

Temporal trends in hip fracture incidence, mortality, and morbidity in Denmark from 1999 to 2012

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Submitted 2017-11-01. Accepted 2017-12-09

Background and purpose — While development in hip fracture incidence and mortality is well examined, none has yet looked at the temporal trends regarding prevalence of co-morbidities. Therefore we investigated changes in incidence of first hip fracture, co-morbidity prevalence, 30 day- and 1-year mortality in hip fracture patients in the Danish population during the period 1999 to 2012.

Patients and methods — Patients > 18 years admitted with a fractured hip in Denmark between 1996 and 2012 were identified with data for the period 1999–2012 being analyzed regarding prevalence of co-morbidities, incidence, and mortality.

Results — 122,923 patients were identified. Incidence in the whole population declined but sex-specific analysis showed no changes for men. For the whole study population, 30-day and 1-year mortality remained unchanged. Age at time of first hip fracture also remained unchanged. Of the included co-morbidities a decrease in prevalence of malignancy and dementia in women was found while there was an increase in the prevalence of all remaining co-morbidities, except hemi- or paraplegia for both sexes, rheumatic diseases for women, and for men diabetes with complications, myocardial infarction, AIDS/HIV, and malignancy.

Interpretation — While hip fracture incidence declined for women it was unchanged for men; likewise, 30-day and 1-year mortality rates together with age at first fracture remained unchanged. When these results are compared with the relatively large increase in the prevalence of co-morbidities, it does not seem likely that the increased disease burden is affecting either the incidence or the mortality.

Patients sustaining a hip fracture are known to have increased mortality and morbidity compared with the general population and as the population gets older an increased incidence of hip fractures could be expected (Kanis 1993). Studies on the development in hip fracture incidence have found diverging results with some reporting decreasing incidence (Kannus et al. 2006, Abrahamsen and Vestergaard 2010, Lippuner et al. 2011, Nilson et al. 2013, Jean et al. 2013, Korhonen et al. 2013) and others increasing incidence (Mann et al. 2008). Also, hip fracture patients have an excess mortality (Haentjens et al. 2010) with risk factors including co-morbidity (Barone et al. 2009). While the development in hip fracture incidence and mortality has already been examined, few studies have looked at the development in co-morbidity and it is unclear whether hip fracture incidence and mortality change with the prevalence of co-morbidities. The purpose of this descriptive study was to investigate the changes in incidence of first hip fracture, co-morbidity, 30-day and 1-year mortality in hip fracture patients in the Danish population during the period 1999 to 2012.

Patients and methods

Study population

Data were collected from the Danish National Patient Registry (DNPR) on all patients above 18 years, sustaining a hip fracture (ICD-10 codes: DS720, DS721 or DS722) during the period January 1, 1996 to December 31, 2012. For patients sustaining more than 1 hip fracture during the period, only the first was included and used as index fracture for survival analysis. 154,062 patients sustained a hip fractures during

this period. To make sure that only the first hip fracture was included and thus reducing the risk of finding a false decrease in hip fracture incidence and co-morbidities, data for the first 3 years were excluded as a washout period. As such, only data from the period 1999 to 2012 were analyzed resulting in the inclusion in the study of 122,923 patients with a hip fracture. Data collected on the individual patient included age, sex, fracture type, co-morbidity, and time of death. The co-morbidities found in the Charlson Co-morbidity Index (CCI) were included in the study with data on co-morbidities registered prior to the fracture being retrieved from the DNPR and coded as described by Quan et al. (2005). The following co-morbidities were thus included: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, moderate or severe liver disease, mild liver disease, diabetes without chronic complication, diabetes with chronic complication, hemiplegia or paraplegia, metastatic solid tumor, any malignancy, AIDS/HIV, and renal disease.

National patient registry data

In Denmark, all citizens have a unique, non-reusable, 10-digit civil registration number (CRN) assigned by the Civil Registration System (CRS). The CRS contains demographic information on all citizens residing legally in Denmark including vital status and emigration. The CRN is used in all public records making it possible to link different information from national registries for the unique individual. This provides excellent traceability and allows almost complete follow-up (Schmidt et al. 2014).

Through the use of the CRN, all contacts and admissions to Danish hospitals are registered in the DNPR which contains information on all non-psychiatric hospital admissions dating back to 1977 and has since 1995 also included data on outpatient visits and psychiatric admissions (Lynge et al. 2011). For this study, data on discharge diagnosis or secondary diagnostic codes were used in the form of International Disease Classification 10 (ICD-10) codes. When using data from registries 2 important measures of quality are validity and completeness, which vary with the different diagnosis codes (Schmidt et al. 2015). To our knowledge no completeness study has been performed on hip fractures reported to the DNPR, but since data completeness depends on hospitalization patterns and diagnostic accuracy, one would expect that conditions such as hip fracture, which should always lead to a hospital encounter, are registered consistently in the DNPR with a high level of completeness.

Data on the Danish population size for the different years during the period 1999–2012 were obtained from <http://www.dst.dk/da/Statistik/statistikbanken>.

Statistics

All included continuous variables were non-normally distributed and were thus analyzed using Mann–Whitney U-tests.

The Cochran–Armitage trend test was used to test for trends in development in prevalence of co-morbidities. The development in incidence and mortality over time was assessed using negative binomial regression analysis since overdispersion was found when performing Poisson regression analysis, with patients sustaining a fracture being removed from the population at risk for the purpose of calculating incidence rates. Person-time was calculated based on the number of individuals at risk on January 1 each year in Denmark assuming all were followed for the subsequent year. P-values < 0.05 were considered significant. Statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Ethics, funding, and potential conflicts of interest

According to Danish law, ethical committee approval is not required for this type of observational database study. The data were obtained through secure remote access to Statistics Denmark (ref. 704670). The study was approved by the Danish Data Protection Agency. No funding was received for this study. No competing interest was declared for any of the authors.

Results

122,923 patients sustained their first hip fracture during the study period (Table 1). From 1999 to 2012, the hip fracture incidence in the whole population declined from 182 to 137 per 100,000 ($p < 0.001$) but gender-specific analysis showed that a decrease was evident only for women (256 to 181 per 100,000, $p < 0.001$) since the changes for men were not statistically significant (107 to 93 per 100,000, $p = 0.09$) (Figure 1). At the same time, the median age at time of first hip fracture remained largely unchanged (Figure 2). For the whole population, 30-day together with 1-year mortality remained unchanged (9.7% to 10.3%, $p = 0.9$ and 28.2% to 27.4%, $p = 0.4$, respectively) with sex-specific analysis showing the same trends for men (13.7% to 12.5%, $p = 0.5$ and 33.5% to 31.3%, $p = 0.5$) and women (8.1% to 9.1%, $p = 0.9$ and 26.0% to 25.5% $p = 0.2$) (Figures 3 and 4).

Of the included co-morbidities a trend with a decrease in prevalence of malignancy and dementia in women was found while an increase in the prevalence of all remaining co-morbidities, except hemi- or paraplegia for both genders, rheumatic diseases for women, and for men diabetes with complications, myocardial infarction, AIDS/HIV, and malignancy was found, with the largest increase in prevalence seen for congestive heart failure, moderate to severe liver disease, and renal disease, with the largest increments found for congestive heart failure (men: 6.5% to 10.7%, women: 5.9% to 13.1%), moderate to severe liver disease (men: 0.1% to 0.7%, women: 0.1% to 0.4%) and renal disease (men: 0.4% to 2.0%, women: 0.3% to 1.1%) (Table 2, see Supplementary data).

Table 1. Basic characteristics. Values are frequency (%) unless otherwise stated

	Alive after 30 days	Dead within 30 days	p-value	Alive after 1 year	Dead within 1 year	p-value
Number	110,702 (90.1)	12,221 (9.9)	–	88,541 (72.0)	34,382 (28.0)	–
Male	32,968 (29.8)	5,175 (42.4)	< 0.001	25,497 (28.8)	12,646 (36.8)	< 0.001
Female	77,734 (70.2)	7,046 (57.6)		63,044 (71.2)	21,736 (63.2)	
Median age (range)	80 (18–107)	86 (18–109)	< 0.001	79 (18–107)	84 (18–111)	< 0.001
Median Charlson-score (range)	1 (0–15)	1 (0–19)	< 0.001	0 (0–16)	1 (0–19)	< 0.001
Myocardial infarction	2,451 (2.2)	530 (4.3)	< 0.001	1,722 (1.9)	1,259 (3.7)	< 0.001
Congestive heart failure	10,229 (9.2)	1,490 (12.2)	< 0.0001	7,772 (8.8)	3,947 (11.5)	< 0.0001
Peripheral vascular disease	2,648 (2.4)	412 (3.4)	< 0.0001	1,978 (2.2)	1,082 (3.2)	< 0.0001
Cerebrovascular disease	7,114 (6.4)	1,044 (8.5)	< 0.0001	5,369 (6.1)	2,789 (8.1)	< 0.0001
Dementia	4,381 (4.0)	849 (7.0)	< 0.0001	2,896 (3.3)	2,334 (6.8)	< 0.0001
Chronic pulmonary disease	3,964 (3.6)	635 (5.2)	< 0.0001	2,973 (3.4)	1,626 (4.7)	< 0.0001
Rheumatic disease	1,364 (1.2)	174 (1.4)	0.4	1,099 (1.2)	439 (1.3)	0.6
Peptic ulcer disease	3,778 (3.4)	568 (4.7)	< 0.0001	2,832 (3.2)	1,514 (4.4)	< 0.0001
Mild liver disease	705 (0.6)	82 (0.7)	0.7	575 (0.7)	212 (0.6)	0.5
Diabetes without chronic complication	1,065 (1.0)	148 (1.2)	0.008	815 (0.9)	398 (1.2)	0.0002
Diabetes with chronic complication	2,283 (2.1)	290 (2.4)	0.02	1,773 (2.0)	800 (2.3)	0.0004
Hemiplegia or paraplegia	300 (0.3)	17 (0.1)	0.006	250 (0.3)	67 (0.2)	0.007
Renal disease	746 (0.7)	204 (1.7)	< 0.0001	483 (0.6)	467 (1.4)	< 0.0001
Any malignancy	2,862 (2.6)	475 (3.9)	< 0.0001	2,074 (2.3)	1,263 (3.7)	< 0.0001
Moderate or severe liver disease	252 (0.2)	32 (0.3)	0.5	198 (0.2)	86 (0.3)	0.4
Metastatic solid tumor	665 (0.6)	166 (1.4)	< 0.0001	293 (0.3)	528 (1.5)	< 0.0001
AIDS/HIV	14 (0.0)	0 (0.0)	0.2	13 (0.0)	1 (0.0)	0.08

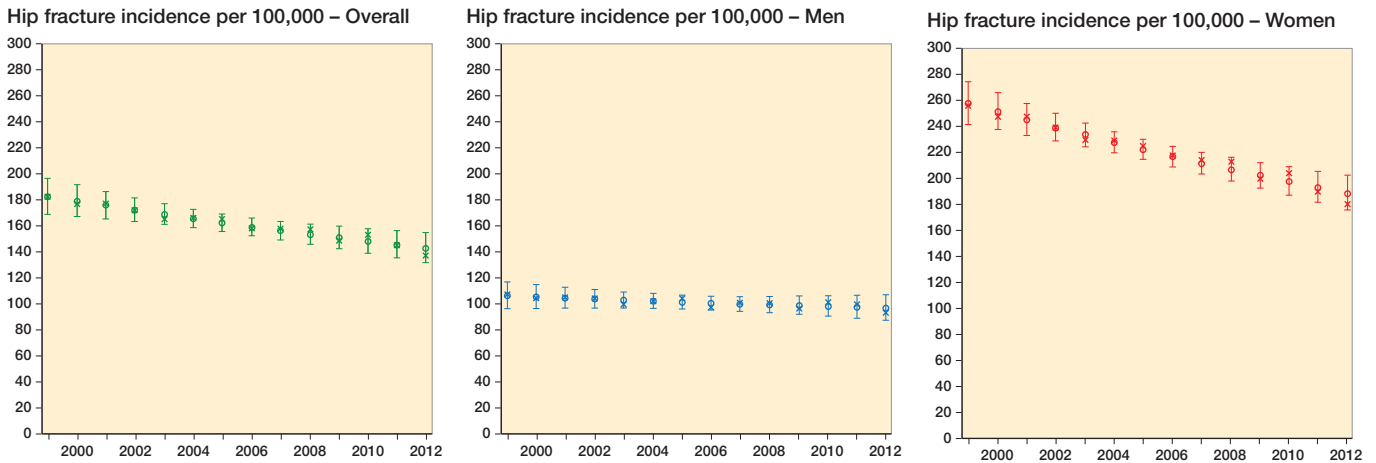


Figure 1. Overall and sex-specific hip fracture incidence. O: fitted values. X: observed values. P-values and 95% confidence intervals are derived from negative binomial regression. Overall $p < 0.0001$, men $p = 0.09$, and women $p < 0.0001$.

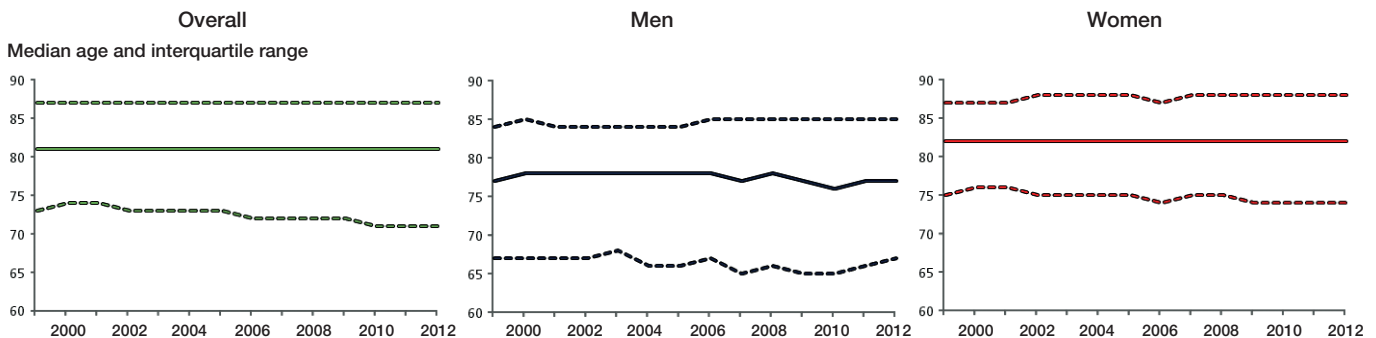


Figure 2. Overall and sex-specific median age and interquartile range at time of first hip fracture.

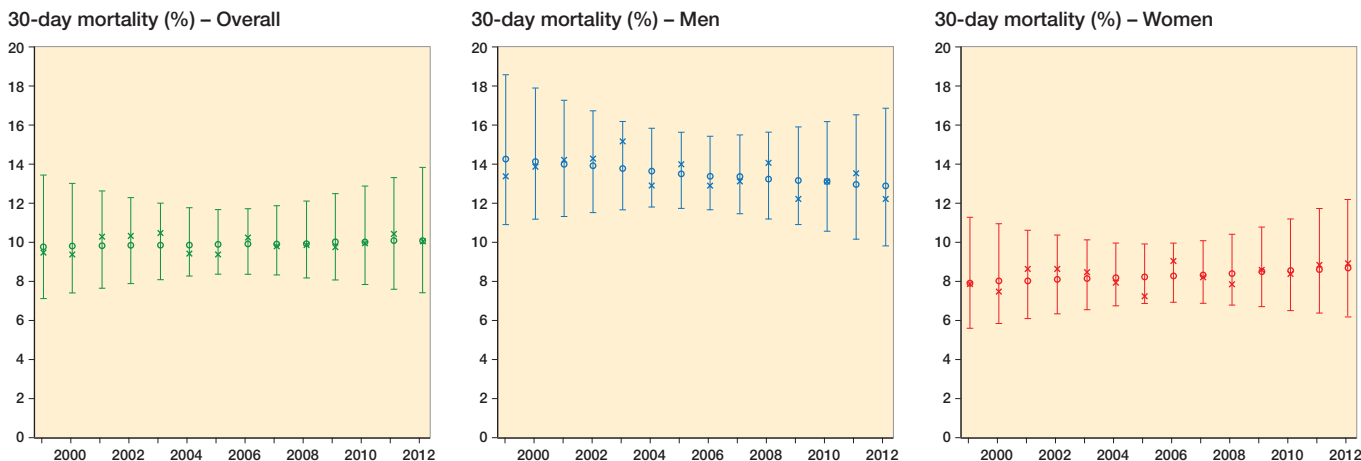


Figure 3. Overall and sex-specific 30-day mortality. O: fitted values. X: observed values. P-values and 95% confidence intervals are derived from negative binomial regression. Overall $p = 0.9$, men $p = 0.5$, and women $p = 0.9$.

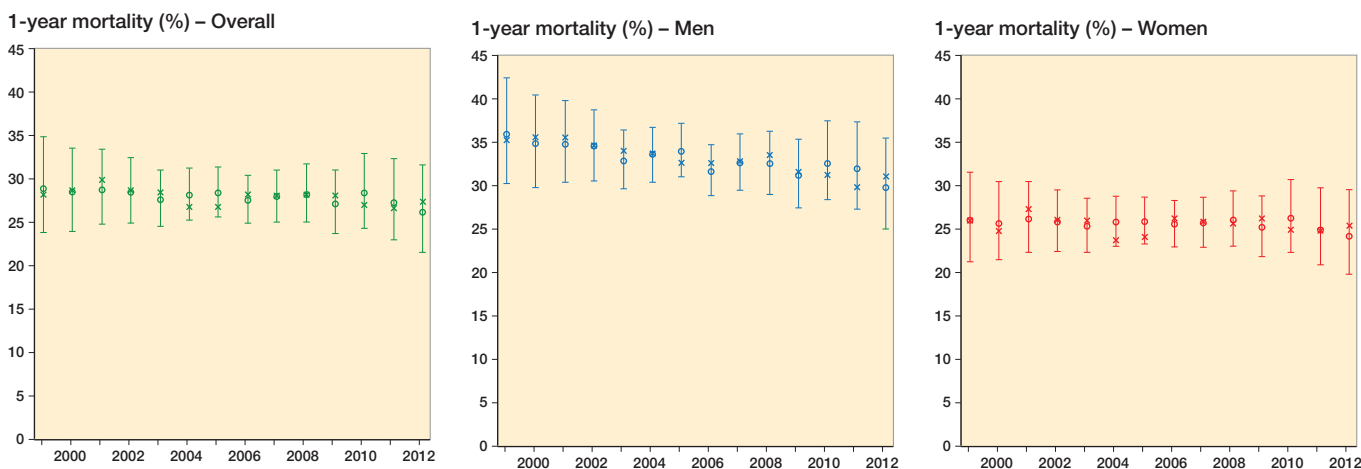


Figure 4. Overall and sex-specific 1-year mortality. O: fitted values. X: observed values. P-values and 95% confidence intervals are derived from negative binomial regression. Overall $p = 0.4$, men $p = 0.5$, and women $p = 0.2$.

Discussion

Hip fractures represent the most serious complication of osteoporosis in terms of morbidity, mortality, disability, and medical costs (Melton III 1993) and in 1993 it was estimated that the incidence of hip fractures would increase rapidly towards 2016 (Kanis 1993). This hypothesis was further supported by another study in which it was projected that the increasing size of the elderly population would lead to a 50% increase in the number and cost of osteoporotic fractures by 2025 (Burge et al. 2007). While this tendency towards an increased incidence is supported by data from Austria (Mann et al. 2008), other studies from Denmark, Sweden, Canada, Switzerland, and Finland have shown a decline (Kannus et al. 2006, Abrahamsen and Vestergaard 2010, Lippuner et al. 2011, Jean et al. 2013, Korhonen et al. 2013, Nilson et al. 2013).

In line with these studies, we found that the incidence of hip

fractures during the period 1999 to 2012 declined in the general population by 25%. Earlier data have shown that hip fractures occur more commonly in women than in men (Seeman 1995). This difference is also supported by our results showing a higher incidence of hip fractures for women during the whole period and even though the reduction in incidence was higher for women than for men the incidence was still twice as high in 2012 (181 vs. 93 per 100,000). Different explanations for the declining incidence have been proposed and include more widespread preventive measures, diagnosis, and treatment of osteoporosis (Jean et al. 2013) which in part could explain why the incidence in the Austrian population was found to increase since the lack of a structured nationwide osteoporosis prevention approach has been reported (Mann et al. 2008). While anti-osteoporotic treatment has been proposed as one of the major contributors to the declining inci-

dence, it has also been suggested that the decrease is too large to be explained by the extent of anti-osteoporotic treatment with other potential explanations being changes in smoking habits, obesity, improved general health, and vitamin D supplements (Abrahamsen and Vestergaard 2010). But even though a decreasing incidence has been found during the last decade in Denmark it has been proposed in a recent study by Rosengren et al. (2017), in which age-period-cohort effects for hip fractures were analyzed, that increasing fracture rates would be expected due to aging of more recent birth cohorts with a higher relative risk of sustaining a hip fracture.

Hip fracture patients constitute one of the most vulnerable groups of patients with a high level of co-morbidity, with earlier data showing that 90% of male hip fracture patients suffered from some sort of chronic disease with two-thirds having a disease affecting sensory or motor function and one-tenth having chronic alcoholism (Huuskonen et al. 1999). Likewise, different co-morbidities have been found to influence the risk of sustaining a hip fracture. It has thus been shown that patients suffering from systemic lupus erythematosus (Wang et al. 2013), Parkinson's disease (Pouwels et al. 2013), dementia (Jorgensen et al. 2014), former stroke (Pouwels et al. 2009), heart failure, peripheral atherosclerosis, ischemic heart disease (Sennerby et al. 2009), hemodialysis, liver cirrhosis, prior fracture, and osteoporosis all have an increased risk of sustaining a hip fracture (Lin et al. 2014). For COPD and asthma diverging results have been found with some reporting an increased risk of sustaining a fracture (Vestergaard et al. 2007) while others have not (Dam et al. 2010). The same applies to diabetes, where one study found an increased risk for patients suffering from type-2 diabetes (Schwartz et al. 2011) while another study found an increased risk only in patients with type-1 diabetes (Hothersall et al. 2014). Also, it has been found that patients who sustained a hip fracture were more likely to be women, living in long-term institutional care, using neuroleptics, dependent in activities of daily living (ADL), with a history of previous stroke with hemiparesis, Parkinsonism, and/or lower BMI than those who did not sustain a fracture after a fall on the hip (Willig et al. 2003).

Since different co-morbidities have been found to increase the risk of sustaining a hip fracture, a general reduction in the disease burden in the population could be hypothesized as one of the reasons for the reduced incidence (Jorgensen et al. 2014) but, contrary to this, our results on the temporal development of the 17 included co-morbidities showed a trend with a decrease in prevalence of malignancy and dementia in women, while there was an increase in the prevalence of all remaining co-morbidities, except hemi- or paraplegia for both sexes, rheumatic diseases for women, and for men diabetes with complications, myocardial infarction, AIDS/HIV, and malignancy, with the largest increase in prevalence seen for congestive heart failure, moderate to severe liver disease, and renal disease. Of the included co-morbidities, the most preva-

lent in 1999 were congestive heart failure (men 6.5%, women 5.9%), cerebrovascular disease (men 5.7%, women 4.8%), dementia (men 3.4%, women 3.2%), and chronic pulmonary disease (men 4.2%, women 2.5%) and during the period these co-morbidities were also subjected to the largest increments resulting in these also being the most prevalent in 2012 (congestive heart failure: men 10.7%, women 13.1%, cerebrovascular disease: men 7.4%, women 6.9%, dementia: men 4.0%, women 3.9%, and chronic pulmonary disease: men 5.1%, women 3.8%).

While an increased disease burden would be expected to lead to an increase in incidence of first hip fracture, this was not evident in our study. Reasons for the lack of increase in the incidence despite an increased disease burden could be better treatment of the individual diseases or more intensive diagnostic measures resulting in earlier detection and treatment of the diseases and thus less impact on the individual patient.

A potential reason for the higher disease rate we found could be increased age at the time of the first hip fracture but the median age of patients sustaining a hip fracture remained almost unchanged at 81 for the whole population, 82 for women, and between 76 and 78 for men. Therefore, changes in age at the time of fracture do not seem to be a probable explanation for the changes in co-morbidity, which instead could be a consequence of more extensive diagnostic measures in the hospital setting in the years prior to the fracture.

During the study period, 30-day and 1-year mortality for the whole study population and for both sexes remained unchanged with no significant changes. At the same time a higher mortality was evident for men at both 30 days and 1 year. This difference in mortality has been shown earlier in several studies (Kellie and Brody 1990, Myers et al. 1991, Jacobsen et al. 1992). This is further supported by a meta-analysis showing an excess mortality in both men and women after a hip fracture with higher mortality in men compared with women at all ages (Haentjens et al. 2010). The effect of co-morbidities on 30-day mortality has previously been investigated and an increased risk of early death was found in patients suffering from central nervous system diseases (dementia, Parkinson's, hemiplegia), diabetes, circulatory disorders, nutritional deficiencies, COPD, chronic renal disease, and other chronic diseases (liver, pancreas, intestine) (Barone et al. 2009). We also found a significant association between low socioeconomic status and the risk of early death. As such, one would expect a concomitant increase in mortality rates with the increase in prevalence of the co-morbidities increases. One explanation for why this phenomenon was not observed in our study could be better and more effective treatment of the different co-morbidities and/or better and faster management of hip fracture leading to a smaller effect on the mortality rates.

A limitation of this study is that it is only concerned with the first hip fracture and as such data on incidence represent this and not the total incidence during the period, which

would be expected to be higher and, even though a washout period of 3 years was included, there is a small risk that the fracture included is not the first but the second fracture or a complication from an earlier fracture. Also, while a decrease in incidence was found during the study period it is important to remember that the data shown are based on ICD-10 codes given on discharge and since no completeness study has been performed it is possible that the incidences shown could be influenced by lacking or inappropriate coding. Another limitation includes data on co-morbidity, which are based on ICD-codes given to the patient on discharge. As such, a reason for the increase could be more focus on allocating codes to the patients on discharge at the end of the study period, but against this are results from a recent Danish study (Jørgensen et al. 2015) on patients undergoing first-time coronary angiography during the period 2000 to 2009. In this study a general tendency towards lower prevalence of co-morbidities was found and when these results are compared with ours it seems likely that the increase in disease burden found in our study is real and not based on a change in coding practice. In addition, a correlation between time of inclusion and length of window of registration for co-morbidities is present in the study with patients included later having a longer window. While this would lead to a hypothetical increased risk of accumulating co-morbidities for the patients included towards the end of the study period we are sure that any substantial co-morbidities would lead to contact with the healthcare system within a 3-year period and as such the risk would be minimally increased due to the effect of the initial 3-year data washout period in the study. Also, since our data do not contain information on changes in mortality and disease burden in the background population, it is not possible to conclude whether or not the changes are isolated to the hip fracture population or are a result of changes in the background population. The strengths of the study include the large number of patients in the study, covering all Danish hip fracture patients, and the use of the Danish national registries, which ensure that data are collected unbiasedly. As the study covers an entire population, it also increases the generalizability of the results and it is likely that the trends observed in the Danish population match those of other Western countries.

In summary, this observational study shows that during the period 1999 to 2012 the incidence of first hip fracture has declined for women but remained unchanged for men. For 30-day mortality, rates have increased for women even though there are no changes in 1-year mortality. On the contrary, 30-day mortality for men is unchanged while 1-year mortality has declined. When these results are compared with the relatively large increase in the prevalence of the different co-morbidities it does not seem likely that the increased disease burden is affecting the incidence or the mortality.

Supplementary data

Table 2 is available as supplementary data in the online version of this article, <http://dx.doi.org/10.1080/17453674.2018.1428436>

CJ: Statistical analyses, wrote the paper. CMM, JBL: Critical review of the manuscript. HLJ: Statistical analyses, critical review of the manuscript.

Acta thanks Jan-Erik Gjertsen and Björn Erik Rosengren for help with peer review of this study.

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