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25 year trends in first time hospitalisation for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study

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Abstract

Objectives To examine 25 year trends in first time hospitalisation for acute myocardial infarction in Denmark, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity.

Design Nationwide population based cohort study using medical registries.

Setting All hospitals in Denmark.

Subjects 234 331 patients with a first time hospitalisation for myocardial infarction from 1984 through 2008.

Main outcome measures Standardised incidence rate of myocardial infarction and 30 day and 31–365 day mortality by sex. Comorbidity categories were defined as normal, moderate, severe, and very severe according to the Charlson comorbidity index, and were compared by means of mortality rate ratios based on Cox regression.

Results The standardised incidence rate per 100 000 people decreased in the 25 year period by 37% for women (from 209 to 131) and by 48% for men (from 410 to 213). The 30 day, 31–365 day, and one year mortality declined from 31.4%, 15.6%, and 42.1% in 1984–8 to 14.8%, 11.1%, and 24.2% in 2004–8, respectively. After adjustment for age at time of myocardial infarction, men and women had the same one year risk of dying. The mortality reduction was independent of comorbidity category. Comparing patients with very severe versus normal comorbidity during 2004–8, the mortality rate ratio, adjusted for age and sex, was 1.96 (95% CI 1.83 to 2.11) within 30 days and 3.89 (3.58 to 4.24) within 31–365 days.

Conclusions The rate of first time hospitalisation for myocardial infarction and subsequent short term mortality both declined by nearly half between 1984 and 2008. The reduction in mortality occurred for all patients,

independent of sex and comorbidity. However, comorbidity burden was a strong prognostic factor for short and long term mortality, while sex was not.

Introduction

Despite considerable improvements in prophylaxis and treatment,^{1–3} myocardial infarction remains a common life threatening disease and an enormous burden on Western healthcare systems.¹ The incidence of and mortality from myocardial infarction are not continuously monitored by surveillance registries, despite the critical need for ongoing evaluation of its primary and tertiary prevention.

As people age, they are more likely to develop chronic medical conditions. About 45% of the adult population has at least one chronic disease.⁴ This proportion increases to 90% in persons older than 65 years,⁴ who represent more than half of patients with myocardial infarction.⁵ Myocardial infarction shares risk factors with many chronic diseases (such as obesity, diabetes, chronic obstructive pulmonary disease, and cancer⁶), increasing the prevalence of comorbidity among patients with myocardial infarction.^{7,8} Comorbidity potentially modifies effectiveness of therapies and the clinical course of a myocardial infarction.^{8,9} However, clinical guidelines for treatment of myocardial infarction are based on the results of trials that often exclude patients of advanced age or with a large number of comorbid conditions.¹⁰

With the availability of new therapies that also benefit older patients,¹¹ it has become increasingly important to understand the impact of comorbidity on the prognosis of myocardial

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Supplementary figures A and B
Supplementary tables A–D

infarction and to determine whether trends in survival apply to all patients with myocardial infarction.¹² Previous studies on this topic have been limited by size (<4100 participants),^{9 13} inclusion period (<6 years),^{9 13} or selective inclusion of patients from specific hospitals^{9 13} or age groups.⁹ Also, the prognostic impact of sex remains unclear because of conflicting study findings.¹⁴⁻¹⁷ We therefore conducted a nationwide, population based, cohort study to examine trends in first time hospitalisation for myocardial infarction over the 25 year period from 1984 to 2008, subsequent short term and long term mortality, and the prognostic impact of sex and comorbidity.

Methods

Setting

We conducted this cohort study in Denmark, which has 5.4 million inhabitants. The Danish National Health Service provides universal, tax supported, healthcare, guaranteeing unfettered access to general practitioners and hospitals and partial reimbursement for prescribed drugs. Accurate and unambiguous linkage of all registries at the individual level is possible in Denmark by means of the unique central personal registry number assigned to each Danish citizen at birth and to residents on immigration.¹⁸

Acute myocardial infarction

We used the Danish National Registry of Patients¹⁹ to identify all first time hospitalisations for myocardial infarction from 1 January 1984 to 31 December 2008 among Danish born inhabitants aged 15 years or older. This registry contains data on dates of admission and discharge from all Danish non-psychiatric hospitals since 1977 and from emergency room and outpatient clinic visits since 1995.¹⁹ Each hospital discharge or outpatient visit is recorded in the registry with one primary diagnosis and one or more secondary diagnoses classified according to ICD-8 (international classification of diseases, 8th revision) until the end of 1993 and ICD-10 (10th revision) thereafter.¹⁹ Patients with myocardial infarction are included in the Danish National Registry of Patients if they died in the ambulance on the way to the hospital or during the hospital admission, but not if they died at home. We used ICD-8 codes 410.09 and 410.99 and ICD-10 code I21 to identify myocardial infarction.

Mortality

We obtained information on all cause mortality until the end of 2009 from the Danish Civil Registration System.^{18 20} This registry has recorded all changes in vital status and migration for the entire Danish population since 1968, with daily electronic updates.¹⁸

Comorbidity

We obtained information on comorbid conditions from inpatient and outpatient hospital diagnoses (all available primary or secondary diagnoses) recorded in the Danish National Registry of Patients in the five years before the myocardial infarction. To avoid inclusion of complications caused by the myocardial infarction, secondary diagnoses coded during the admission for myocardial infarction were excluded. We categorised the severity of comorbidity using the Charlson comorbidity index,²¹ a scoring system that has been adapted for use with hospital discharge data⁹ and validated for patients with acute and chronic ischaemic heart disease.^{8 9 22 23} The index assigns between one and six points to a range of diseases, depending on the strength

of their relation to mortality in the subsequent year (during the era when the Charlson comorbidity index was developed): one point for myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, and diabetes without end organ damage; two points for diabetes with end organ damage, hemiplegia, moderate to severe renal disease, non-metastatic solid tumour, leukaemia, and lymphoma; three points for moderate to severe liver disease; six points for metastatic cancer and AIDS. We computed the total Charlson score for each patient and defined four categories of comorbidity as used in the Predicting Risk of Death in Cardiac Disease Tool (PREDICT) study—that is, total scores of 0 (normal), 1 (moderate), 2 (severe), and ≥ 3 (very severe).²² Myocardial infarction was not included in the scoring. The Charlson comorbidity index and associated ICD codes are provided in web extra table A on bmj.com.

Statistical analysis

We computed and illustrated graphically the incidence rate of myocardial infarction (standardised to the age distribution of the Danish population in the year 2000) and subsequent 30 day and 31–365 day mortality (standardised to the age distribution of the population diagnosed with myocardial infarction in the year 2000) for men and women from 1984 through 2008.²³ We calculated confidence intervals using the approximate bootstrap method.^{24 25} We repeated the analyses for subgroups of patients aged 35–49, 50–59, 60–69, 70–79, and ≥ 80 years.

We then characterised patients with myocardial infarction according to sex, age, and comorbidity category, overall and for five calendar periods of diagnosis (1984–8, 1989–93, 1994–8, 1999–2003, and 2004–8). We calculated the prevalence of individual Charlson comorbidities registered in the five years preceding the admission for myocardial infarction. We illustrated graphically the change in median age from 1984 through 2008 for both men and women.

We followed all patients until the date of death, emigration, or one year of follow-up, whichever came first. Using the Kaplan-Meier estimator,²⁵ we computed the 30 day and 31–365 day mortality risk associated with each calendar period of diagnosis and comorbidity category. We used Cox proportional hazards regression to estimate the mortality rate ratio (specifically, the hazard ratio) associated with calendar period of diagnosis and comorbidity category within 30 days and 31–365 days after myocardial infarction.

First, we compared mortality rates across calendar periods, using the earliest period as the reference and adjusting for sex, age groups, and comorbidity categories. To evaluate the potential for residual confounding by age and comorbidity, we repeated the analysis modelling age and comorbidity by three knot cubic splines.²⁵ The results were consistent with the categorical modelling strategy and are therefore not reported further. Second, we compared mortality rates across comorbidity categories, using normal comorbidity category as the reference and adjusting for sex and age groups. Within the 2004–8 calendar period of diagnosis, we also examined the 30 day and 31–365 day mortality rate ratios associated with the individual Charlson comorbidities, adjusting for the other comorbidities, age, and sex. The proportional hazards assumption was assessed graphically by plotting $\log(-\log(\text{survival function}))$ against time for all exposure variables and found to be valid.²⁵

Results

Incidence

We identified 234 331 first time hospitalisations for myocardial infarction in Denmark from 1984 through 2008. The Danish population in this 25 year period consisted of 5 610 039 Danish born inhabitants aged 15 years or older. The annual standardised incidence rate of myocardial infarction (per 100 000 people) decreased during this period, by 37% for women (from 209 to 131) and by 48% for men (from 410 to 213) (fig 1). A transient increase in incidence occurred between 2000 and 2004 (fig 1). It was driven by the incidence among people aged ≥ 70 years, particularly those aged ≥ 80 years (fig 2). For patients younger than 70 years, the incidence steadily decreased throughout the 25 year period (fig 2).

Patient characteristics

Although the female proportion of patients with myocardial infarction increased slightly between the first five year calendar period (35.8%) and the last (38.8%), men still accounted for the majority (62.1%) of all hospitalisations for myocardial infarction (table 1). The median age at time of diagnosis was 75 years for women and 68 for men. While the median age held fairly steady at about 68 years for men, it increased for women from 74 years in 1984 to 77 years in 2008 (web extra fig A on [bmj.com](http://www.bmj.com)). The prevalence of patients with normal comorbidity burden fell from 75.5% to 63.8% between the earliest and latest calendar period (table 1). The percentage of patients with moderate comorbidity increased from 13.2% to 16.2%, the percentage with severe comorbidity increased from 7.4% to 10.5%, and the percentage with very severe comorbidity increased from 3.9% to 9.6% (the prevalence for Charlson scores 1 to 10 is provided in web extra table B). The most prevalent Charlson comorbidities were diabetes (7.0%), stroke (7.0%), congestive heart failure (5.8%), chronic pulmonary disease (5.8%), peripheral vascular disease (5.3%), cancer (5.4%), ulcer disease (2.5%), connective tissue disease (2.1%), and severe renal disease (1.6%).

Mortality

The standardised 30 day and 31–365 day mortality risks after first time myocardial infarction were similar for men and women, decreasing comparably between 1984 and 2008 (fig 3). The 30 day mortality declined from 31.4% (95% confidence interval: 31.0% to 31.8%) during 1984–8 to 14.8% (14.5% to 15.2%) during 2004–8 (table 2). The one year mortality declined overall from 42.1% (41.7% to 42.5%) during 1984–8 to 24.2% (23.8% to 24.7%) during 2004–8; and among 30 day survivors it fell from 15.6% (15.2% to 16.0%) during 1984–8 to 11.1% (10.7% to 11.4%) during 2004–8. When the latest five year period was compared with the earliest, the mortality rate ratio adjusted for age and comorbidity category was 0.37 (95% confidence interval 0.35 to 0.38) within 30 days and 0.48 (0.47 to 0.51) within 31–365 days. Age stratified analyses revealed no difference in mortality among men and women within age categories (web extra fig B on [bmj.com](http://www.bmj.com)).

Prognostic impact of comorbidity

The improvement in mortality after myocardial infarction between 1984 and 2008 was observed for all patients in all age groups, independent of their comorbidity category (fig 4). The 30 day and 31–365 day mortality risks were strongly associated with the patient's category of comorbidity for all five year calendar periods (web extra table C on [bmj.com](http://www.bmj.com)). With normal

comorbidity category as the reference, the mortality rate ratios adjusted for age and sex among patients with moderate comorbidity in 2004–8 were 1.35 (95% confidence interval 1.26 to 1.45) within 30 days and 1.83 (1.68 to 2.00) within 31–365 days (table 3). Comparing patients with very severe and normal comorbidity in 2004–8, the adjusted mortality rate ratios were 1.96 (1.83 to 2.11) within 30 days and 3.89 (3.58 to 4.24) within 31–365 days (table 3). The magnitude of the increased mortality rate ratios associated with increasing comorbidity categories was similar across calendar periods (web extra table C). Consistent with the principle that effect estimates are higher among those at lower baseline risk, we found that age modified the mortality rate ratio associated with each comorbidity category, with higher estimates in younger age groups (web extra table D).

Among the individual non-malignant comorbidities, liver disease and dementia were each associated with a roughly doubled mortality rate within 30 days after myocardial infarction compared with patients without comorbidity (table 4). Within 31–365 days, twofold increased mortality rate ratios were also observed for patients with moderate to severe liver or renal diseases. Congestive heart failure, peripheral or cerebrovascular disease, chronic pulmonary disease, and ulcer disease were associated with a 1.2 to 1.3-fold increased mortality rate ratio within 30 days, increasing to 1.5-fold within 31–365 days. Diabetes with end organ damage was associated with 1.3-fold increased short term and long term mortality rate ratios, whereas connective tissue disease was not.

Discussion

In this nationwide cohort study, we found an almost 50% reduction both in the first time hospitalisation for myocardial infarction between 1984 and 2008 and in subsequent short term mortality. During the same period, one year mortality among 30 day survivors declined by a third. The improved survival since 1984 applied to all myocardial infarction patients independently of sex and comorbidity. However, the comorbidity burden measured five years before admission was a strong predictor of mortality within 30 days after myocardial infarction and during the remainder of the first year, whereas sex was not.

Strengths and limitations of study

Several issues should be considered in interpreting our results. The population based design in a country with universal healthcare reduced selection biases stemming from selective inclusion of specific hospitals, health insurance systems, or age groups. All patients were followed until death, emigration, or end of follow-up, and hence no one had incomplete registration.

The positive predictive values of diagnoses in the Danish National Registry of Patients have previously been validated and found to exceed 90% for both myocardial infarction ($>90\%$)²⁶ and the Charlson comorbidities (98% overall).²⁷ A potential limitation was that patients with sudden cardiac death outside hospital or ambulance or who did not receive a resuscitation attempt at the emergency room were not registered in the Danish National Registry of Patients. To address this limitation, we compared over time the proportion of patients who had myocardial infarctions recorded as cause of death in the Danish Register of Causes of Death without having it or a previous myocardial infarction recorded in the Danish National Registry of Patients. This supplementary analysis revealed that such patients could not account for the observed incidence and mortality trends.

Other diseases such as diabetes and chronic pulmonary disease are likely to be under-represented in the Danish National Registry of Patients, because some patients are treated in primary care only. Although the 7% prevalence of diabetes among patients with myocardial infarction is substantially lower than in other Western countries,² it is only slightly lower than reported in the second Danish trial on Acute Myocardial Infarction (DANAMI-2) (11%).²⁸ Also, because the comparisons were made within a population of patients with myocardial infarction, underascertainment of comorbidities is unlikely to influence substantially the relative mortality estimates associated with comorbidity categories. The mortality data from the Danish Civil Registration System are virtually complete.¹⁸

As suggested for stable angina pectoris patients,²³ the Charlson comorbidity index could potentially be made even more appropriate for patients with myocardial infarction by assigning greater weight to some diseases (such as liver and renal disease) and omitting others lacking prognostic significance among patients with myocardial infarction (such as connective tissue disease) or with low prevalence (such as hemiplegia, leukaemia, and AIDS).^{23–29} Also, peripheral and cerebrovascular disease may to some extent represent “disease staging” of underlying atherosclerosis that has progressed to multiple vascular systems, rather than representing separate disease entities.²⁹ However, despite these limitations regarding individual comorbidities, the Charlson comorbidity index in its original form has proved an adequate tool for measuring the prognostic impact of total comorbidity burden in patients with myocardial infarction.^{9–30}

Comparison with other studies

Our study is the first to examine nationwide 25 year trends in myocardial infarction epidemiology. Its results are in line with previous US,^{31–41} UK,^{42–43} Australian,⁴⁴ and multinational^{3–45} studies examining trends in the incidence and outcomes of myocardial infarction. Compared with our study, these studies were conducted over shorter time periods,^{34–45} with data collection before the definition of myocardial infarction was amended in 2000,^{32–34–38–42–45} or in modest sized cohorts such as the Atherosclerosis Risk in Communities Study,³⁵ Framingham Heart Study,^{32–33} Minnesota Heart Survey,³⁴ Perth MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) cohort,⁴⁴ or Worcester Heart Attack Study.^{31–39}

It is estimated that half of the decline in mortality since 1980 is attributable to primary prevention of myocardial infarction—that is, reduction in the prevalence of major cardiovascular risk factors such as smoking, sedentary lifestyle, and uncontrolled high blood pressure.^{1–2} The other half is attributable to the introduction of thrombolysis, coronary artery bypass grafting, percutaneous coronary intervention, and improved tertiary medical prevention with antiplatelet regimens, β blockers, angiotensin converting enzyme inhibitors, and statins.^{1–3} It is noteworthy that the incidence of myocardial infarction has continued to decline despite increased prevalence of obesity and diabetes.^{1–2} The transient increase in incidence between 2000 and 2004 with local maximum in 2002 was presumably attributable to new diagnostic criteria that included troponin as the main diagnostic biomarker of myocardial infarction.⁴⁶ Although we did not discriminate between ST segment and non-ST segment elevation myocardial infarction, the changing biomarker use is likely to have increased the detection rate of smaller infarcts and thus predominantly the rates of non-ST segment elevation myocardial infarction.^{35–36}

We observed a larger decrease in myocardial infarction incidence among men than women until 1997, after which the

decreasing trend seemed independent of sex. One explanation for this difference is that cardiovascular disease previously was considered primarily a man's disease, and thus cardiovascular disease prevention primarily focused on risk modification among men. Also, within the last two to three decades, the lifestyles and risk behaviours of women and men became more similar with regard to smoking, sedentary work, and working outside the home. We observed that sex did not influence the prognosis of myocardial infarction as previously suggested.^{14–15} Thus, age is the single most important prognostic factor to control for when comparing mortality from myocardial infarction between men and women.^{16–17–47}

Our study is also the first to examine the short and long term mortality risks and rates associated with comorbidity burden in a nationwide population. We observed increased levels of comorbidity over time. This trend may, however, be explained partly by the increase in age at time of diagnosis, a more complete disease registration (owing to the addition of outpatient clinic diagnoses in the Danish National Registry of Patients) from 1995 onwards, and the introduction of the diagnosis related group system as a prospective payment system around 2000. Because short term mortality is likely to be closely related to the severity and progression of myocardial infarction, it is notable that comorbidity had a substantial influence on 30 day mortality. Also important, we found that improvements in survival among patients with myocardial infarction occurred independently of their comorbidity burden. In contrast, survival improvements for other major diseases, such as breast cancer, depend on patients' comorbidity categories, with poorer survival improvement among those with severe comorbidity.¹²

Our large study, including nearly 250 000 patients, extends the results of two smaller studies that also examined the prognostic impact of comorbidity burden as classified by the Charlson comorbidity index.^{9–13} O'Connell et al based their analysis on the MONICA study of 4081 people aged 25–69 years who were admitted for myocardial infarction between 1988 and 1994 and who survived for at least 28 days.⁹ Their reported association between comorbidity and mortality (adjusted hazard ratio 1.36 (95% confidence interval 1.07 to 1.72) for moderate to severe comorbidity and 2.74 (1.73 to 4.34) for very severe comorbidity) was consistent with our results. Núñez et al examined the association between comorbidity and mortality among 1035 patients admitted to hospital with myocardial infarction between 2000 and 2003.¹³ The 30 day and one year mortality rate ratios that they reported were consistent with our results for the calendar period 1999–2003.

Comorbidity may influence the prognosis of myocardial infarction in several ways. Comorbid conditions may directly alter the effectiveness of treatments and affect the course of myocardial infarction. Although comorbidities are likely to increase non-cardiac mortality in particular,⁴⁸ the increased short term mortality also suggests an impact on cardiac mortality. Underuse of coronary reperfusion therapy among patients with comorbid diseases may account for some of the increased mortality associated with comorbidity within the first 30 days after hospitalisation for myocardial infarction.⁷

Generalisability, implications, and conclusions

The observed trend for incidence and mortality of myocardial infarction are likely generalisable to most industrial Western societies where changes in lifestyle, risk factor modification, and increasing use of aggressive medical and interventional treatment have followed international recommendations.²

Furthermore, the ratio of mortality rates associated with comorbidity categories should be unbiased because the comparisons over time were made between patients all with myocardial infarction.²⁵

Our findings have implications for research and clinical care. Clinical trials should include patients with prevalent comorbid illness so that results may be extrapolated to the entire spectrum of patients with myocardial infarction.⁵ Cardiovascular disease registries should measure comorbidities to permit fair inferences regarding mortality, process of care, and risk stratification after myocardial infarction.^{8, 22} Finally, comorbidity should be considered in individual patient counselling, with treatment optimised to improve the outcome both of the comorbid condition and the myocardial infarction. Our findings are particularly important for elderly people, given their high prevalence of comorbidity⁴ and the increasing numbers of people of advanced age facing treatment decisions for coronary artery disease.^{4, 5}

In conclusion, we found that the rate of first time hospitalisation for myocardial infarction and subsequent short term mortality both declined by nearly half between 1984 and 2008. The reduction in mortality occurred for all patients, independent of sex and the severity of comorbidity. However, comorbidity burden was a strong prognostic factor for short and long term mortality, while sex was not.

Contributorship: MS, JBJ, and HTS conceived the study idea and designed the study. JBJ and HTS collected the data. MS, HEB, and HTS reviewed the literature. MS, JBJ, TLL, and HTS directed the analyses, which were carried out by JBJ. All authors participated in the discussion and interpretation of the results. MS organised the writing and wrote the initial drafts. All authors critically revised the manuscript for intellectual content and approved the final version. HTS is the guarantor.

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Ethical approval: Not needed.

Data sharing: No additional data available.

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What is already known on this topic

A marked decrease in incidence of acute myocardial infarction and associated mortality has occurred since 1980

As the population ages, an increasing proportion of patients with myocardial infarction will have comorbidities

What this study adds

This study of all 234 331 patients hospitalised in Denmark with first time myocardial infarction between 1984 and 2008 showed a near halving of incidence and short term mortality of myocardial infarction

The reduction in mortality occurred for all patients with myocardial infarction independent of sex and comorbidity

Comorbidity burden was a strong independent predictor of short term and long term mortality, while sex was not

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Tables

Table 1 | Numbers (percentages) of people with a first time hospitalisation for myocardial infarction in Denmark in five year periods from 1984 through 2008 by sex, age, and comorbidity category

	Calendar periods of diagnosis					Total (n=234 331)
	1984–8 (n=56 454)	1989–93 (n=50 249)	1994–8 (n=42 261)	1999–2003 (n=44 365)	2004–8 (n=41 002)	
Sex:						
Female	20 201 (35.8)	18 691 (37.2)	16 238 (38.4)	17 652 (39.8)	15 926 (38.8)	88 708 (37.9)
Male	36 253 (64.2)	31 558 (62.8)	26 023 (61.6)	26 713 (60.2)	25 076 (61.2)	145 623 (62.1)
Age (years):						
15–34	206 (0.4)	196 (0.4)	223 (0.5)	228 (0.5)	224 (0.5)	1 077 (0.5)
35–49	3 845 (6.8)	3 521 (7.0)	2 974 (7.0)	3 172 (7.1)	3 185 (7.8)	16 697 (7.1)
50–59	8 334 (14.8)	7 241 (14.4)	6 176 (14.6)	6 859 (15.5)	6 296 (15.4)	34 906 (14.9)
60–69	15 610 (27.7)	12 978 (25.8)	10 020 (23.7)	9 604 (21.6)	9 227 (22.5)	57 439 (24.5)
70–79	18 465 (32.7)	16 080 (32.0)	13 309 (31.5)	12 617 (28.4)	10 526 (25.7)	70 997 (30.3)
≥80	9 994 (17.7)	10 233 (20.4)	9 559 (22.6)	11 885 (26.8)	11 544 (28.2)	53 215 (22.7)
Comorbidity category*:						
Normal	42 645 (75.5)	37 771 (75.2)	30 041 (71.1)	28 323 (63.8)	26 157 (63.8)	164 937 (70.4)
Moderate	7 455 (13.2)	6 845 (13.6)	6 409 (15.2)	7 599 (17.1)	6 633 (16.2)	34 941 (14.9)
Severe	4 168 (7.4)	3 701 (7.4)	3 571 (8.4)	4 592 (10.4)	4 295 (10.5)	20 327 (8.7)
Very severe	2 186 (3.9)	1 932 (3.8)	2 240 (5.3)	3 851 (8.7)	3 917 (9.6)	14 126 (6.0)

*Categories of comorbidity were based on Charlson comorbidity index scores of 0 (normal), 1 (moderate), 2 (severe), and ≥3 (very severe).

Table 2| 30 day and 31–365 day mortality risk and mortality rate ratio after first time hospitalisation for myocardial infarction in Denmark in five year periods of diagnosis from 1984 through 2008

Period of diagnosis	No of patients	Median age (years)	30 day mortality			31–365 day mortality		
			Mortality risk % (95% CI)	Mortality rate ratio (95% CI)		Mortality risk % (95% CI)	Mortality rate ratio (95% CI)	
				Unadjusted	Adjusted*		Unadjusted	Adjusted*
1984–8	56 454	70	31.4 (31.0 to 31.8)	1 (reference)	1 (reference)	15.6 (15.2 to 16.0)	1 (reference)	1 (reference)
1989–93	50 249	70	27.4 (27.1 to 27.8)	0.86 (0.84 to 0.88)	0.84 (0.82 to 0.86)	13.2 (12.9 to 13.6)	0.83 (0.80 to 0.87)	0.79 (0.76 to 0.82)
1994–8	42 261	71	23.8 (23.4 to 24.2)	0.73 (0.71 to 0.75)	0.68 (0.67 to 0.70)	11.7 (11.3 to 12.0)	0.73 (0.70 to 0.76)	0.63 (0.60 to 0.66)
1999–2003	44 365	72	18.1 (17.8 to 18.5)	0.54 (0.52 to 0.55)	0.46 (0.45 to 0.47)	12.2 (11.8 to 12.5)	0.76 (0.73 to 0.79)	0.56 (0.54 to 0.58)
2004–8	41 002	71	14.8 (14.5 to 15.2)	0.43 (0.42 to 0.44)	0.37 (0.35 to 0.38)	11.1 (10.7 to 11.4)	0.69 (0.66 to 0.72)	0.48 (0.47 to 0.51)

*Adjusted for age, sex, and comorbidity category.

Table 3| 30 day and 31–365 day mortality risk and mortality rate ratio after first time hospitalisation for myocardial infarction in Denmark between 2004 and 2008 associated with comorbidity category

Comorbidity category*	No of patients	30 day mortality			31–365 day mortality		
		Mortality risk % (95% CI)	Mortality rate ratio (95% CI)		Mortality risk % (95% CI)	Mortality rate ratio (95% CI)	
			Unadjusted	Adjusted†		Unadjusted	Adjusted†
Normal	26 157	10.8 (10.4 to 11.2)	1 (reference)	1 (reference)	6.2 (5.9 to 6.5)	1 (reference)	1 (reference)
Moderate	6633	19.2 (18.3 to 20.2)	1.85 (1.73 to 1.98)	1.35 (1.26 to 1.45)	15.5 (14.6 to 16.5)	2.64 (2.42 to 2.87)	1.83 (1.68 to 2.00)
Severe	4295	21.4 (20.2 to 22.7)	2.09 (1.94 to 2.25)	1.52 (1.41 to 1.64)	20.6 (19.3 to 22.1)	3.61 (3.30 to 3.96)	2.50 (2.29 to 2.74)
Very severe	3917	27.1 (25.7 to 28.5)	2.72 (2.53 to 2.91)	1.96 (1.83 to 2.11)	31.2 (29.5 to 32.9)	5.80 (5.34 to 6.31)	3.89 (3.58 to 4.24)

* Categories of comorbidity were based on Charlson comorbidity index scores of 0 (normal), 1 (moderate), 2 (severe), and ≥3 (very severe).

†Adjusted for sex and age.

Table 4| 30 day and 31–365 day mortality rate ratios associated with individual comorbidities after first time hospitalisation for myocardial infarction in Denmark between 2004 and 2008

	Adjusted mortality rate ratio (95% CI)*	
	30 day	31-365 days
No comorbid diseases	1 (reference)	1 (reference)
Congestive heart failure	1.30 (1.20 to 1.41)	1.62 (1.48 to 1.78)
Peripheral vascular disease	1.23 (1.13 to 1.34)	1.47 (1.33 to 1.62)
Cerebrovascular disease	1.21 (1.12 to 1.30)	1.52 (1.39 to 1.65)
Dementia	1.81 (1.60 to 2.05)	1.52 (1.28 to 1.81)
Chronic pulmonary disease	1.21 (1.12 to 1.31)	1.54 (1.41 to 1.68)
Connective tissue disease	0.95 (0.82 to 1.09)	1.05 (0.89 to 1.23)
Ulcer disease	1.24 (1.10 to 1.39)	1.50 (1.31 to 1.72)
Mild liver disease	2.00 (1.48 to 2.71)	1.80 (1.22 to 2.67)
Diabetes without end organ damage	0.99 (0.89 to 1.09)	1.19 (1.05 to 1.34)
Diabetes with end organ damage	1.30 (1.16 to 1.46)	1.25 (1.09 to 1.44)
Hemiplegia	1.32 (0.79 to 2.19)	1.68 (0.97 to 2.89)
Moderate to severe renal disease	1.26 (1.11 to 1.42)	2.08 (1.83 to 2.36)
Non-metastatic solid tumour	1.22 (1.12 to 1.34)	1.69 (1.53 to 1.87)
Leukaemia	1.85 (1.32 to 2.59)	1.89 (1.21 to 2.95)
Lymphoma	1.40 (1.07 to 1.83)	1.60 (1.15 to 2.22)
Moderate to severe liver disease	2.21 (1.34 to 3.64)	1.97 (0.94 to 4.10)
Metastatic cancer	1.58 (1.25 to 2.01)	2.91 (2.33 to 3.63)

AIDS was omitted from the table because of its low prevalence (<0.1%).

*Adjusted for the other comorbidities, age, and sex.

Figures

Transient increase in incidence starting around 2000 was presumably due to new diagnostic criteria for myocardial infarction^{41 46}

Fig 1 Standardised incidence rates for first time hospitalisation for myocardial infarction in Denmark between 1984 and 2008 among men and women

Transient increase in incidence starting around 2000 for older age groups was presumably due to new diagnostic criteria for myocardial infarction^{41 46}

Fig 2 Standardised incidence rates for first time hospitalisation for myocardial infarction between 1984 and 2008, for men and women within age groups

Fig 3 Standardised 30 day and 31–365 day mortality after first time hospitalisation for myocardial infarction among men and women between 1984 and 2008.

Fig 4 30 day and 31–365 day mortality after first time hospitalisation for myocardial infarction between 1984 and 2008, according to comorbidity category.