Age and Ageing 2023; **52:** 1–9
https://doi.org/10.1093/ageing/afad201

RESEARCH PAPER

Imminent fall risk after fracture

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Abstract

Rationale: Adults with a recent fracture have a high imminent risk of a subsequent fracture. We hypothesise that, like subsequent fracture risk, fall risk is also highest immediately after a fracture. This study aims to assess if fall risk is time-dependent in subjects with a recent fracture compared to subjects without a fracture.
Methods: This retrospective matched cohort study used data from the UK Clinical Practice Research Datalink GOLD. All subjects ≥50 years with a fracture between 1993 and 2015 were identified and matched one-to-one to fracture-free controls based on year of birth, sex and practice. The cumulative incidence and relative risk (RR) of a first fall was calculated at various time intervals, with mortality as competing risk. Subsequently, analyses were stratified according to age, sex and type of index fracture.
Results: A total of 624,460 subjects were included; 312,230 subjects with an index fracture, matched to 312,230 fracture-free controls (71% females, mean age 70 ± 12, mean follow-up 6.5 ± 5 years). The RR of falls was highest in the first year after fracture compared to fracture-free controls; males had a 3-fold and females a 2-fold higher risk. This imminent fall risk was present in all age and fracture types and declined over time. A concurrent imminent fracture and mortality risk were confirmed.
Conclusion/Discussion: This study demonstrates an imminent fall risk in the first years after a fracture in all age and fracture types. This underlines the need for early fall risk assessment and prevention strategies in 50+ adults with a recent fracture.

Keywords: imminent fall risk, imminent fracture risk, clinical practice research datalink, risk, accidental falls, older people

Key Points

- This study found an imminent fall risk for both males and females after an index fracture compared to a matched fracture-free control cohort.
- Males and females had a 3-fold and 2-fold higher risk of falls in the first year after index fracture, respectively.
- This imminent fall risk pattern was present in all age groups and was found for all individual fracture types.

Introduction

Fractures and falls comprise an important health concern in our ageing population, causing significant morbidity and mortality and a decrease in quality of life [1]. In the UK the total costs of incident fractures are €5.5 billion yearly [1]. Subjects with a history of fracture have twice the risk to sustain subsequent fractures [2, 3], and this risk is the highest in the first 2 years after initial fracture [2, 4]. This imminent subsequent fracture risk has been reported after fractures at all major fracture sites [5–7].

Recent falls have been associated with the imminent subsequent fracture risk, amongst other factors such as cognitive and physical decline [7–10]. Up to 90% of all fractures in older persons are caused by a fall and fracture patients have a high prevalence of fall risk factors [11–14]. Recent findings of a fracture liaison service (FLS) cohort showed that falls were the main cause of subsequent fractures, and subjects with an incident fall after the initial fracture had an almost 9-fold risk of sustaining a subsequent fracture during 3 years of follow-up [11]. Moreover, a higher fall rate was reported in the first year after fracture, compared to later years. Thus, the imminent subsequent fracture risk could probably, at least partially, be explained by an imminent fall risk after a fracture.

Several studies reported fall incidence after different types of fractures, but comparability between the studies is low due to differences in fall- or fracture intervention strategies, population characteristics and length of follow-up [15–26]. Importantly, most studies measure fall incidence at one time point, which does not allow to detect changes in fall risk over time. A study of Wong et al. reported a high short-term annual fall incidence rate after an initial fracture that declined steadily during the first 5 years after fracture [27]. However, they did not account for mortality as a competing risk, which is important, especially in an older fracture population. This study aims to assess if fall risk is time-dependent in subjects ≥50 years with a recent fracture compared to fracture-free controls.

Methods

Data source

This descriptive, retrospective study cohort was conducted using the Clinical Practice Research Datalink (CPRD) GOLD database. CPRD collects routinely recorded computerised medical data from over 650 general practices in the United Kingdom (UK) [28]. The cohort encompasses data of ∼7% of the UK population and has been shown to be largely representative of the UK population in terms of age, sex and ethnicity [28, 29]. Clinical information of the CRPD is recorded using Read codes; a clinical classification system for registration of diseases and mortality [28, 30]. Registrations in CPRD have been proven to be fairly accurate for mortality [31, 32], and hip and vertebral fractures diagnosis showed a high validity [33]. The CPRD has obtained ethics approval for purely observational research using anonymised data from the National Research Ethics Service Committee (IRAS ID 242149). The research protocol for this study (ID 22_002143) was approved by the Independent Scientific Advisory Committee for the Medicines and Healthcare Products Regulatory Agency Database Research.

Study population

The fracture cohort consisted of all subjects aged 50+, with an incident fracture between 1 January 1990 and 31 December 2015. The first 3 years of follow-up were excluded due to low numbers of included subjects, thus all further analysis were carried out between 1 January 1993 and 31 December 2015. All fracture types were included except for pathological fractures and fractures due to prosthetic failure. All subjects with an incident fracture were matched based on year of birth, sex and practice to a fracture-free control subject using incidence density sampling [34]. The date of the fracture determined the index date for both fracture subjects and their matched controls. Follow-up started after a lead-in period of 30 days, to limit the possibility of including falls or fractures related to the index event twice. Subjects were followed from the index date until occurrence of the outcome of interest, the subjects moving out of the practice, registered death in the database, end of data collection of the practice, or the end of study period (31 December 2020), whichever came first.

Outcome

The primary outcome of interest were 'GP-reported falls' and secondary outcome measures were 'GP-reported fractures' and all-cause mortality. A fall was defined as an event in which the GP recorded a diagnosis of the patient experiencing a 'fall'. Falls and fractures were defined using Read codes, and were checked by individuals with expert knowledge (JB, HW, Appendix 1 and 2) [35]. 'GP-reported fractures' were defined as fractures during follow-up, excluding the index fracture location or a fracture of unspecified location, as differentiation between consultations regarding the follow-up of an index fracture or a new fracture of the same fracture site was not possible [30].

Imminent risk

We defined imminent fall risk in accordance with the definition of imminent fracture risk; a high short-term risk within 12–24 months after the index fracture, that declines over time [2, 4, 36].

Statistical analysis

Population characteristics were described using means and standard deviations (SD) for normally distributed and medians and interquartile ranges (IQR) for non-normally distributed data. To adequately interpret fall data, first, secular trends of falls were explored; subjects in both the fracture and control cohort were followed from their index date until a fall or fracture, censoring or 1 year of follow-up, whichever

Table 1. Population characteristics

	Fracture Cohort		Control cohort	
	Females	Males	Females	Males
Number of subjects	221,932	90,298	221,932	90,298
Mean age ± SD	70 (60–80)	66 (57–77)	70 (60–80)	66 (57–77)
Age in years *n* (%)				
50–54	23,169 (10.44)	15,118 (16.74)	23,169 (10.44)	15,118 (16.74)
55–59	27,564 (12.42)	13,579 (15.04)	27,564 (12.42)	13,579 (15.04)
60–64	27,668 (12.47)	12,427 (13.76)	27,668 (12.47)	12,427 (13.76)
65–69	27,311 (12.31)	10,804 (11.96)	27,311 (12.31)	10,804 (11.96)
70–74	27,025 (12.18)	10,089 (11.17)	27,025 (12.18)	10,089 (11.17)
75–79	28,345 (12.77)	10,013 (11.09)	28,345 (12.77)	10,013 (11.09)
80–84	27,187 (12.25)	9,069 (10.04)	27,187 (12.25)	9,069 (10.04)
85–89	20,893 (9.41)	6,444 (7.14)	20,893 (9.41)	6,444 (7.14)
90–94	10,240 (4.61)	2,434 (2.70)	10,240 (4.61)	2,434 (2.70)
95+	2,530 (1.14)	32 (0.36)	2,530 (1.14)	321 (0.36)
Median years of follow-up (IQR)	5.7 (2.5–9.7)	5.5 (2.2–9.5)	5.9 (2.7–9.7)	6.0 (2.8–10.0)
Reason of end of follow-up				
Death during follow-up *n* (%)	62,661 (28.23)	28,543 (31.61)	55,796 (25.14)	22,726 (25.17)
End of data collection *n* (%)	118,266 (53.29)	45,961 (50.90)	121,455 (54.73)	49,382 (54.69)
End of study period *n* (%)	41,005 (18.48)	15,794 (17.49)	44,681 (20.13)	18,190 (20.14)

came first. To calculate the 1-year fall incidence rates (IR), all first reported falls were divided by the total time at risk, expressed as falls/1,000 person years (PYs). Results were stratified by calendar year. Trends over time in IRs for both groups were described using Poisson regression, and were compared between groups using incidence rate ratios (IRRs). As a sensitivity analysis, all (not only first) falls during the 1-year follow-up were counted. Similarly, 1-year IR and IRR for first fracture and mortality were calculated.

For the assessment of imminent fall risk, the cumulative incidence of first falls (defined as first falls after the index date) was assessed at multiple time intervals using the cumulative incidence competing risk (CICR) method with mortality as competing risk [37, 38]. Relative risks (RR) of falls were calculated between the fracture group and the fracture-free control group by dividing the cumulative incidence of the fracture group by the cumulative incidence of the control group at each time point. For the first 5 years of follow-up, proportions of subjects with a first fall were calculated by dividing all subjects with a first fall at a specific year of follow-up by all subjects with a first fall during follow-up. Lastly, the cumulative incidence and RR between groups was calculated for fractures and mortality.

Outcomes were stratified to index fracture type, sex and/or age categories. Fracture types were grouped according to Center *et al.*: (i) hip fractures, (ii) major fractures; vertebra, multiple rib, proximal humerus, pelvis, femur (non-hip) and proximal tibia and (iii) minor fractures; all remaining, except fingers and toes (which were excluded) or the International Osteoporosis Foundation (IOF) classification: (i) major osteoporotic fractures (MOF); hip, vertebra, proximal humerus and distal radius, (ii) non-major osteoporotic (non-MOF); all remaining [39].

All analyses were carried out using SAS 9.4 (SAS Institute, Cary, NC), graphs were produced in GraphPad Prism 9.5 (GraphPad Software, San Diego, CA, USA).

Results

A total of 624,460 subjects were included between 1993 and 2015; 312,230 subjects were identified with an index fracture (Table 1) and matched to 312,230 fracture-free controls (flowchart for inclusion, Appendix 3). Of those, 71% were female and the median age at inclusion was 70 (60–80) years for females and 66 (57–77) years for males. The fracture and control cohort had a median follow-up of 5.7 (2.4–9.6) for and 6.0 (2.7–9.8) years and in 29.2% and 25.1% death was the reason for end of follow-up, respectively.

Secular trends

From 1993 to 2015 the mean overall IRR of a first fall was 1.8 (95% CI 1.7–1.81) for females with a fracture and 2.4 (95% CI 2.2–2.5) for males with a fracture compared to their fracture-free controls (Appendix 4). The IRR of all reported falls was the same compared to the IRR of first falls. Appendix 5 shows IRs and IRRs of first falls over the inclusion period for the fracture cohort compared to the controls. The trend in fall IRs over time in the fracture cohort was slightly higher than in the control cohort (RR females: 1.01 (1.00–1.01), *P*-value 0.006, RR males: 1.02 (1.00–1.03), *P*-value 0.006).

One-year IRR of first falls, fractures and mortality

In Figure 1A–C the 1-year IRR of first falls, first fractures and mortality is displayed for all index fracture groups (Center

and IOF classifications) and individual fracture types compared to their controls. The 1-year IR for a first fall was higher for all index fracture classification groups and for all individual fracture types compared to their controls (Figure 1A). For all index fracture groups the IRR was higher for males; ranging from 2.3 to 2.6, compared to females; IRR ranging from 1.7 to 1.9. Similarly, the 1-year IR for a subsequent fracture was higher in all fracture classification groups and for all individual fracture types for both males and females (panel B). Panel C shows the 1-year mortality rate after fracture which was higher for all index fracture classification groups, except for females with a minor fracture. The IRR of mortality differed between individual fracture types.

Imminent fall risk

Cumulative incidences of first falls were time-dependent, were higher for females compared to males and were highest in the first years after index fracture (Appendix 6A–C). For both the fracture and control cohort the incidence of first falls was highest in the first years after index date. Of females in the fracture cohort, 41.3% had a first fall during follow-up versus 33.7% in the control cohort. Of the 41.3% fallers, 12.2% fell in year one (7.2% in month 2–6 and 4.9% in month 6–12) and 8.2%, 7.1%, 6.0% and 5.5% in year 2, 3, 4 and 5, respectively. For the 33.7% fallers in the female control cohort fall incidence was 8.9%, 7.5%, 6.4%, 5.9% and 5.4% in year 1, 2, 3, 4 and 5, respectively. Of males in the fracture cohort, 28.3% had a first fall during follow-up versus 23.8% in the control cohort. Of the 28.3% fallers, most males fell in year one 13.8% (8.3% in month 2–6 and 5.4% in month 6–12), and 8.4%, 6.8%, 5.8% and 5.0% in year 2, 3, 4 and 5, respectively. For the 23.8% fallers in the male control cohort, this was 7.4%, 5.7%, 5.6%, 5.0% and 5.0% in year 1, 2, 3, 4 and 5, respectively.

The RR of first falls for the fracture cohort compared to their controls is displayed in Figure 2. In both males and females, the RR of falls was highest in the first years after fracture and declined over time. In females, the RR of first falls after fracture was 1.7 in the year 1 (2.2 in months 1–3, 1.9 in months 3–6 and 1.7 in months 6–12), and stabilised afterwards between year 2 (RR: 1.5) and 5 (RR 1.4). In males, the RR of first falls after fracture was 2.2 in the first year (3.1 in month 1–3, 2.6 in month 3–6) and 2.0, 1.8, 1.7 and 1.6 in year 2, 3, 4 and 5. Similar patterns of high imminent fall risk were present in all index fracture classification groups (Appendix 7A–E), and in all age groups (Appendix 8A and B).

Imminent fracture and mortality risk

The RR of subsequent fractures was also highest in the first few years after index fracture compared to controls and declined over time (Figure 2B). This imminent fracture risk was present for both females and males, but higher in males compared to females. A similar pattern was shown for the RR of mortality (Figure 2C).

Discussion

This large population-based cohort study found an imminent fall risk for males and females after an index fracture compared to a matched control cohort. Males and females had a 3-fold and 2-fold higher risk of falls in the first year after index fracture, and a 2-fold and 1.5-fold risk in the second year after index fracture, respectively. This risk gradually declined during the years thereafter, but remained higher throughout the follow-up period. This imminent fall risk pattern was similar to the pattern of the concurrent imminent fracture and mortality risk and present in all age groups and for all individual fracture types and fracture type classifications groups (Center, IOF).

Several studies previously established the presence of an imminent subsequent fracture risk [2, 4, 7, 40]. However, imminent fall risk is less frequently reported and has not yet been described in a large nationwide population study before. The finding of an imminent fall risk after an index fracture is in line with recent smaller cohort studies [11, 19]. Vranken *et al.* assessed falls and fracture incidences prospectively during 3 years of follow-up in a population of 488 FLS patients (mean age 65, 71% females) [11]. Of females and males respectively, 38% and 41% fell in the first year, of which 25% and 29% occurred <6 months and 51% and 49% had experienced a fall at the end of the second year. Of all fall-related subsequent fractures, the majority occurred at the first fall [11]. Additionally, Wong *et al.* reported the highest fall incidence in the first years after distal radius, proximal humerus or hip fracture in a 50+ Hong Kong population [27]. Lastly, a randomised controlled trial studying a fall-intervention programme after femur fracture (mean age 82, 76% females), reported the highest fall incidence in the first 4 months after fracture [19]. Although the fall incidences of our study and aforementioned studies are subject to differences in fall registration and characteristics of the population, the pattern of an imminent fall risk is clear in all studies, showing the highest risk of falls in the first year after fracture and a declining risk over time. As the majority of all fractures and subsequent fractures are caused by a fall, it is likely that the imminent risk of subsequent fractures can be explained to a great extent by an imminent fall risk.

Our study shows an imminent fall risk for all ages and different index fracture groups and this risk was higher for males compared to females, but females had a higher absolute risk. The yearly fall incidence of both the fracture and control cohort declined after the first years. This is inherent to the outcome 'first falls' and the censoring of the patients experiencing this outcome after their first fall during follow-up. Consequently, in the following years a 'cohort' remains that is less prone to falling. In our study the RR of falls and fractures remained >1 during 24 years of follow-up. This is in line with studies assessing imminent fracture risk with long term follow-up [2, 40].

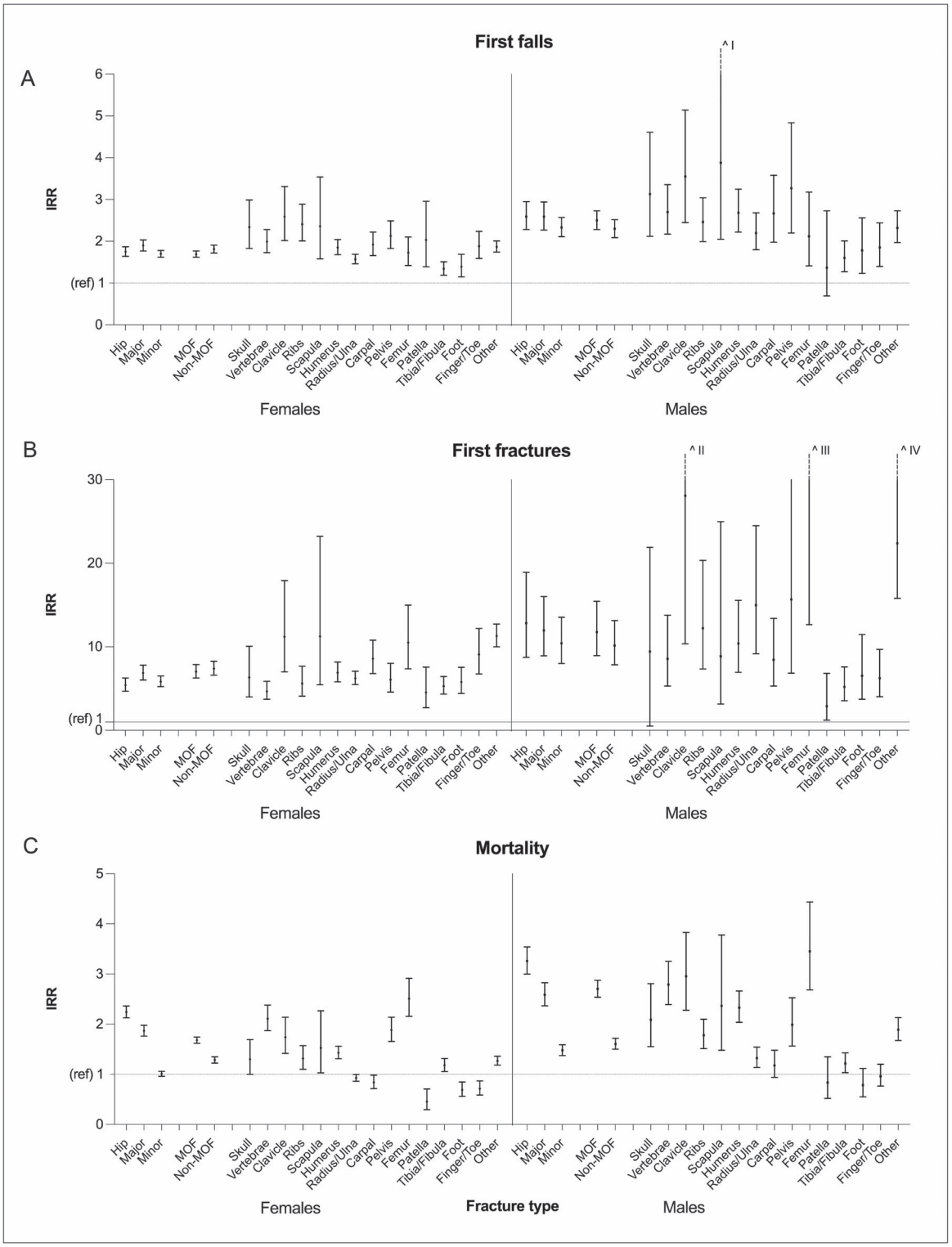

Figure 1. One-year incidence rate ratios of first falls (A), first fractures (B) and mortality (C) of subjects with fracture compared to fracture-free controls. IRR = incidence rate ratio; ref = reference point at IRR = 1. Figure 1 shows the IRR of the first year after fracture for first falls (A), first fractures (B) and mortality (C), stratified to fracture classification groups and individual fracture types. Major = vertebral, multiple rib, pelvis, distal femur and proximal humerus fractures (Center classification), Minor = all fractures not including hip or major fractures (Center classification), MOF = Hip, vertebral, distal radius and proximal humerus fractures (IOF classification), non-MOF = all fractures that are not included in MOF group (IOF classification). Results are presented as mean IRR ± 95% confidence interval (CI). ^ I: upper limit 95% CI = 7.34, ^II: upper limit 95% CI = 76.16, ^III: mean IRR = 51.36 and upper limit 95% CI = 208.61, ^IV: upper limit 95% CI = 15.79.

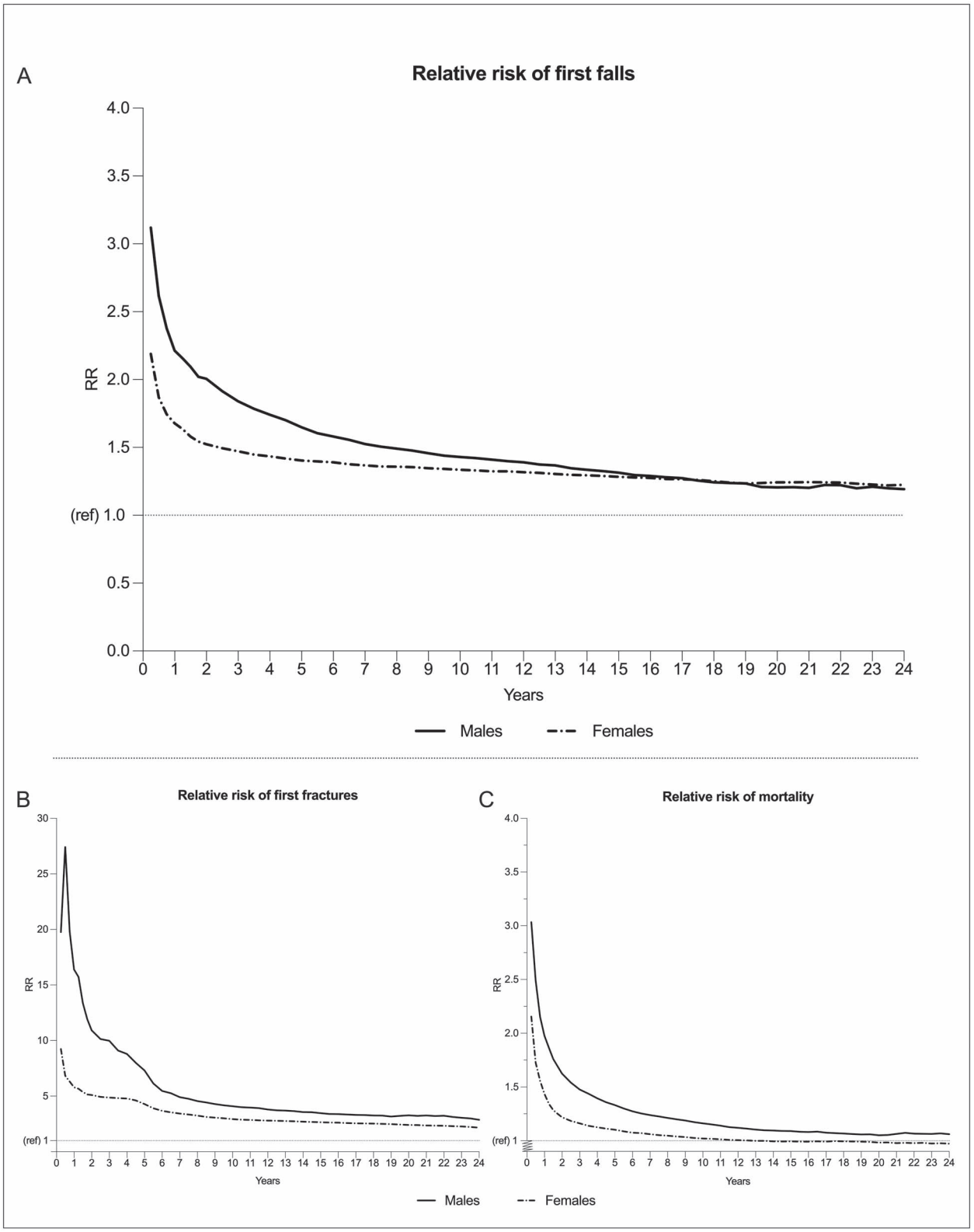

Figure 2. RR of first falls (A), first fractures (B) and mortality (C) of the fracture cohort compared to the control cohort. RR = relative risk, ref = reference point at RR = 1. Figure 2 shows the RR of first falls (A), first fractures (B) and mortality (C) of the fracture population compared to the control population, stratified by sex. The RR was calculated by dividing the cumulative incidence of first falls (A), first fractures (B) and mortality (C) of the fracture cohort by the cumulative incidence of first falls (A), first fractures (B) and mortality (C) of the control cohort, respectively.

Our results underline the need for early fall risk assessment and multiple component fall prevention interventions in fracture patients. These interventions, including exercise and medication review have proven to be effective [41, 42]. Fall risk assessment is only recently included in recommendations for FLS and post-fracture care and only a small number of fracture patients receive a fall assessment [1, 43, 44]. As our study was descriptive, assessment of clinical characteristics was beyond our scope. However, it is likely that the fracture population has different clinical characteristics compared to their controls. Fracture patients often have a high proportion of fall risk factors, such as low physical performance, a high proportion with frailty and a history of falls [11, 14, 45–47]. Possible determinants of imminent fall risk are age, sex, medication use, history of falls, ADL difficulties, physical performance and specific comorbidities [9, 48, 49]. Future studies should focus on the identification of determinants of imminent fall risk. For now, emphasis should lay on immediate identification of those with high fall risk, using existing fall guidelines, to prevent future falls and fall-related fractures, as the time-window for prevention is small [11, 50].

Strengths and limitations

This study has several strengths; the results are based on a large nationwide cohort of over 600,000 subjects and the risk of falls after fracture was assessed time-dependently, whilst accounting for mortality as a competing risk. Competing risks analysis is essential to prevent over-reporting of falls, especially in studies with older populations and high mortality rates, both inherent to fracture populations [37]. Moreover, this study combined fall data with cumulative fracture and mortality incidence data. This study also has limitations; due to the retrospective design, causality could not be assessed. Thus, all findings should be further assessed in prospective studies. Second, the 1-month lead-in period could cause an underestimation of imminent fall and fracture risk as the highest fall incidence might be in the first months after fracture [19] and institutionalisation after the initial fracture could increase fracture rates [51]. Third, fall incidence was subject to large underreporting and lower compared to the yearly incidence reported in older general populations (30%) or fracture populations (31–55%) [11]. This was due to several causes; first, there was no systematic regular inquiry about fall incidence during follow-up by the GP or by use of fall diaries, leaving fall registration subject to recall bias [52]. Moreover, underreporting could occur if a fall diagnosis was not recorded electronically, recorded in free text or solely the medical consequence of the fall (e.g. fracture, tissue injury), and not the fall itself was recorded. It is likely that patients mostly report injurious falls, not all falls to their GP [53] and in case of an ER visit, some falls will only be reported at the hospital. Lastly, a fracture diagnosis might prompt the GP to do additional evaluations, such as a fall assessment, possibly increasing falls registration in fracture patients.

Conclusion

This study demonstrates an imminent fall risk after fracture, in a large population-based study, accounting for the competing risk of mortality. This imminent fall risk was demonstrated in all age groups and all index fracture types. Corresponding time-dependent risk patterns were found for subsequent fractures and mortality after fracture. This study underlines the need for fall risk assessment and fall-intervention strategies early after a fracture.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Declaration of Conflicts of Interest: JB reports fee for lectures and the position in the advisory board from UCB and Amgen, outside the submitted work. HW reports a speakers fee for lectures from UCB and Amgen, outside the submitted work.

Declaration of Sources of Funding: None.

Data Availability: Data that was obtained from the Clinical Practice Research Datalink (CPRD) GOLD is available for on-site audit purposes to qualified auditors, subject to further discussion and contractual agreements with the licensor of CPRD GOLD data.

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Received 28 April 2023; editorial decision 1 September 2023