for hip fracture. Patients with a read code for unspecified fractures or unspecified femoral fractures before the index date were excluded, since it was uncertain if the index fracture was actually the first hip fracture of the patient.

### *Selection of controls*

To determine (changes in) relative one-year mortality we matched each hip fracture patient to up to four control patients without a read code for a hip fracture by age, sex, calendar time (index date), and practice using the incidence density sampling technique.

### *Outcomes*

The primary outcome of interest was one-year all-cause mortality. All patients were followed from the index date to either the end of the study period (up to 365 days after the index date), the date of transfer of the patient out of the practice area, or the patient's death as recorded in the CPRD database, whichever came first. The secondary outcome was one-year cause-specific mortality (using all entries recorded on the death certificates) and was assessed in the population eligible for linkage between CPRD and ONS data. Patients were censored at the end of the study period if it occurred before the date of death. Specific causes of death were grouped into the following categories using the International Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10): cardiovascular disease (ICD-10: I0–I5, I7–I9), cerebrovascular disease (ICD-10: I6), respiratory infections (ICD-10: J0–J2), non-respiratory infections (ICD-10: A0–B9, N39.0), malignant neoplasms (ICD-10: C), non-infectious respiratory diseases (ICD-10: J3–J9), injuries (ICD-10: S, T0–T14), dementia (ICD-10: F00–F03, G30), and all other causes of death.

### *Definition of covariates*

General risk factors/possible confounders (according to the presence of CPRD read codes) for mortality that were considered for analyses were age, sex, smoking status (a record of currently smoking, ex-smoking, non-smoking), alcohol use (yes, no), the most recent record of the body mass index (BMI) before the index date (<20, 20–25, >25), a history of chronic diseases (ischemic heart disease, cerebrovascular disease, heart failure, chronic kidney disease, chronic obstructive pulmonary airway disease [COPD], dementia), major infections (sepsis, meningitis), major osteoporotic fracture (radius/ulna, humerus, clinical vertebrae), malignant neoplasms, and secondary osteoporosis. A record for pneumonia was assessed within six months before the index date [4, 11]. Furthermore, a prescription record for anti-diabetic drugs and for psychotropic drugs, glucocorticoids and bisphosphonates in the six months before the index date were considered since these drugs are associated with falls and fractures and may therefore influence mortality risk [12–16]. Besides age, all covariates were handled as categorical variables in the analyses.

### *Statistical analyses*

Hazard ratios [HRs] for one-year all-cause and cause-specific mortality were estimated by Cox proportional hazards regression (SAS 9.2 PHREG procedure). One-year all-cause mortality following hip fracture was compared between calendar years of the total study period (according to the year of first hip fracture [index date]) using the year 2000 as a referent group. Based on these results, cut-off points were defined to compare the one-year all-cause and cause-specific mortality risks between year periods, stratified by sex. The HRs were adjusted for significant determinants for one-year mortality after hip fracture, which were defined by stepwise backward elimination with a significance level of 0.05. Kaplan–Meier plots were used to visualize the age- and gender-specific cumulative incidence rates for one-year all-cause mortality over time, and were stratified by year periods (log-rank test for comparison).

Furthermore, we estimated HRs for the relative differences in one-year mortality between hip fracture patients and control subjects. HRs for relative one-year all-cause and cause-specific mortality were estimated for each year period, and were compared by including an interaction term into the model (calendar year cut-off point * indicator variable for hip fracture). HRs were adjusted for all covariates that changed the beta-coefficient of hip fracture with ≥1% in an age-adjusted analysis.

Since for some of the covariates (BMI, smoking status and alcohol use) missing data were present multiple imputation was used. Data were imputed five times using the automatic multiple imputation method in SPSS version 19.0. All analyses were performed separately for the five imputed datasets and HRs were pooled using the MIANALYZE procedure in SAS 9.2.

In sensitivity analyses changes in one-year all-cause mortality in hip fracture patients and relative to control subjects were estimated after restriction of the study population to those eligible for linkage of CPRD data to the Office for National Statistics, and after restriction to a population without missing data for life-style factors (complete-case analysis).