SHORT COMMUNICATION



Educational gradient in hip fracture incidence in Norway. The Norwegian Epidemiologic Osteoporosis Studies (NOREPOS)

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Abstract

Summary Examining fracture dynamics by socioeconomic status may inform healthcare and prevention. We found a higher risk of hip fracture in men and women with lower educational level in Norway. However, by age 90 + years, the cumulative incidence was higher in those with higher education, due to their higher life expectancy.

Purpose Socioeconomic gradients are seen for several health outcomes in high-income countries. We aimed to examine possible educational gradients in risk of hip fracture in Norway and to describe the cumulative incidence of hip fracture by educational level.

Methods In a population-wide cohort of Norwegians aged \geq 50 years, information on attained education from Statistics Norway was linked to hospital-treated hip fractures and deaths during 2002–2019. We estimated relative fracture risk by educational level (primary, secondary or tertiary) in Cox proportional hazards regression. We also examined the cumulative incidence over attained age by gender and educational level in competing risk regression.

Results The population included N = 1,389,858 individuals with 135,938 incident hip fractures. Compared with men who had attained tertiary education, hazard ratios (95% confidence intervals) for hip fracture were 1.44 (1.40, 1.49) in men with primary education only and 1.26 (1.22, 1.29) in men with secondary education. In women, the corresponding estimates were 1.28 (1.25, 1.31) and 1.16 (1.13, 1.19). In the age range 50 to 90 years, the highest cumulative incidence of hip fracture was seen in those with primary education. The gradient gradually diminished with advancing age and was reversed in the oldest (>90 years) in both genders.

Conclusions There was a clear educational gradient in hip fracture incidence in both men and women in Norway, with a higher risk in people with lower education. Despite this, the cumulative incidence of hip fracture in old age was highest among people with higher education, due to their higher life expectancy.

Keywords Education · Hip fracture · Norway · Registry-based epidemiology · Socio-economic status

Introduction

A gradient in excess mortality and morbidity by socioeconomic status (SES) is well-established [1]. The socioeconomic gradient in health-related measures has been reported in many settings worldwide, also in egalitarian high-income countries with well-functioning welfare systems such as Norway [2]. A study from Norway showed a difference in life expectancy between the richest and poorest one percent of 8.4 years for women and 13.8 years for men [3]. Social inequalities in health lead to serious loss of health for individuals and society, but the losses also represent preventable measures, which can be targeted in preventive strategies [4].

Scandinavia has among the world's highest incidence rates of hip fractures, and despite declining age-specific rates, the societal burden of hip fractures is projected to increase in the upcoming decades due to the ageing population [5–7]. Observational cohort studies have shown a link between SES and fracture risk. A meta-analysis found a pooled 23% increased risk of fragility fractures at low compared with high educational level [8], with large between-studies heterogeneity. There is a scarcity of longterm population-wide studies with hip fractures as outcome.

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A multicentre meta-analysis that combined data from six cohorts in Europe showed a pooled hazard ratio (HR) of 0.75 (95% confidence interval (CI) 0.65, 0.85) for hip fracture in women with medium or high education compared with low education, but no association in men [9]. The authors did not report fracture incidence taking into account the competing risk of death.

Given the well-described SES differences in life expectancy [3, 10] and the high age at which hip fractures commonly occur, life expectancy may affect the variation in fracture incidence by SES, particularly in older age groups. It has therefore been recommended to report fracture burden as cumulative incidence, thus considering the competing risk of death [11].

Using attained educational level as a measure of SES, we aimed to investigate if there are socioeconomic gradients in risk of hip fracture in Norwegian men and women. In addition, we aimed to describe the cumulative incidence of hip fractures in Norway by educational level, age, and gender.

Methods

Study population

A nationwide population sample was available from the Population and Housing Census conducted by Statistics Norway in November 2001, where household questionnaires were distributed to the total population and filled in individually. We included all inhabitants aged 50 years and older with information about attained educational level in 2001 (available for 98.9%), who were alive and resided in Norway on 1 January 2002 and had not had a hip fracture during the last eight years (look-back to 1 January 1994, see below), comprising N = 1,389,858 individuals.

Hip fractures

In Norway, all persons who suffer a hip fracture are admitted to hospital for surgical treatment. Information on hip fractures treated in hospitals from 1994 through 2019 was available in the Norwegian Epidemiologic Osteoporosis Studies (NOREPOS) hip fracture database (NORHip) [7]. This database includes inpatient data obtained directly from the hospitals' patient administrative systems (1994–2007) and from the mandatory Norwegian Patient Registry (2008–2019). We have identified up to two hip fractures in each individual during the 26-year period by applying a comprehensive algorithm that considered the combination of hip fracture diagnosis codes (International Classification of Diseases, 9th edition (ICD-9): 820; 10th edition (ICD-10): S72.0, S72.1 and S72.2), surgical procedure codes, other accompanying diagnosis codes and time between hospitalizations. The database has been thoroughly validated (www.norep os.no/documentation). The information from NORHip was linked to the other data sources using the unique 11-digit personal identification number assigned to every resident in Norway. For our purpose, only first-time hip fractures occurring between 1 January 2002 and 31 December 2019 were included.

Educational level

Administrative registry data on attained educational level in 2001 was obtained from Statistics Norway, grouped according to the Norwegian Standard Classification of education [12]. Education levels were combined into three categories corresponding to primary education (compulsory education), secondary education (upper secondary school including post-secondary schooling) and tertiary education (college/university education, including undergraduate, graduate, and postgraduate education).

Observation time

Residency status and dates of emigration and death from the National Population Register were provided by Statistics Norway. All individuals were followed from 1 January 2002 to their first incident hip fracture, emigration, death, or 31 December 2019, whichever occurred first, yielding a maximum observation time of 18 years.

Statistical analyses

Data preparation and statistical analyses were performed in R for Windows, version 4.3.0. To assess possible educational gradients in risk of hip fracture, we performed Cox proportional hazards regression with age in 2002 as entry time and attained age at hip fracture or censoring as exit time using the coxph function in the survival package [13], hence estimating HR with 95% CI for hip fracture according to attained education with tertiary education as reference level. Statistical interaction between gender and educational level on risk of hip fracture was tested by including interaction terms in the overall (genders combined) analysis. The proportional hazards assumption was evaluated by investigating plots of Schoenfeld residuals of educational level over attained age, using the cox.zph function in the survival package [13]. Considering that the differential life expectancy by education [10] could be expected to influence the proportion of hip fractures across educational levels in old age, we obtained the cumulative incidence of hip fracture by gender, age, and educational level from a multistate survival analysis with hip fractures and all-cause deaths as competing outcomes, using the survfit function with the mstate option in the survival package [13]. For this

analysis, the outcome was assigned a value of 0 for censored individuals (followed to date of emigration or end of follow-up), 1 for individuals who suffered a hip fracture in the observation period, and 2 for individuals who died without experiencing a hip fracture. To obtain the corresponding Kaplan–Meier cumulative hazard function presented in Online Resource 1, we used the survfit function with hip fracture (0/1) as outcome, censoring individuals on their date of death, date of emigration or end of follow-up.

Results

Risk of hip fracture by educational level

The study population comprised 652,012 men and 737,846 women (Table 1). While 36% had primary education as their highest attained educational level, 47% had secondary education and 17% had tertiary education. Compared with women, a higher proportion of men had tertiary education (20% vs. 14%). With higher education being more prevalent in younger age cohorts, there was an inverse gradient with decreasing age through increasing educational levels (Table 1). During a mean observation time of 13.4 years, 135,938 incident first hip fractures occurred. Plots of Schoenfeld residuals over attained age did not indicate violation of the proportional hazards assumption for educational attainment. The hazard of hip fracture showed an

Table 1 Person-years of observation time and number of hip fractures across gender and attained educational level, and hazard ratios (HR) with 95% confidence intervals (95% CI) for hip fracture in persons with primary and secondary education compared with those with tertiary education.¹ Men and women 50 years and older in the Norwegian Population and Housing Census 2001 (n = 1 389 858 individuals with135 938 hip fractures during follow-up until 31.12.2019)

inverse gradient through levels of education. With age as timescale and adjusting for gender and year of birth, people with only primary education had a 34% higher risk of hip fracture (95% CI 31% to 36%) compared with those who had tertiary education, and people with secondary education had a 20% higher risk of hip fracture (95% CI 18% to 22%) compared with those who had tertiary education (Table 1). The inverse relationship between educational level and hip fracture was observed in both men and women, but it was more pronounced in men (p for interaction < 0.001), with a 44% higher risk in men who had attained only primary compared with tertiary education, and a 28% higher risk in women who had attained only primary compared with tertiary education (Table 1). The cumulative hazard function showed a steep increase in hip fracture risk by age in all educational level groups (Supplementary Figure SI1, Online Resource 1).

Cumulative incidence of hip fracture by educational attainment

In survival analyses treating hip fractures and all-cause deaths as competing outcomes, there were in men 41,487 incident hip fractures and 270,688 competing deaths (i.e., deaths in those without hip fracture) during 2002–2019, while in women there were 94,451 incident hip fractures and 260,784 competing deaths. The cumulative incidence of hip fracture increased steeply by age in all educational groups (Fig. 1). In the age range 50–90 years, the highest overall

	Ν	Age at entry Median (IQR)	Person-years	n (%) hip fractures	Model 1 HR (95% CI) ²	Model 2 HR (95% CI) ³
All	1 389 858	63 (55, 74)	18 682 401	135 938 (9.8)		
Primary	495 686	69 (60, 78)	5 776 730	64 340 (13.0)	1.37 (1.35, 1.40)	1.34 (1.31, 1.36)
Secondary	657 456	61 (55,71)	9 274 751	57 380 (8.7)	1.21 (1.19, 1.24)	1.20 (1.18, 1.22)
Tertiary	236 716	58 (53, 66)	3 630 921	14 218 (6.0)	1.00 (ref)	1.00 (ref)
Men	652 012	61 (55, 72)	8 767 166	41 487 (6.4)		
Primary	199 691	67 (58, 76)	2 320 755	16 355 (8.2)	1.47 (1.42, 1.51)	1.44 (1.40, 1.49)
Secondary	318 956	60 (54, 70)	4 427 712	19 083 (6.0)	1.26 (1.23, 1.30)	1.26 (1.22, 1.29)
Tertiary	133 365	58 (54, 66)	2 018 699	6 049 (4.5)	1.00 (ref)	1.00 (ref)
Women	737 846	64 (56, 75)	9 915 235	94 451 (12.8)		
Primary	295 995	71 (61, 79)	3 455 974	47 985 (16.2)	1.31 (1.28, 1.35)	1.28 (1.25, 1.31)
Secondary	338 500	61 (55, 72)	4 847 039	38 297 (11.3)	1.17 (1.15, 1.20)	1.16 (1.13, 1.19)
Tertiary	103 351	58 (53, 66)	1 612 221	8 169 (7.9)	1.00 (ref)	1.00 (ref)

¹ Cox proportional hazards regression with tertiary education entered as reference level. Attained educational level in 2001 obtained from Statistics Norway and grouped according to the Norwegian Standard Classification of Education. Primary education: Up to 9th class level (compulsory levels); Secondary education: Upper secondary school including post-secondary schooling; Tertiary education: College/university education, including undergraduate, graduate, and postgraduate education. Values in bold font indicate totals across all educational levels

² Age as timescale, gender included as covariate in the analysis in men and women combined

³ As model 1 + year of birth (continuous) included as covariate

Fig. 1 Cumulative incidence (%) with 95% confidence intervals of hip fracture by gender, attained age and educational level in the population of Norway aged \geq 50 years, accounting for competing deaths. Based on 1,389,858 individuals with 135,938 incident hip fractures and 531,472 competing deaths during up to 18 vears of observation (1 Jan 2002 through 31 Dec 2019). Men: 41,487 incident hip fractures and 270,688 competing deaths, mean 13.4 years follow-up. Women: 94,451 incident hip fractures and 260,784 competing deaths, mean 13.4 years follow-up. Obtained by fitting a multistate survival model and applying the 'survfit' function in the 'survival' package in R [13].



cumulative incidence was observed in the primary education group in both genders. However, this gradient gradually diminished with advancing age and finally reversed after the age of 90 in both genders. Women with tertiary education had a 25.6% probability of suffering a hip fracture by the age of 95 years, compared with 24.0% for women with primary education. For men, the corresponding probabilities were 13.4% with tertiary education and 12.2% with primary education (Fig. 1).

Discussion

In this population-wide study including 652,012 men and 737,846 women followed for up to 18 years we found a clear educational gradient in the incidence of hip fracture, with a higher risk among those with primary education only. Our findings emphasize the need to invest effort in reaching lower socio-economic groups for fracture prevention. However, with advancing age this educational gradient was attenuated and ultimately reversed in the oldest old in both genders.

Norway and the other Scandinavian countries experience the highest rates of hip fractures globally. Despite declining age-specific rates over time, the societal burden of hip fractures is projected to increase in the upcoming decades due to the aging population [5–7]. Fractures are preventable but given limited resources, there is a need for knowledge to help identify high-risk groups.

A socioeconomic gradient is commonly seen for life expectancy and several chronic diseases, also in egalitarian high-income countries with well-functioning welfare schemes [4]. Socioeconomic differences in health outcomes may be mediated through several mechanisms and may partly be determined by variation in health seeking behaviour and partly by variation in lifestyle-related risk factors. Several of the well-studied risk factors for chronic diseases, including physical inactivity, smoking, and excess alcohol consumption, are also associated with a higher risk of hip fracture, while, in contrast, a higher body weight is protective [14, 15]. We believe that parts of the observed socio-economic gradient in fracture risk in our data may be mediated by lifestyle factors such as physical inactivity and smoking. However, since alcohol use is more frequent at higher educational level, and the higher average body mass index in lower socio-economic groups is protective against hip fracture, these factors may serve to counter-mediate the observed educational gradient. Beyond the individual lifestyle factors, unequal access to resources, healthcare, and social support, genetic factors, and unequal exposure to environmental risk factors and psychological stressors are also considered important contributors to the socioeconomic gradient in health [16]. Actions to narrow the socio-economic gap need to be implemented on many levels through community planning and structural interventions.

Individual SES can be operationalized as measures such as income, occupation, education, or social class, each of which may convey different dimensions of SES. A study from Sweden found that income performed best for SES adjustment in old age [17], but the authors argued that when examining effects of SES on health outcomes, the choice of indicator should be theoretically guided, i.e., it should reflect the assumed mechanisms that one aims to capture. Valentin et al. noted that "educational level is important for occupation and income, is a resource that reflects human capital and non-material resources, and is a SES variable relatively stable through adulthood, unaffected by future health conditions" [8]. Further, educational level is tied to modifiable lifestyle and behavioral factors [18].

There has been a secular decrease in hip fracture incidence, and the role of SES may have changed over time. Older age cohorts have lower attained education on a group level than younger cohorts. Particularly in women, educational level may be a less sensitive marker of SES in older age cohorts. In addition, lifestyle and health behavior patterns across SES may have shifted over time. E.g., the socioeconomic differences in smoking prevalence have widened, as smoking used to be widespread in high-SES groups, but smoking cessation was successful at an earlier stage in the high-SES groups. We may speculate that cohort effects contribute to the observed diminished educational gradient in old age. Adjustment for birth cohort explained a minor fraction of the relative educational gradient in hip fracture, leading to a slight attenuation of the HR for primary vs. tertiary education.

Low SES has been linked to increased fracture risk in several countries. A meta-analysis established a pooled 23% increased risk of fragility fractures at low compared with high educational levels, with large heterogeneity between studies [8]. Concerning hip fractures, a multicentre metaanalysis combining data from six cohorts in Europe showed a pooled HR of 0.84 (95% CI: 0.72, 0.95) for hip fracture in people with medium or high education compared with those with low education [9]. In contrast to our results, the association was statistically significant in women (HR 0.75, 95% CI: 0.65, 0.85) but not in men (HR 0.97, 95% CI: 0.82, 1.13). In line with our results, a registry-based study from Sweden found a higher risk of hip fracture in individuals who had attained compulsory education only, compared with those with higher education: Age-standardized incidence of first hip fracture was 4.3 and 6.2 per 1,000 person-years in men and women with basic education compared with 3.7 and 5.6 per 1,000 person-years in men and women with higher education [19]. However, to our knowledge, no previous studies assessing the risk of hip fracture by educational level have considered the competing risk of lower life expectancy in those with lower education.

Strengths and limitations

We had access to a population-wide cohort of approximately 1.4 million people with more than 135,000 hip fractures during 18 years of observation time. Due to universal public healthcare coverage and the personal identification number of all residents, population registries and mandatory national health registries could be individually linked, and our study

was not affected by selection bias. The information on educational level and hip fractures was based on objective data collected in the same way for all subjects. Valid information on attained educational level for all individuals is available through national registries, and educational level has also been shown to be strongly associated with life expectancy even among the oldest old (\geq 90 years) [10]. Only 1.1% of the population had missing information on attained educational level. The large sample size yielded high precision in the estimates. An ideal scenario would involve tracking all individuals within the population across their lifespan. The limited study period, with individuals entering and exiting the study population at different ages depending on their birthyear, prevents disentanglement of the effects of age, period, and birth cohort. Furthermore, our data does not include individual information on clinical risk factors and behaviours to help shed light on possible mediating pathways for the educational effects. Future studies should be carried out in broad unselected populations and cover both individual-level and community-level determinants, combining the influence of genetics, living conditions, psychosocial aspects and social support, and individual lifestyle behavioural factors.

Conclusion

There was a clear educational gradient in the risk of hip fracture in men and women in Norway, with a 34 percent higher risk in people with primary education compared to those who had completed college or university education. This educational gradient was diminished in older age and reversed in the oldest, with the highest cumulative incidence in those with tertiary education at ages above 90 years. While it is appropriate to target fracture prevention efforts to high-risk groups with low SES given their increased early risk, it should be recognized that the lifetime risk of suffering a hip fracture is higher in those with high education, due to their longer life expectancy.

Abbreviations ICD-9: International Classification of Diseases, 9th edition; ICD-10: International Classification of Diseases, 10th edition; NOREPOS: The Norwegian Epidemiologic Osteoporosis Studies; NORHip: The Norwegian Epidemiologic Osteoporosis Studies (NOREPOS) hip fracture database; SES: Socio-economic status

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Data Availability The data that support the findings of this study are available upon application to the respective data owners (Norwegian

Institute of Public Health, Norwegian Directorate of Health, and Statistics Norway) but restrictions apply to the availability of these data, which were used under approval for the purpose of the current research project, and so are not publicly available.

Declarations

Ethics approval The study and the data linkages have been approved by the Regional Committee for Medical and Health Research Ethics (REC South East A, ref 15538), the Norwegian Institute of Public Health, the Norwegian Directorate of Health (Norwegian Patient Registry), Statistics Norway and the Norwegian Data Protection Authority. The data have been handled in accordance with the General Data Protection Regulation, and a Data Protection Impact Assessment has been conducted in consultation with the Data Protection Officer in the Norwegian Institute of Public Health.

Disclaimer Data from the Norwegian Patient Registry have been used in this publication. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the Norwegian Patient Registry is intended nor should be inferred.

Consent for publication Not applicable.

Conflict of interest Kristin Holvik, Cecilie Dahl, Sven Ove Samuelsen, Anne-Johanne Søgaard, Siri Marie Solbakken, Grethe S Tell, Mari Hoff, Berit Schei, Helena Kames Kjeldgaard, Ellen M Apalset, Bente Morseth, Guri Grimnes, Haakon E Meyer and Tone Kristin Omsland declare that they have no conflict of interest.

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