EXAMINATION OF THE EPIDEMIOLOGY OF ACUTE MYOCARDIAL INFARCTION IN ENGLAND USING LINKED HOSPITAL AND MORTALITY DATA

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Examination of the epidemiology of acute myocardial infarction in England using linked hospital and mortality data

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ABSTRACT

Background Acute myocardial infarction (AMI) is a major public health concern. There are limited recent national-level population-based epidemiological data on AMI in England. As a result, the current burden of disease is difficult to quantify.

Aim This thesis addresses gaps in knowledge on AMI in England. It aims to provide a comprehensive analysis of AMI epidemiology over the last decade.

Methods This is a population-based study using person-linked routine hospital and mortality data for England for the period from 1 April 1998 to 31 March 2008. Main outcome measures include: trends in event rate, case fatality, and mortality for AMI, as well as trends in characteristics of, and hospital care for, the AMI patient population between 1999 and 2007; rates of occurrence and case fatality for first and recurrent AMI in 2007; and five-year survival and risk of a second AMI for 2003 to 2007.

Results Total age-standardised AMI mortality rate fell by around half, while the age-standardised event rate and case fatality rate each declined by around one third between 1999 and 2007. Approximately half of the decline in AMI mortality was attributed to a decline in event rate and half to improved survival. During the 2000s, the hospitalised AMI patient population became increasingly elderly, presented with more comorbidities, underwent more revascularisation procedures, and spent less time in hospital. In 2007, approximately 90,000 AMIs occurred in England, of which around one third were fatal, one in seven were reinfarctions, and three quarters were AMIs in those aged 65 years and older. Among 30-day survivors of a first AMI, around one in three men and one in four women died within five years, and about one in eight men and one in six women experienced a second AMI in the same time period.

Conclusions There have been substantial improvements in AMI occurrence, survival, and mortality over the last decade in England. This was driven by improvements in prevention and acute medical treatment. The results in this thesis emphasise the importance of both.

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THE ROLE OF THE AUTHOR

The initial idea for the research and the thesis outline was developed by me together with my supervisors, Professor Michael Goldacre and Dr. Michael Rayner. Dr. Lucy Wright joined the supervisory team after my first year. Together, the supervisory team guided my research and helped me with the interpretation and presentation of the results.

I was provided with a raw data file of linked hospital and mortality records from the Unit of Health-Care Epidemiology, Department of Public Health, University of Oxford. I cleaned the file, prepared it for analyses, and wrote all the analytical syntax to answer the research questions. I conducted all the data analyses and performed the literature search myself. The contents of this thesis have been written by me.

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To my parents,

Andrei Smoline and Marina Smolina



ABBREVIATIONS

AMI acute myocardial infarction

BRHS British Regional Heart Study

CABG coronary artery bypass graft

CFR case fatality rate

CHD coronary heart disease

CI confidence interval

CVD cardiovascular disease

ESP European Standard Population

FCE finished consultant episode

GOR Government Office Region

HR hazard ratio

ICD International Classification of Diseases

IMD Index of Multiple Deprivation

HES Hospital Episode Statistics

MINAP Myocardial Ischaemia National Audit Project

MONICA Monitoring of Trends and Determinants in Cardiovascular Disease Project

NSF National Service Framework

ONS Office for National Statistics

OR odds ratio

PPV positive predictive value

PTCA percutaneous transluminal coronary angioplasty

SMR standardised mortality ratio

UK United Kingdom

WHO World Health Organisation

GLOSSARY

Admission a continuous period of hospital care for AMI

AMI event an emergency hospital admission with a main discharge diagnosis of AMI (ICD-10 codes I21 or I22) or a sudden death with AMI coded as the underlying cause of death on the death certificate

Case fatality see *hospitalised case fatality* and *overall case fatality*

Cause of death the underlying cause of death recorded on the death certificate

Comorbidity any condition listed as a secondary diagnosis alongside the primary discharge diagnosis of AMI in the index admission or in any subsequent admission within 30 days of the date of AMI

Deprivation category one fifth of the study population, ordered from least deprived (quintile 1) to most deprived (quintile 5) based on the Index of Multiple Deprivation 2004

Event rate the annual rate of occurrence of any new AMI event per 100,000 population

Fatal AMI a sudden AMI death or a hospitalised AMI event with a death record within 30 days of a hospital admission for AMI, irrespective of the cause or place of death

Finished consultant episode a continuous period of time a patient spends in hospital under care of a particular consultant or allied healthcare professional at a single healthcare provider

First AMI event an index AMI event in 2007 that occurred in individuals with no record of hospital admission for AMI during the previous nine years[a]

Government Office Region (GOR) a geographical location of residence within England, based on the borders defined by the English government and Office for National Statistics

Hospitalised case fatality proportion of hospitalised AMI cases who died within 30 days

Incidence the annual rate of occurrence of first AMI events per 100,000 population

[a] In Chapter 8, first AMI events are used to mean an index AMI event that occurred between 2003 and 2007 in individuals with no record of a hospital admission for AMI during the previous five years.

Index AMI event for each person, the first occurrence of a hospital admission for AMI or a death due to AMI in the dataset

Length of stay the total number of days that a patient spent in hospital care during their index admission for AMI

Main diagnosis main condition treated or investigated during the relevant episode of care

Mortality the annual rate of occurrence of deaths with AMI recorded as the underlying cause of death per 100,000 population

Overall case fatality proportion of all AMI cases (including hospitalisations for AMI and sudden AMI deaths) who died within 30 days of the event

Postdischarge mortality the proportion of hospitalised AMIs that end in death following discharge from hospital, irrespective of the cause of death, within a specified time period

Recurrence rate the rate of occurrence of recurrent AMI events, per 100,000 population

Recurrence risk cumulative incidence of second AMI among the survivors of first AMI

Recurrent AMI an AMI event that occurred in individuals with a clinical history of a previous AMI and at least 30 days since the date of admission for the previous event

Reinfarction see *recurrent AMI*

Revascularisation procedure either PTCA or CABG procedure recorded in any operative field in hospital records for a patient within 30 days of the date of AMI

Sudden AMI death a death record with AMI coded as the underlying cause of death and with no linked hospital admission for AMI in the previous 30 days

Sudden AMI death rate the rate of occurrence of sudden AMI deaths per 100,000 population (Chapters 3, 7); the proportion of all AMIs that are sudden deaths (Chapter 4)

Standardised mortality ratio (SMR) the ratio of the observed number of deaths over the expected number of deaths (adjusted for age and sex), multiplied by 100

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

This chapter introduces the thesis and provides an overview of the epidemiology of coronary heart disease and acute myocardial infarction globally and in England. Specifically, the following epidemiological measures are discussed: mortality, incidence, case fatality, prevalence, survival, recurrence, hospital admissions, length of hospital stay, treatments, and economic costs. Attention is also drawn to some important risk factors that influence epidemiological trends, including sex, age, comorbidities and socioeconomic deprivation. The rationale for the study, the main aims and objectives, and the structure of the thesis are stated at the end of the chapter.

Introduction

Cardiovascular disease (CVD) is an important public health issue because of the major burden of disease in terms of morbidity and mortality it poses on the population. CVD is a class of conditions that affect the heart and circulatory system, including: coronary heart disease, cerebrovascular disease, peripheral vascular disease, hypertension, heart failure, and others. Coronary heart disease (CHD) is the single most common cause of death among adults in the world.[1] Global and regional projections estimate that CHD will remain the leading cause of death at least up to 2030.[2] Acute myocardial infarction (AMI) is an emergency life-threatening manifestation of CHD. AMI is the cause of approximately three quarters of all deaths from CHD and accounts for roughly half of all hospital admissions for CHD.[3, 4] Because of the high burden of disease in terms of

incidence, case fatality, and mortality, AMI is one of the most extensively studied diseases.[5] A considerable amount of research and technological innovations have been invested into studying the biological, epidemiological, social, and other aspects of this disease, as well as the risk factors influencing its development.

In general, studies indicate that mortality from CHD has declined during the past three decades in the developed world.[3, 6-13] General declines have also been observed in CHD incidence and case fatality[10, 14-17] but trends have shown great variation by country, time period, sex, and age group. The situation regarding the interrelationship between AMI mortality, incidence, and case fatality is not clear because of inconsistencies in existing research findings. There is also conflicting evidence regarding the extent and nature of the contribution of changes in risk factors and treatment to the observed time trends in CHD progression. Furthermore, despite the considerable amount of current knowledge, many gaps still remain because of the variable nature of the disease in different geographic locations and different population sub-groups.

Country-specific, reliable, and representative epidemiological data are needed to further inform policy and economic models and to support decision making processes in health service delivery and planning. However, studies of CHD and AMI epidemiology from other countries cannot serve as reliable indicators of epidemiological developments in England. Firstly, the use of different methods makes direct comparisons challenging and it is difficult to draw any definitive conclusions. Secondly, the causes of changes in disease pattern over time are different in different populations and at different time periods. Thirdly, most studies are limited in size and their generalisability and representativeness could be called into question. Finally, CHD in older populations has been much less researched than in middle-aged populations, as many studies limit

enrolment to individuals aged below 65 or 75 years. Yet most CHD events occur among those aged 65 years and older.

Mortality from AMI has attracted recent political attention in the context of the National Health Service (NHS) reforms as an important health outcome indicator used to compare the population health in England with that of other countries.[18, 19] However, internationally comparable epidemiological data on AMI in England, other than mortality, are sparse. There are no published, comprehensive, population-based national-level estimates of AMI incidence, case fatality, or survival. The several large studies published to date were local, did not necessarily include all age groups or distinguish between first and recurrent events, and are by now out of date. As a result, assessments of the current burden of disease of AMI in the UK have substantial limitations, which could lead to clinical and policy decisions to be made based on incomplete, and possibly inaccurate, information.

Possible sources of epidemiological information for nation-wide studies are the routinely collected national hospital admission and death certificate data. However, linkage of data between these two sources is necessary in order to undertake a comprehensive analysis of person-based disease occurrence. Without linkage, national hospital data provide an incomplete profile of AMI because a large proportion of people who die from AMI die suddenly out of hospital,[20] while national mortality data similarly provide an incomplete profile of AMI because for many, AMI is not fatal.[3] Since 1998, it has been possible to link routinely collected hospital and mortality data for the entire population of England. Using a linked dataset of these national statistics, this thesis provides a comprehensive analysis of the epidemiology of AMI in England over the last decade. It also explores and reports on the methodological complexities of using routine administrative hospital and mortality data in the study of AMI.

Literature Review

This literature review presents an overview of the epidemiology of CHD and AMI globally and in the UK. The objective of the review is to describe the current state of knowledge and identify and describe any existing gaps. The major epidemiologically-relevant measures that are covered by the review are those that will be examined in this thesis and thus this review also serves as a background for the chapters that follow. This review is not meant to be a systematic examination of the literature, but rather a comprehensive overview of major studies in the field.

Methods

Electronic databases MEDLINE, Ovid SP, Web of Science, and Google Scholar were searched from 1990 until present to identify key studies investigating the epidemiology of AMI and CHD in the UK and globally. The following search terms were used, in various combinations: "myocardial infarction", "acute coronary syndrome", "coronary heart disease", "coronary artery disease", "isch(a)emic heart disease", "England", "United Kingdom", "mortality", "incidence", "event rate", "case fatality", "survival", "recur(ent/ence)", "subsequent", "reinfarction". References of identified articles were examined and any relevant articles or reports were included; some sources identified this way dated prior to 1990, but were still included if they were deemed to be important.

Pathophysiology of CHD

Coronary heart disease is a collective term used to describe a number of conditions, which can be characterised by a lack of adequate blood supply to the heart. They include

AMI, unstable angina, stable angina, and chronic CHD. AMI is the most acute and fatal manifestation of CHD. The most common underlying pathology of CHD is atherosclerosis, or a build-up of fatty deposits in the coronary arteries (arteries that supply the heart muscle).[21] These fatty deposits narrow the artery lumen, restricting blood flow to the heart muscle (myocardium). An AMI is triggered when a coronary artery becomes significantly restricted or blocked, resulting in inadequate or no blood supply to some areas of the myocardium. This leads to the heart muscle being deprived of oxygen, which could trigger an AMI and/or cause death of the affected areas if oxygen supply is not restored in sufficient time. Damage to the myocardium can be detected through a rise in cardiac markers in the blood (e.g. creatine kinase, troponins).

Clinically, the diagnosis of AMI is divided into ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI). STEMI is a more severe form of AMI, while NSTEMI is often used interchangeably with the diagnosis of unstable angina. More recently, "acute coronary syndrome" has evolved as a widely used umbrella term that captures the spectrum of CHD diagnoses from unstable angina to both types of AMI.[22] However, this shift in terminology use has not yet been reflected in the World Health Organisation's International Classification of Diseases diagnostic codes, and AMI and unstable angina are still coded as separate conditions in the discharge summaries of hospital records.

Epidemiology of CHD

Mortality

Mortality is the most commonly reported epidemiological measure of disease burden in a population. Many clinical, policy, and other decisions are based on mortality data. In

general for CHD, international literature shows that around three quarters of fatal events occur as sudden deaths outside of hospital.[3, 20, 23-29] For many individuals, sudden death is the first and only manifestation of CHD.[30-33] It is much more common in men than women, with age-standardised mortality rates being two to three times higher in men.[31, 34-37] Death rates increase exponentially with age for both men and women.[38, 39]

Mortality rates from CHD have been well studied in the developed world over the course of the 20th century. Generally, CHD mortality increased from the beginning to the middle of the century, and declined afterwards in North America and Western Europe, including England.[18, 38, 40] The increase in CHD mortality in the first half of the 20th century observed in England and other countries is a result of the "epidemiological transition" in the health and disease profiles of the populations – in other words, a shift in the major causes of death from infectious diseases and malnutrition to chronic non-communicable diseases. This transition was driven by industrialisation, urbanisation, improved hygiene, better socioeconomic situation, improved health care, and longer life expectancy.[41, 42] Higher standards of living, in turn, led to changes in lifestyles, which were accompanied by increased intake of dietary fat, sugars, and calories in general; smoking; and less physical activity – all of which accelerated the progression of atherosclerosis.

In the second half of the 20th century, CHD mortality started to decline in many developed countries.[7, 9, 10, 24, 32, 43, 44] In England, CHD mortality rates have been declining since the early 1960s.[45] However, the rates of decline for total age-standardised mortality as well as mortality in those aged under 75 years were small until the mid-1980s, after which the rates of decline increased.[45] For men aged under 55 years, CHD mortality peaked in mid-1970s and declined thereafter, and for women under 55 years, the rates showed a plateau until 1980 and a decline thereafter.[45]

Outside the UK, one of the major epidemiological studies of CHD was the population-based prospective Framingham Heart Study in the United States (US), which reported declines in CHD mortality of 44% in men and 51% in women between 1950 and 1989.[46] The Framingham Heart Study also coined the term "coronary risk factor" by identifying associations between high blood pressure, high levels of blood cholesterol, diabetes, obesity, smoking and incidence and case fatality from CHD. The Framingham study suggested that more than half of the observed decline in CHD mortality in women and one third to one half in men could be attributed to improvements in these coronary risk factors in the population.[46]

The epidemiological drivers behind the decreasing trends have been the subject of many research studies. The mortality rate for any disease is a product of the number of new cases of a disease and of the survival rate of those who have already been diagnosed with the disease. Therefore, any observed changes in mortality can either be the result of a change in incidence or in survival rates. Given that different determinants of mortality decline have fundamentally different implications for clinicians and policy makers, it is not surprising that the factors driving the observed mortality declines are, and still remain, an important research topic.

The seminal study that addressed this topic is the World Health Organization's Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) project. In 21 countries across the world, 38 MONICA centres were established to study and monitor CHD epidemiology and trends in rates, risk factors, and treatment within defined populations aged 35-64 years over the period of 10 years from the mid-1980s to the mid-1990s.[3] This large-scale international study produced a dataset on 166,000 events with consistent definitions of variables, clinical characteristics, and risk factor information. The two key research questions were: Are the reported declines in CHD mortality over

the last decades genuine? And, if they are, how much of the decline is attributable to improved survival rather than to declining coronary event rates? The MONICA study's findings were heterogeneous and revealed a lot of regional variation in event rates, mortality, and survival between different populations. Overall, MONICA results confirmed the declining CHD rates observed by others in the US and other countries, and attributed two thirds of the decline in mortality to a decline in coronary event rates and one third to a decline in case fatality during the period from the 1980s to 1990s.[3]

However, the MONICA study design had a number of limitations and thus its findings need to be interpreted with the following in mind. First, there is a question of generalisability: it is well known that rates of disease vary geographically within each country, thus making it difficult to state whether the figures from one or two single centres are representative of the whole population. For instance, within the UK, coronary event rates in Oxfordshire for the same time period were much lower than rates reported by the two UK MONICA centres in Glasgow and Belfast;[26] there was no MONICA centre in England. Further, the MONICA study results may not be representative of national trends since the study did not encompass all age groups, only including individuals aged under 65 years. Yet it is well established that most AMIs occur in individuals over 65 years of age.[47-49] (The age group limitation is not restricted to the MONICA project but also applies to many other previous studies of CHD.)

Studies that followed MONICA attributed the fall in mortality to different factors in different populations at different points in time. Some emphasised a decline in incidence, driven by improved risk factor profiles in the population and thus primary prevention, while others drew attention to the decline in case fatality due to improved cardiac treatments, particularly in the period of the 1980s and 1990s.[24, 25, 50-52] For example, in Sweden, just under 50% of the reduction in mortality from AMI has been attributed to a

decline in case fatality and just over 50% to decline in incidence.[16] In Finland, the drivers of decline differed by region: while a decline in recurrent coronary events accounted for most of the CHD mortality decline in eastern Finland, the decline in case fatality rates played a major role in south-western Finland.[12]

A number of modeling exercises have been undertaken to explain the observed declines in CHD mortality based on changes in major risk factors and evidence-based therapies in a given population. The IMPACT model, originally developed and validated in Scotland, has been used to explain CHD mortality declines in Scotland,[53] England and Wales,[54] Ireland,[55] US,[8] Canada,[56] Sweden,[57] Spain,[58] and New Zealand.[59] In Scotland, England and Wales, the model attributed approximately 60% of the mortality decline to reductions in population risk factors and the remaining 40% to the improvements in CHD treatments. In other non-UK countries, the results pointed to an approximately equal split between the contributions of improvements in risk factors and treatment modalities.

Pronounced geographical variation in mortality from CHD has been observed within and between countries around the world.[3, 60] In Europe, there are clear east-to-west and north-to-south gradients, with the highest CHD mortality rates in Central and Eastern Europe and lowest CHD mortality rates in the southern countries.[37] Regional differences in CHD mortality have also been observed in the UK, with a consistent north-to-south gradient.[61] [61-63] In 2008, the CHD mortality rate per 100,000 population for those aged under 75 years in Scotland was almost 50% higher than the rate in England (81 compared with 59 for men and 28 compared with 19 for women, respectively).[61] The majority of the large-scale geographic variation in CHD mortality in the UK can be explained by unhealthy lifestyles and area deprivation, however environmental factors also play a role.[64]

Incidence

Incidence is another crucially important measure of the extent of a disease in a population. Incidence can be defined either as the occurrence of a first-ever event or the occurrence of each new event. The latter is also referred to as the event rate or attack rate. The rate of occurrence of new AMI events is of great interest to researchers because it serves as an important indicator of the effectiveness of preventive measures and management of risk factors through health promotion and other public health initiatives. The main sources of data on AMI incidence are records of hospital admissions and certified deaths. There is a well known pattern of higher AMI incidence among men than women, with the rates in men more than double those for women.[15, 16, 65-67] In general, sex differences decrease with increasingly older age;[15, 65, 66] however, incidence increases exponentially with older age in both sexes.[5, 67]

There are few population-based studies that have reported AMI incidence for England. The Oxford Record Linkage Study (ORLS) estimate of AMI incidence per 100,000 population in the Oxford region from 1994-98 stands at 360 for men and 160 for women.[5] The Oxford Myocardial Infarction Incidence Study (OXMIS) showed that AMI incidence among individuals aged under 80 years was 273 for men and 66 for women in 1994-95.[26] The more recent Oxford Vascular Study (OXVASC) presented incidence rates of 162 for men and 92 for women, respectively, in 2002-05.[67] Even though these three studies were all conducted in Oxfordshire, they report quite different results; it is thus unclear to what extent these results are generalisable to the whole of England. Finally, data from The Health Information Network (THIN), a primary care database comprising patient data from general practices across the UK estimated that in 2005, the incidence of first AMI in England was 230 for men and 130 for women, respectively.[68]

In general, the incidence of AMI has decreased in a number of countries during the past three decades,[3, 10, 14, 15, 24, 69-72] including the UK.[5, 49, 68, 73-75] Data from Oxfordshire show declines in AMI incidence in both men and women and in all age groups.[5] Some studies have found that the declines in AMI event rate were greater in men than women,[9, 70, 76, 77] but others did not.[10, 14, 15] The observed falls are likely to be driven by changes in risk factors, and, to a lesser extent, improvements in treatment.[14, 73, 78, 79]

Regional variation in CHD incidence between and within countries has been well documented.[3, 14, 63, 80-84] In the UK, there have been two prospective cohort studies that examined the regional variation in the CHD incidence and CVD prevalence rates, respectively: the British Regional Heart Study (BRHS)[85, 86] and the British Women's Heart and Health Study (BWHHS).[62, 87, 88] The study population for BRHS consisted of men aged 40-59 years recruited between 1978 and 1980, and the study population for BWHHS consisted of women aged 60-79 years recruited between 1999 and 2001.

These two studies reported higher CHD incidence and CVD prevalence rates in Scotland and northern England than in southern England. The results also indicated that variation in prevalence of the main cardiovascular risk factors can explain most of the regional variation in CHD in men, but not CVD in women. In particular, BRHS reported that 79% of the variation in CHD incidence rate for middle-aged men could be explained by age, smoking, social class, systolic blood pressure, physical activity, height, and body mass index.[85] On the other hand, BWHHS showed that, even after adjusting for major risk factors, socioeconomic position, and health service utilisation, geographical variation in CVD prevalence was attenuated, but still persistent among older women.[62, 88]

The exact causes of geographical differences in CHD occurrence are not well understood and still represent a major research interest, with a variety of possible explanations that

are currently under investigation. Nonetheless, it is clear that the observed regional differences are a result of a multitude of factors, including not only cardiovascular risk factor prevalence, socioeconomic deprivation, and health services use, but also disease severity, primary health care delivery, and a variety of environmental influences, such as climate, population density or urbanicity, quality of air and water, cultural differences, and psychosocial factors, such as stress and depression.

Diagnostic criteria

A diagnosis of AMI is usually made based on a combination of clinical evidence, including symptoms, electrocardiographic (ECG) findings, and biomarkers of myocardial injury. The criteria for a clinical diagnosis of AMI have changed in the last decade. In 2000, the European Society of Cardiology and the American College of Cardiology introduced new diagnostic criteria, which rely on the use of more sensitive biochemical markers of damage to myocardium (troponins) for detection of AMI along with symptoms and ECG results.[89] Troponins are much more sensitive and specific biomarkers compared with the previously used creatine kinase (CK) and its MB fraction, and are able to detect very small amounts of damage to the heart muscle. However, the use of troponins for diagnosis also has a downside. Biologically, a rise in troponins can occur in any situation that causes enough stress to the heart to damage the myocardium, including, but not limited to, AMI.[90] Troponins thus lead to identification of a certain number of false AMIs by the virtue of their high sensitivity.

The greater sensitivity of troponins also means that some cases that previously would have been diagnosed as unstable angina could now be diagnosed and coded as AMI, thus artificially inflating the apparent event rate of new AMIs in a population.[91] Studies from a number of countries, and the US in particular, have shown increases in identified

hospitalised cases of AMI as a result of the new criteria.[72, 92-101] For example, a US study in Olmstead County reported a 41% increase in the number of AMIs identified using troponins; however, less than half of these newly identified cases were actually recorded as AMI in medical records.[95] A subsequent Olmstead County study that examined trends over time in AMI incidence found no changes between 1987 and 2006 when the new criteria was included, and a 20% decline when the same (old) diagnostic criteria were applied.[72] It was also found that the effect of new criteria was stronger in women than men and in older compared with younger individuals.[93-96] Previous UK studies have shown that the introduction of troponins would increase the number of identified AMIs by 23-27%, when comparing the number of AMIs identified using only the old criteria with the number of AMIs identified using only the new criteria.[102-104] However, in real-life clinical practice, where the adoption of new criteria happens over time, the increase in AMIs would be more gradual and may not attain these levels due to the variation between hospitals and physicians in the uptake over time of the new diagnostic methods.

Furthermore, there are substantial differences between countries in the characteristics of the AMI patient population, clinical practice, the use of troponins for diagnosis before the introduction of the new criteria, and the speed of adoption of the new criteria, among others. The interpretation of the data on the effect of troponins on AMI diagnoses is further complicated by the differences across studies in the use of biomarker type (troponin T versus I), the assays (there are several generations), manufacturers, normal ranges, and diagnostic thresholds.[91] Moreover, the percentage increase in the number of AMIs is also dependent on the reference criteria used. Finally, troponins have been used, although not as widely, in the diagnosis of AMI since the mid-1990s, while the older biomarkers are still being used in many hospitals throughout the world.[105] Overall, it is

difficult to know the exact extent and speed of the uptake of troponins in clinical practice, as well as how it has affected the epidemiological measures for AMI.

Case fatality

In general, case fatality indicates the proportion of individuals (cases) with a particular condition (e.g. AMI) who die within a certain time period. As a measure, it may refer just to patients admitted to hospital for the condition, or it may refer more broadly to all cases with the condition, including those that die from the condition outside of hospital. The former is termed hospitalised case fatality, and the latter is usually termed overall or total case fatality. Hospitalised case fatality rates are often used as indicators of hospital performance, while overall case fatality rates serve a broader measure of disease burden and outcomes in a population. For AMI, case fatality (either hospitalised or overall) generally refers to the rate of death within one month (typically, 28 or 30 days, depending on the study) of the date of occurrence of AMI.

Most deaths in AMI patients occur relatively soon after the event. Overall 30-day case fatality has been reported to be around 40-50%.[3, 28] Of the deaths that occur within 30 days, most happen in the first few days after AMI.[14, 106, 107] For example, in a recently published study from Scotland, 81% of the 28-day fatalities among incident AMI cases occurred within the first 24 hours.[107] Of the deaths within one year after admission to hospital for AMI, about two thirds occur within the first 30 days and most happen in hospital.[106, 108] Deaths at longer intervals occur mainly after hospital discharge.[106]

Sex differences have been observed in AMI case fatality. Studies have consistently reported a higher one-month case fatality in young women compared with young men, but a lower case fatality in older women compared with older men.[15, 39, 66, 109, 110] Also,

while 30-day case fatality rates that included sudden out-of-hospital deaths were higher in men than women, case fatality rates in those who survive long enough to be admitted to hospital were higher in women than men.[35, 39, 48, 66, 109, 111-113]

A steady decline in both hospitalised and overall case fatality for AMI has been observed in a number of countries since the 1980s, including the US,[24, 114-116] Canada,[43, 117] Denmark,[94, 118] Finland,[10] Netherlands,[108] Norway,[110] Sweden,[14, 119] Switzerland,[120] and the UK.[5, 26, 49, 68, 73-75, 121] Reductions in case fatality among hospitalised AMI patients are often attributed to improvements in acute treatment and coronary care, such as more widespread use of thrombolysis, statins, beta blockers, ACE inhibitors, and aspirin.[14, 15, 51]

While changes in hospitalised case fatality can serve as a good indicator of changes in acute care, hospital treatment is not the only explanation for the observed trends. Case fatality, both hospitalised and overall, also reflects changes in the progression and severity of disease and the population risk factor profile.[48, 61] In particular, recent studies in the US demonstrated a decreasing severity of AMI over the past two decades.[72, 100, 122-124] Results from the Atherosclerosis Risk in Communities Study (ARIC) study showed that between 1987 and 2002, the proportion of STEMIs to all AMIs fell at a rate of 1.9% per year.[122] Findings from the Olmstead County that covered 1987-2006 also showed that the severity of AMIs has declined, similarly evidenced by the decreasing incidence of STEMI and increasing incidence of NSTEMI.[72] The declining AMI severity likely reflects, at least in part, the more widespread use of preventative medications and better control of risk factors.[125] It thus appears that both primary and secondary prevention, in addition to improvements in acute treatment, have contributed to the declining trends in AMI case fatality. The change in the diagnostic criteria for AMI in 2000[89] has been shown not to affect trends in hospitalised case fatality rates.[94, 102, 104, 126]

Regional variation in AMI case fatality has been reported in a number of studies.[82, 118, 127-129] However, unlike incidence and mortality, geographical differences in the UK did not follow a north-to-south gradient.[127, 130] An observational study based on data from the Myocardial Ischaemia National Audit Project (MINAP) attributed the observed regional variation in 30-day mortality among patients hospitalised for AMI to regional differences in evidence-based hospital care.[130] Another UK study that examined differences between the UK constituent countries using information from a primary care database reported higher 30-day case fatality in Scotland and lower case fatality in Wales and Northern Ireland compared with England in 2001-05, after adjusting for age, smoking, and area deprivation; however, the differences between countries were not statistically significant.[68] The study attributed the observed geographical variation to the underlying differences in the prevalence of risk factors and acute care.

Survival

The epidemiological concept of survival refers to the period of time from a specified event, usually the onset of a condition (or performance of a procedure), to the time of death. Survival after an AMI has been the subject of extensive research because understanding survival patterns is an important element of understanding CHD progression.

Of patients who experience an AMI and survive the first 30 days, around 40% die within five years.[35, 131-133] In the first year following the event, survivors of AMI have about a three-fold higher risk of death compared with the general population.[134, 135] As time from AMI increases, cause of death changes from predominantly AMI and CHD to other causes.[106, 108, 134] For example, data from Oxfordshire indicate that cause of death certified as AMI declined from 85% of deaths occurring within 29 days of AMI event to 66% of

deaths occurring between 30 and 89 days to 47% of deaths occurring between 90 and 364 days.[106] Similar to short-term case fatality, younger women have a worse long-term prognosis compared with men in the same age category, but the direction of survival advantage changes in old age, with a higher risk of mortality in older men compared with older women.[15, 39, 66, 110, 133, 136-140]

In general, survival after AMI has improved over the past three decades in a number of countries, in all age groups, and for both sexes. Improvements in survival have been observed both in the UK[49, 141] and other developed countries.[110, 118, 134, 142-147] For example, in Sweden between 1984 and 1991, two-year survival after AMI improved from 64% to 75%;[146] in New Zealand, three-year survival rose from 86% in 1983-84 to 92% in 1991-92;[142]and in Scotland, five-year survival increased from 48% in 1986 to 54% in 1991.[49] Data from a sample of general practices across the UK showed a 28% increase in three-year survival among three-month AMI survivors during the 1990s.[141]

Improved survival after AMI has been attributed to the use of evidence-based treatments, such as thrombolysis, revascularisation procedures, and medications.[134, 141, 143-145, 147-149] For example, in the Australian Perth MONICA cohort, treatments during the index admission, and within the subsequent one year, fully explained the survival improvement after AMI between 1991 and 2005.[143] Another study from the US on the survivors of AMI aged 65 years and older showed that adjustment for the use of statins, beta blockers, ACE inhibitors, and antiplatelet drugs after discharge completely eliminated the association between time and mortality between 1995 and 2004.[147] The study concluded that the increased use of medications fully explained the decline in long-term mortality. In the UK, the reduction in three-year mortality after AMI between 1991 and 2002 was paralleled by a marked increase in the use of secondary prevention drugs.[148]

Recurrence

A considerable proportion of those who survive their first AMI experience a recurrent event (or reinfarction) in subsequent years. Nowadays, with increased use of medical interventions and a range of secondary prevention and treatment options, increasingly more AMI patients are likely to survive the initial episode and go on to experience another event.[15] A recurrent non-fatal AMI is a strong and independent risk factor for an increased risk of complications and/or subsequent death.[150-157]

For example, during the mean six-year follow up in the population-based FINMONICA register of individuals aged under 65 years, 28% of women and 34% of men experienced at least one recurrent event over the study period.[158] This study reported that in those who experienced a reinfarction, it occurred on average 2.4 years after the incident event; multiple recurrent events occurred closer in time to each other; and time to recurrent event was not greatly affected by sex or comorbidities. A hospital-based Canadian study found that within one year after an AMI event, 7.7% of AMI survivors were readmitted for a second AMI, with the highest readmission rates for AMI observed in those aged 75 years and older for both men and women.[48] Another recently published study from Sweden of over 775,000 AMI events between 1972 and 2001 found that the recurrence risk for patients with a first AMI was the highest in the year immediately following the event.[159] The risk fell sharply from around 20% to around 5% by two years, reached a minimum of around 4% by five years, and slowly increased thereafter.[159] The mean time to a new event was 2.5 years for women and 3.3 years for men.

Only three UK studies could be identified that reported the risk of recurrent AMI. Data from the Nottingham Heart Attack Register for the years 1992 and 1996 indicated that 11% of AMI patients who were discharged alive were readmitted for a non-fatal definite

AMI within four years.[155] Follow-up of the OXMIS cohort showed that 14% of men and 15% of women who survived their first AMI experienced a coronary death or a non-fatal reinfarction by six years.[160] A population-based study from Scotland using linked hospital and mortality records reported that 9.9% of men and 6.3% of women experienced a recurrent non-fatal AMI within five years of the admission date for the initial event.[132]

Even though time trends for first AMI or any AMI (without distinguishing first or recurrent) have been well documented, there is little research on trends in recurrence. The studies generally report that the recurrence rate of AMI has declined since the 1970s. In the ARIC study in the US, declines in the recurrence rate of 2.6% and 1.9% per year were noted for men and women aged under 75 years, respectively, from 1987 to 1994.[24] The Minnesota Heart Survey also showed a 20-30% fall in the recurrence rate between 1985 and 1997 in the US.[50] The FINMONICA study reported a similar decline in recurrent AMIs between 1983 and 1997.[12, 161] In Sweden, the recurrence risk fell by 36% in women and 40% in men between the late 1970s and the late 1990s.[159] A northern Swedish MONICA study also reported a decline in recurrence between 1985 and 1998.[76] Finally, the British Regional Heart Study reported that recurrence rate of major coronary events among middle-aged men has declined at a rate of 3.9% per year from 1978 to 2000.[73]

Studies have also reported an improving short-term and long-term prognosis for patients experiencing a recurrent AMI.[12, 24, 50, 162 149] For example, in a population based study in Denmark from 1985 to 2002, one year case fatality rate was higher for recurrent AMIs than for first AMIs, but prognosis had improved over time, with a relative decrease in one-year case fatality of about 50% for both first and recurrent AMI.[162]

Prevalence

Improvements in short-term and long-term survival after AMI have lead to an increase in disease prevalence over the past two decades. An analysis of general practice records from a sample of practices in the THIN database showed that there was a slight, but significant, increase in the age-standardised prevalence of CHD in the UK between 1996 and 2005, from 8.1% to 9.2% in men and from 5.5% to 6.3% in women.[74] The average annual rates of increase were 1.3% in men and 1.7% in women per year, producing overall increases of 13% in men and 15% in women over the study period.[74] With regards to the prevalence of ever having had an AMI, Health Survey for England data show that while the overall rates have not changed very much between 1998 and 2006, the prevalence of prior AMI among the middle-aged individuals decreased and the prevalence among men and women aged over 65 years increased.[45]

Currently in the UK, there are over 1.6 million men and one million women living with CHD, and about one million men and 500,000 women who have had an AMI.[61] The prevalence of CHD is higher in men than women and increases with older age in both sexes. Health Survey for England data for 2006 show that while 4.1% of men and 1.7% of women have ever been diagnosed with myocardial infarction overall, the figures for those aged 75 years and older are 16.6% and 9.1%, respectively.[163] There is also geographical variation in the prevalence of CHD within the UK, with higher rates in Scotland and northern England and lower rates in southern England.[61] For comparison, data from the US National Health and Nutrition Examination Survey between 2003 and 2006 indicate that CHD prevalence was 9.1% in men and 7.0% in women.[164] The corresponding figures were 4.7% and 2.6% for ever having had an AMI.[164] In Western Australia, the average annual age-standardised CHD prevalence between 1995 and 2005 was 8.8% in men and 4.0% in women.[165]

Risk factors for AMI

Several personal attributes, or risk factors, that are associated with the development of CHD or poor prognosis following AMI have been identified – some of them can be modified by lifestyle changes or medications while others cannot.[166-168] Non-modifiable risk factors include age, sex, ethnicity, family history of heart disease, and genetic predisposition. Modifiable risk factors include smoking, excessive alcohol consumption, high blood pressure, high blood cholesterol levels, overweight and obesity, poor diet, and physical inactivity. There are also other risk factors that contribute to the risk of CHD but are subject only to limited control/modification, including certain comorbidities (e.g. diabetes), stress, depression, and socioeconomic deprivation.

The seminal INTERHEART case-control study of AMI in 52 countries showed that smoking, history of hypertension or diabetes, waist-to-hip ratio, dietary patterns, physical activity, consumption of alcohol, blood apolipoproteins, and psychosocial factors account for 90% of the risk of AMI in men and 94% in women.[169] Table 1 shows the population-attributable risk for each risk factor, which is the proportion of the overall risk of AMI in a population – in other words, it is the excess risk of AMI in a population that would be eliminated if the exposure (risk factor) was eliminated.

Factors that are usually available for research using routinely collected data include age, sex, comorbidities, and socioeconomic deprivation. These are the variables that will be examined in the studies presented in this thesis. They are now discussed.

Table 1. Risk factors for AMI in the INTERHEART study.[169]

Risk factor	Population-attributable risk, % (95% CI)
Current and former smoking	36.4 (33.9-39.0)
Diabetes	12.3 (11.2-13.5)
Hypertension	23.4 (21.7-25.1)
Abdominal obesity	33.7 (30.2-37.4)
Psychosocial*	28.8 (22.6-35.8)
No vegetable or fruit intake	12.9 (10.0-16.6)
No exercise	25.5 (20.1-31.8)
No alcohol intake	13.9 (9.3-20.2)
High apolipoprotein ratio	54.1 (49.6-58.6)
All together	*90.4 (88.1-92.4)*

**Includes depression, general stress, low locus of control, and major life events*

Age

Age is the most powerful single predictor of AMI occurrence and prognosis, with elderly patients having significantly more events and higher risk of death and recurrence than younger patients.[35, 39, 48, 49, 69, 121, 132, 133, 139, 170] The annual rates of decline in CHD mortality have also been observed to decrease with increasing age.[78, 138, 171-173] Therefore, older individuals represent a higher-risk group of patients in which improvements in health outcomes are harder to achieve. Yet, more AMI patients are falling into this category over time.

Over the past few decades, AMI has changed from a disease of middle-aged men to a disease of older age, where the majority of the oldest patients are women.[174] Numerous studies have demonstrated a shift in the occurrence of AMI towards older age groups.[43,

[71, 114, 116, 119, 138, 173, 175, 176] This demographic shift in the patient population has important implications for in-patient care and treatment because older individuals tend to have more complex clinical profiles, with more concurrent conditions and more in-hospital complications, and may not be eligible for all available treatment options.

Sex

There is a well known pattern of sex differences in AMI occurrence and mortality in men and women. The literature suggests the following general trends: in absolute numbers, more men than women experience AMI; a higher proportion of women than men die from AMI if it occurs at a young age; and higher proportion of women than men survive an AMI if it occurs at an older age. These will now be described in more detail.

The exact reasons for the observed higher incidence of AMI events in men are unclear. A number of factors are suspected to be at play, including that pre-existing CHD is more common in men,[145, 177] and the possibly protective effect of estrogen in women.[21] However, the evidence on the importance of sex hormones in development of CHD is unclear and conflicting.[21, 40] It has also been widely noted that women typically have their first AMI at an older age than men.[16, 66, 109, 133, 139, 158, 178] The INTERHEART study showed that the earlier onset of AMI in men can be largely explained by the higher prevalence of cardiovascular risk factors in younger men compared with younger women, particularly abnormal lipid levels and higher rates of smoking.[179]

After AMI occurs, sex differences persist for case fatality. However, because of the much later onset in women, it is more informative to examine sex differences in prognosis after AMI within different age groups rather than overall age-adjusted rates. Generally, studies report that younger men fare better than younger women, but older women fare better

than older men.[39, 66, 109, 110, 139, 145] For instance, the two seminal studies in the US on this topic showed that among patients aged less than 50 years, the 30-day case fatality rate was about twice as high in women than men during hospitalisation for AMI, and about 50% higher within two years of admission.[39, 139] The higher risk in younger women still persisted even after adjustment for the available demographic and clinical factors. These studies also demonstrated that sex differences decreased with age and became non-significant after the age of approximately 70 years. A study from Sweden showed that women aged under 50 years had a higher rate of mortality, but after the age of 70 years, women had better 28-day and one-year survival than men.[66] A Canadian study showed that sex differences in five-year mortality were eliminated after adjustment for baseline characteristics in all age groups, except for women younger than 65 years.[140]

A number of explanations have been put forward to explain the poorer prognosis in younger women. From a physiological point of view, given the usually later onset, occurrence of AMI among young women could be considered a premature event and serve as an indicator of poor health or genetic susceptibility.[39] In addition, women usually have a higher prevalence of comorbid conditions (especially diabetes), suffer from more severe AMIs, have atypical symptom presentation, develop more in-hospital complications, and are less likely to receive thrombolysis and revascularisation procedures at the time of admission to hospital. [39, 66, 112, 136, 137, 139, 140, 158, 180-183]

It is also important to note that men are more likely to die from AMI before hospital admission, while women are more likely to die in hospital after being admitted, especially in younger age groups.[11, 16, 20, 35, 66, 109, 145, 184] A Scottish study has demonstrated that the excess deaths occurring out of hospital in men offset the excess risk of death following admission to hospital in younger women.[109] Therefore, differences between sexes depend not only on age but also the type of event (sudden AMI death or hospitalisation for AMI).

With regards to long-term survival, most studies report no large sex differences in overall age-adjusted rates.[109, 133, 178, 185] However, the studies that presented age-specific long-term survival for men and women have found a similar pattern to short-term survival, with younger women having a slightly higher mortality compared with younger men, but older women exhibiting a survival advantage over older men.[15, 39, 66, 110, 133, 136-140, 145]

Comorbidities

As individuals age, their disease profile changes to one in which more concurrent diseases are present.[186-188] Hospital patients with multiple health problems are more difficult to treat and may require special pathways of care. There is a growing recognition of the importance of accounting for multimorbidity in patients with chronic disease, and CVD in particular, both in terms of the associated complexity of clinical care as well as a risk adjustment tool for future prognosis.[189-191] Conditions that are associated with increased risk of AMI as well as increased risk of death if AMI occurs include cancer, respiratory disease, renal disease, cerebrovascular disease, hypertension, arrhythmia, heart failure, peripheral vascular disease, CHD, and diabetes.[49, 71, 132, 144, 190, 192-196]

Diabetes is a particularly important prognostic factor for having an AMI event and for decreased survival thereafter.[49, 133, 154, 175, 197-202] A recent meta-analysis of international data on vascular risk factors combining 102 prospective studies showed that diabetes confers around a two-fold increased risk for CHD.[203] A study using national hospital data for England and Wales for 2003-06 reported that the relative risks of death or recurrence within 90 days and 91-365 days of an AMI were 1.2 and 1.5 in diabetics compared with non-diabetic patients, after controlling for age, sex, heart failure, and surgery.[202] In general, studies show that diabetic patients are older, more often female, more likely to

have previous CVD or have other comorbidities, and less likely to be treated with effective cardiac therapies, such as revascularisation procedures, compared to non-diabetic patients.[204-207] In the UK, the diabetes prevalence has increased and the number of AMI admissions with type 2 diabetes rose from 7.2% to 14% over the last decade[208, 209] – this rise in diabetes might contribute to a future resurgence in CHD.

Socioeconomic deprivation

There are two main ways to measure socioeconomic inequalities in a given population: using individual-level characteristics, such as education, occupation, and income, or area-based deprivation measures related to area of residence. Both approaches are widely used in the literature; the first is commonly referred to as socioeconomic class/status/position and the second as area deprivation. Because many studies have used one or both, for the purposes of this thesis, the term "socioeconomic deprivation" will be used to mean socioeconomic differences in general, regardless of the way in which they are measured.

It has long been known that there is an association between socioeconomic deprivation and CHD.[210] Studies from a number of countries have consistently reported higher AMI incidence and mortality in more deprived individuals.[87, 211-223] Importantly, individual-level socioeconomic characteristics and area-based deprivation have been shown to be independently associated with CHD.[87, 220-222, 224, 225] A recent systematic review on the associations between social characteristics of the residential environment and CHD found that most of the studies reported an increased risk of CHD among those living in more deprived areas, after controlling for individual-level socioeconomic variables.[224] A study of British women between 60 and 79 years of age also found that those living in disadvantaged areas experience a higher risk of CHD, even after accounting for personal socioeconomic status.[87] However, the effect of area deprivation was reduced after

accounting for physiological risk factors, suggesting that area deprivation could be an upstream determinant of lifestyle, which in turn affects the prevalence of risk factors.[87]

Other studies have also shown that variation in the incidence of and mortality from AMI and CHD can be largely explained by the distribution of major cardiovascular risk factors across different socioeconomic deprivation categories.[213, 218, 222, 226, 227] However, even if the traditional risk factors explain a good part of the association between socioeconomic deprivation and CHD, they do not explain all of it, and the independent effects of individual-level and contextual-level characteristics point to additional, broader social and economic forces playing an important role in disease manifestation.[87, 222, 228]

Unlike associations with mortality and incidence, there are conflicting findings in the literature on the association between socioeconomic deprivation and case fatality. While most studies found that after adjusting for baseline characteristics, high deprivation was associated with lower survival after AMI,[220-223, 229-232] others did not reach the same conclusion.[121, 219, 233, 234] One English study found that socioeconomic deprivation was inversely associated with short-term, but not long-term, case fatality.[229] A Scottish study found no socioeconomic gradient for in-hospital case fatality, but overall case fatality was slightly higher in most deprived areas compared to least deprived.[233]

Finally, a socioeconomic gradient in CHD incidence, mortality, and case fatality has been found to vary by sex, age, and population density. Socioeconomic deprivation appears to play a greater role for women, younger individuals, and those living in the urban environments – these groups are consistently identified to be at increased risk of CHD.[27, 83, 212, 219, 220, 235]

Hospital admissions for AMI

Hospital admission records are an important data source to study the incidence of disease, particularly when linked with mortality data. Hospital records are often used as a proxy for the incidence of an acute condition, such as AMI, in the population and for monitoring temporal trends in disease occurrence.[236] In the case of studies of resource usage, hospital admissions are particularly important for CHD because they account for the majority of the direct economic costs of CHD (see section on Economic Cost below) and thus are central to health services planning and resource allocation.

Studies of hospitalisation trends for AMI generally report declines in age-standardised rates;[3, 43, 50, 78, 138, 171-173, 176, 237, 238] yet, some found little or no change.[24, 71, 116] In the US and Australia, an increase in hospital admission rates was observed up until the mid-1990s, followed by a decline thereafter.[114, 237] As mentioned above, the introduction of the new diagnostic criteria for AMI in 2000 affected estimates of AMI hospitalisation rates during the 2000s in some countries by causing an artificial increase because more cases of acute chest pain were being diagnosed and recorded as AMI.[94] However, studies that used standardised criteria that covered both pre- and post-troponin usage periods have found that the declines in AMI hospitalisation rates observed in the 1980s and 1990s have continued into the 2000s.[72, 73] A recent US study of hospital admission data from 2002 and 2007 (to reduce the impact of the new AMI definition) reported a 23% decline in AMI hospitalisations with an average annual change of -5.8% per year, after adjusting for age, sex, and race.[173]

Length of hospital stay

Hospital length of stay can serve as an indicator of disease severity and is also crucial for assessing health resource utilisation and the associated costs of care. Length of stay is determined by both patient and hospital characteristics as well as hospital transfers that may have occurred.

Over the last three decades, there has been an overall reduction in the mean length of hospital stay for patients admitted with AMI in a number of countries. In general, the mean length of stay has decreased in the developed world from several weeks in the middle of the last century, to two to three weeks in the 1970s and 1980s, to around one week in the 2000s.[239, 240] In Canada, there was a decrease in the average length of stay from 17 days for men and 23 days for women in 1976 to 10.7 days and 13.4 days in 1991, respectively.[9] In Denmark, the median length of stay fell from 10 days to 7 days from 1985 to 2002,[162] and in the Netherlands, the mean length of stay decreased from 10 days to 9 days from 1995 to 2000.[78] In the UK, the mean length of stay fell from 8.7 days to 7.2 days between 1982 and 1992 according to data from the Nottingham heart attack register[175] and from 8 days to 6 days between 1990 and 2000 according to Scottish linked database.[138] The main drivers behind the shortening hospital stay include improvements in acute treatments, earlier mobilisation of patients, and financial cost pressures.[115, 240-242]

The declining length of stay after an AMI episode has raised concerns about the possible negative impact on patients' health.[115, 195, 243] Some feared that shorter stays would lead to the displacement of short-term deaths following AMI from the hospital to the community, thus improving the apparent hospital performance, but not resulting in any real changes in patient outcomes.[144, 195] However, a number of studies that have examined this issue reported no adverse effects of shorter stays on mortality following discharge from

hospital for AMI patients.[101, 115, 240, 241, 243] Most of these studies were in the US and it is unclear whether or not shorter hospital stays have had a negative effect on postdischarge mortality in other countries.

Treatments for AMI

Survival improvement since the 1980s has occurred in parallel with a rapid and progressive use of medical treatments for AMI.[25, 50, 149, 175] Thrombolysis, revascularisation procedures, such as coronary artery bypass surgery (CABG) or percutaneous coronary intervention (PTCA/PCI), and drug treatments (e.g. aspirin, beta blockers, statins, ACE inhibitors) have been associated with increased survival after AMI.[134, 141, 143, 144, 147, 149, 244, 245] For example in Canada, the proportion of AMI patients receiving CABG or PCI during their index admission increased from 3.8% and 4.4% to 8.1% and 13.5%, respectively, from 1984-88 to 1989-93.[134] In Australia, the proportion of AMI survivors who have received CABG or PCI within one year of index event increased from 1% for both in 1984-87 to 20% and 17%, respectively, in 1991-93.[143] In the US between 1985 and 1995, the rates of CABG doubled in men from 5% to 10% but remained stable in women at 7-8%, while rates of angioplasty increased dramatically in both men and women from 5% to over 30%.[50] In the UK, the total number of CABG operations performed for all patients (not just AMI patients) since the late 1970s has increased tenfold from 2,297 in 1977 to 22,846 in 2008.[61] A similar high rate of increase was observed for PCI, which has risen from 9,933 in 1991 to 80,331 in 2008.[61]

The prescription cost analysis data from the Office for National Statistics shows that the rise in the number of drug prescriptions for AMI treatment has been increasing exponentially since the early 1990s in England. In particular, the number of prescriptions

in 2008 compared with 1991 has doubled for beta blockers, increased tenfold for antihypertensives (e.g. ACE-inhibitors) and antiplatelet drugs (e.g. aspirin), and risen 50 times for lipid-lowering drugs (e.g. statins).[61] The proportion of AMI patients prescribed these medications in general practice in the three months following AMI has changed between 1991 and 2002 from 26% to 68% for beta blockers, 11% to 71% for ACE inhibitors, 46% to 86% for antiplatelet drugs, and from 3% to 79% for lipid-lowering drugs.[141] Similar findings were reported in the US, with particularly large increases in the percent of AMI patients who are prescribed statins and antiplatelet drugs.[147]

Despite the favourable trends in treatment, there is still scope for improvement, because the prescription rate remains below the recommended guidelines for most drugs, meaning that not everyone who is eligible for the medications is receiving them.[141, 148, 244, 246, 247] Furthermore, not everyone has equally benefited from the new treatment options: revascularisation and drug prescription rates have been reported to be lower in women,[39, 75, 112, 113, 141, 248] older individuals,[114, 148, 249] diabetics,[204-207] individuals from lower socioeconomic status,[131, 232, 250] and ethnic minorities.[209, 248, 251-253]

In 2000, the UK Department of Health introduced the National Service Framework for CHD, which is a ten-year strategic document that set standards for CHD prevention, diagnosis, treatment, and service delivery, and aimed to improve the quality of care received by individuals suffering from AMI.[247] However, the impact of the Framework remains to be evaluated.

Economic cost of CHD

In addition to a major disease burden in terms of mortality and morbidity, CHD generates large financial expenses: it cost to the UK economy £3.2 billion in 2006.[61] CHD accounts for about one third of direct health expenditure on all cardiovascular diseases in the UK.[61, 254] Hospital inpatient care is the largest cost component, representing over 70% of the total CHD cost.[61, 209, 254, 255] A recent European Union-wide study found that about two thirds of total hospital care expenditure for acute coronary syndrome (including AMI and unstable angina) is spent on intensive care units and coronary care units.[256] Expenditure on pharmaceuticals is relatively small at about 20% of the total cost.[256] From a societal perspective, which includes the indirect costs of informal care, productivity losses, as well as direct healthcare costs mentioned above, the overall costs of CHD more than double. In the UK, the direct healthcare cost of CHD was estimated to be £3.45 billion in 2004 but the total cost of CHD to society to be £8.47 billion.[254]

Rationale for the study

CHD, and AMI as its most life-threatening manifestation, continue to pose major public health challenges, now and in the future. Despite the decline in mortality, CHD is still the leading cause of death in the UK[209] and is likely to remain so over the next few decades. In light of the ageing population,[257] and the increasing prevalence of CHD,[74] the country might soon be facing "an iceberg of hidden cardiovascular disease which will become visible in the near future."[258] Hospital workload is unlikely to decrease because of increasing number of AMI cases in the elderly and a possible rise in the number of younger patients with AMI, if the rates of diabetes continue to climb. In addition, better

medical treatments that improve AMI patients' survival after first events increase the number of people living with CHD and requiring regular medical care both in the hospital and in the community.

Recent, reliable, and representative epidemiological data on AMI are of great importance for clinical practice, public health policy, and planning and prioritising of health resources. Given that trends in disease occurrence and mortality are place- and time period-specific, it is essential to have national representative data for the UK. Yet, currently, there is very limited population-based national epidemiological data on AMI in England. Many of the published studies are out of date, based on data from small geographic areas, and do not necessarily include all age groups. This thesis addresses these gaps in knowledge by providing recent, comprehensive, and representative data on the epidemiology of AMI nationwide for England over the last decade.

AMI was chosen as the subject of focus for a number of reasons. First, AMI plays a central part in assessing the extent of CHD in a population, and important insights in the field of CHD research rely on a good understanding of the epidemiology and trends in AMI. Second, it is a common condition and thus a large sample of cases can be obtained. Third, all patients presenting to hospital with symptoms of AMI are likely to be admitted, minimising the selection bias among patients. Fourth, as a common condition, AMI is a well-coded diagnosis in hospital data and death certificates compared with others.[259, 260] Fifth, any serious consequences of a non-fatal initial event would result in another admission or death, thus allowing the tracking of patients over time. Sixth, diagnostic accuracy is higher for AMI than for unstable angina or CHD.[261-263] Finally, AMI is a severe enough event that most cases can be identified through death certification or hospital treatment.[14, 65, 264] Therefore, a linked dataset comprised of hospital discharges and deaths is likely to contain the majority of AMI events that have occurred in a country.

It is important to note that this thesis did not focus on all CHD because it was not possible to identify reliably all CHD cases using the available data. Although identifying all deaths attributed to CHD is straightforward, identifying all incident cases of CHD is not, because many non-AMI incident cases (e.g. angina) are treated without hospital admission. It is particularly difficult to identify the exact date of onset of incident cases of non-AMI CHD; this in turn makes it impossible to reliably estimate case fatality rates.

Aims and objectives

The aim of this thesis is to provide a comprehensive analysis of the epidemiology of AMI in England over the last decade. In particular, the research objectives are as follows:

- To investigate trends in AMI event rates between 1999 and 2007 (Chapter 3);
- To investigate trends in AMI case fatality between 1999 and 2007 (Chapter 4);
- To examine the relative contributions of changes in event rates and case fatality to changes in total AMI mortality between 1999 and 2007 (Chapter 5);
- To investigate trends in the characteristics of, and hospital care for, AMI patients admitted to hospital between 1999 and 2007 (Chapter 6);
- To provide national estimates of incidence and 30-day case fatality rates for first and recurrent AMI in 2007 (Chapter 7); and
- To examine five-year survival for first and recurrent AMI and to estimate the risk of a second AMI in survivors of first AMI between 2003 and 2007 (Chapter 8).

Structure of the thesis

The main body of this thesis consists of nine chapters. This Introduction is the first chapter. Chapter 2 discusses the methodological aspects of the thesis and provides results of some exploratory research that was undertaken to define key variables. Chapters 3-8 are results-based chapters, with Chapters 3-6 focusing on trends over time and Chapters 7 and 8 focusing on analyses at particular points in time. Chapter 9 summarises key findings, discusses their implications, and suggests directions for future research. Appendix 1 provides more detailed information on the data sources and Appendix 2 describes the record linkage methodology. Appendix 3 provides abstracts of presentations and papers that have been produced based on the results presented in this thesis.

CHAPTER 2: METHODS

This chapter introduces the use of administrative data in research and discusses its validity, strengths, and limitations. It also describes the data sources used in this thesis and the thesis design, and provides the definitions of variables. In addition, the chapter explores some important aspects of methodology and interpretation that are relevant to acute myocardial infarction (AMI) research using linked hospital and mortality records. Some important details about the process of routine administrative data preparation for statistical analysis and the challenges of using routine data for research are addressed. Statistical methods are described fully in the respective chapters.

Introduction

For this thesis, a linked dataset of English national, person-level data from hospital and mortality datasets was used as the main data source. By definition, routine datasets are not designed primarily for research purposes and a number of issues associated with using them for research need to be considered. In addition, given the nature of secondary data analysis, researchers using such datasets are not involved in the design or collection of data, coding rules, or defining the gathered information. Therefore, an extensive exploration of the linked dataset of hospital and mortality records that was used in this thesis was required to gain a full understanding of its design features and to prepare it for statistical analyses.

The objectives of this chapter are:

1. To discuss the use of administrative data in epidemiological and health services research, its validity, and its strengths and limitations;
2. To describe the data sources, thesis design, and study population;
3. To provide definitions of variables used in this thesis; and
4. To present the results of exploratory analyses performed to prepare the dataset.

The use of administrative data in research

Ideal sources of data for epidemiological research include complete, population-level studies or specialised disease registries. However, representative and generalisable studies are rare, and are usually limited in time, sample size, and geographic location. Extensive and up-to-date population-level registries are not widely available, are expensive to maintain, and may have restricted access. As a result of these limitations, administrative data have emerged as an important public health tool.

However, administrative data in their raw form have limited use, because records belonging to the same patient are not linked together, which greatly restricts the analytical potential of the data. Linking information from different sources at an individual level is a long-standing method in population-based research.[265] Efforts have been undertaken in different countries to link two or more data sources such as disease registries, hospital discharge datasets, primary care records, long-term care services, and birth and death registration datasets.[265-267] The current capacity for data linkage means that linked datasets can now be used to answer a diverse range of public health and health service research questions.[268] Linked hospital and mortality data are being increasingly

used to study disease prevalence,[269] trends in incidence and case fatality,[10, 14-16, 35, 49, 65, 264, 270] survival and health outcomes,[82, 131, 132, 134, 162] as well as inequalities among subpopulations based on socioeconomic status[49, 83, 232] and geographic regions.[82, 83, 271]

Validity of administrative data

The strength of any study that uses linked administrative data depends on the validity and accuracy of both the data and the linkage method.[263] For these reasons, routine administrative data are often validated against diagnostic or discharge information in medical records or disease-specific registers.

A literature review to identify key studies examining the accuracy of hospital discharge codes for AMI and underlying cause of death for AMI was conducted using a similar approach as in Chapter 1. Electronic databases MEDLINE, Ovid SP, Web of Science, and Google Scholar were searched from 1980 until present. The following search terms were used, in different combinations: "myocardial infarction," "coronary heart disease," "coronary artery disease," "isch*mic heart disease," "cardiovascular disease," "linked data," "record linkage," "administrative data," "validity," "accuracy," "hospital records," and "death certificates." References of identified articles were examined and any relevant articles or reports were included.

Hospital statistics

Unfortunately, no UK studies that validated the coding accuracy for AMI or CHD in hospital statistics could be identified. Current privacy regulations in England generally preclude access by researchers to the case notes of patients covered by HES; and the

dataset used for this thesis contained no patient identifiers. A very recent systematic review of discharge coding accuracy, published in 2011, identified 32 studies in Great Britain that assessed the accuracy of routinely collected hospital data, but none of them included AMI or CHD within the evaluated diagnostic codes.[272] The review reported an overall median diagnostic accuracy of 80% for all hospital diagnoses. However, these results are for four-digit diagnostic codes; the coding accuracy for three-digit codes (used in this thesis) is likely to be substantially higher.[273, 274] An earlier similar review of literature on the accuracy of routine UK hospital statistics that included studies conducted up to 1998 found a comparable overall diagnostic accuracy rate of 84%.[275]

A recent comparison study of CHD records in HES and general practice from 1997 to 2005 for the participants of the Million Women Study was able to use personal identifiers to check diagnoses across datasets because the participants had given consent for their records to be identified. The study reported an agreement of over 90% for the diagnosis of AMI (ICD-10 codes I21-I22).[276] Another UK comparison study examined the agreement between the Welsh hospital admission system (PEDW) records with data from the Myocardial Ischaemia National Audit Project (MINAP), a database of hospitalised AMI patient population used to assess the management of these patients against the National Service Framework for CHD.[202] The results showed high agreement: of 3,371 AMI patients recorded in MINAP, 99.9% were also found in PEDW.

Despite the paucity of British validation studies of AMI, encouraging results on the accuracy of hospital data have been reported from around the world. Table 2 shows summary results from non-UK studies in a number of other countries that validated the accuracy of AMI coding in the administrative hospital discharge records against medical

records. Most studies reported values for sensitivity and positive predictive value (PPV) that were generally very good (almost all above 80%).

Mortality Statistics

For death records used in mortality statistics, the gold standard for validation is autopsy in combination with clinical findings. Yet autopsy studies are rare and the frequency with which they are performed has been declining in most jurisdictions around the world. They are also usually less representative because of a small patient sample and selection bias towards more complex medical cases, resulting in an underestimation of the coding accuracy.[277] As an alternative to autopsy, the validity of death records can be examined through comparison with diagnostic information available from medical records or disease registers.

Unfortunately, the literature search did not identify any recent UK studies that validated the cause of death coding for AMI and/or CHD. However, an earlier study from Oxford used linked hospital and mortality records to examine the extent to which individual diagnoses, when recorded as being present shortly before death in hospital statistics, were also recorded on death certificates, between 1979 and 1987.[45] It reported that of all people who died within four weeks of hospital admission for AMI, 86% had AMI mentioned as the underlying certified cause on the death certificate.

Table 2. Studies assessing the coding accuracy of acute myocardial infarction diagnoses in hospital discharge records.

First Author	Country	Years validated	Validated cases, n	Comparison database	ICD code(s)	Sensitivity* (%)	PPV** (%)
Martin[278]	Australia	1971-82	1,235	Disease register	410	97	70
Dobson[279]	Australia	1979-85	1,044	Disease register	410	85	70
Boyle[280]	Australia	1986-91	2,071	MONICA	410	79	66
Austin[260]	Canada	1996-00	20,048	Disease register	410	93	89
Levy[191]	Canada	1994	234	Medical records	410	n/a	96
Humphries[281]	Canada	1994-95	817	Medical records	410, 412	83	89
Varas-Lorenzo[282]	Canada	1999-01	193	Medical records	410	n/a	95
Madsen[264]	Denmark	1982-91	4,596	DANMONICA	410	93	94
Joensen[261]	Denmark	1993-04	1,577	Medical records	I21	n/a	82
Mahonen[270]	Finland	1983-90	4,836	FINMONICA	410	80	90
Pajunen[262]	Finland	1988-02	37,062	FINMONICA	410, I21- I22	83	90
Palomaki[283]	Finland	1987-90	734	FINMONICA	410	89	86
Merry[263]	Netherlands	1996-2003	317	Disease register	I21-I22	85	99
Beaglehole[284]	New Zealand	1983	604	Disease register	410	86	67
Lindblad[285]	Sweden	1977-87	432	Physician review	410-411	99	96
Hammar[16]	Sweden	1987-95	1,848	Medical records	410	94	86
Fisher[286]	US	1984-85	7,050	Medical records	410	94	92
Petersen[287]	US	1994-95	5,151	Medical records	410	n/a	97
Kiyota[288]	US	1999-00	2,022	Medical records	410	n/a	94

n/a = not available

**Sensitivity = proportion of actual AMI cases that were correctly coded as AMI in the hospital statistics*

***Positive predictive value = proportion of coded AMIs in hospital statistics that were actual AMI cases based on clinical information*

Table 3 shows non-UK studies that assessed the accuracy of AMI codes in routine mortality statistics. In these studies, death certificate data were linked to other validated records, such as the MONICA study records, by using unique personal identification numbers, death registration numbers, or other identifiers. Overall, the validity of the code for AMI as the underlying cause of death was generally high, with reported values for sensitivity and PPV of over 80%.

Table 3. Studies assessing the coding accuracy of acute myocardial infarction and coronary heart disease diagnoses in mortality records.

Authors	Country	Years validated	Validated cases, n	Comparison database	ICD code(s)	Sensitivity (%)	PPV (%)
Boyle[280]	Australia	1986-91	1,240	MONICA	410	90	96
Madsen[264]	Denmark	1982-91	1,794	DANMONICA	410	89	97
Mahonen[103]	Finland	1983-92	1,677	FINMONICA	410	92	98
Rapola[289]	Finland	1985-91	128	FINMONICA	410	n/a	95
Merry[263]	Netherlands	1996-03	317	Disease registry	I21-I22	85	99
Harteloh[290]	Netherlands	2005	760	n/a – reliability study	I21	89*	n/a
Lloyd-Jones[291]	US	1948-88	942	Framingham Heart Study	410-414	84	78
Goraya[292]	US	1981-94	174	Medical records	410-414	91	96

PPV = positive predictive value; n/a = not available

**Intercoder agreement*

The results from validation studies presented in Table 2 and Table 3 demonstrate high heterogeneity. This is not unusual. While some of the observed variation is a reflection of true differences in data quality between different jurisdictions, the coding accuracy of

hospital and mortality records can be influenced by a number of other factors, including: human error; data recording by staff being in conflict with other competing priorities; lack of information on medical history; inadequate training of physicians in death certification practice; inaccuracies arising from complex circumstances surrounding the death and/or multiple comorbidities; and changes in coding practices and data collection methods over time and across different geographic regions.[277, 293, 294] Therefore, it is not uncommon for studies evaluating the accuracy of routine data to reach different conclusions.

Data sources used in this thesis

Data for this thesis were obtained from two datasets, Hospital Episode Statistics (HES) and mortality statistics, which were linked by the Oxford Record Linkage Study team at the Unit of Health-Care Epidemiology (UHCE), Department of Public Health, University of Oxford. Both datasets cover all of England and include information on all hospital admissions and deaths. The HES dataset provides information on all patients admitted to hospital and whose care is funded by the English National Health Service (NHS). The mortality data are collected by the Office for National Statistics (ONS) and include all deaths that occur in England, whether in hospital or not. These datasets are now briefly described. A more detailed description of the data sources can be found in Appendix 1. A brief description of record linkage methodology can be found in Appendix 2.

Hospital data: Hospital Episode Statistics (HES)

HES records are compiled from data submitted by all NHS-run trusts (including acute hospitals, primary care trusts, and mental health trusts) and independent organisations

that are funded by the NHS. Admissions encompass all public and private patients treated in NHS-run or NHS-funded providers of care in England.

HES information is stored as a collection of records for each financial year of care. The main recording unit is the Finished Consultant Episode (FCE), which is defined as a continuous period of time a patient spends in hospital under care of one consultant at a single healthcare provider.[b] A transfer between consultants or providers generates a new record, and one hospital stay can be composed of multiple FCEs. An FCE record contains over 50 items of data, including the patient's clinical and demographic information.

Diagnoses have been coded in HES according to the International Classification of Diseases, 10th revision (ICD-10) since 1995. Patients' diagnoses as recorded in medical notes are translated into ICD-10 codes by clinical coders. The main discharge diagnosis provides the main reason why the patient was admitted to hospital.[295] The main diagnostic code is assigned at the end of each FCE. Secondary diagnoses describe other conditions relevant to the admission, and may include conditions that patients have at the time of admission or that arose during their stay.[296]

Mortality data: Office for National Statistics (ONS)

The ONS collects all mortality data for England. The conditions mentioned on the death certificate are coded as the underlying cause and contributory causes according to the ICD rules and World Health Organisation (WHO) rules. Mortality statistics are based on the recorded underlying cause of death, defined by WHO as "the disease or injury which initiated the train of morbid events leading directly to death or the circumstances of the

[b] HES Data Dictionary gives several types of healthcare providers: care trust; NHS foundation trust; independent sector provider; primary care trust (PCT); or NHS treatment centre at an independent provider site.

accident or violence which produced the fatal injury" in accordance with the ICD coding rules.[297] The majority of mortality data has been coded by automatic data processing programmes since 1993. Text terms from the death certificates are converted to ICD codes and then selection and modification rules are applied to identify the underlying cause of death using specific software.[c] The ONS switched to ICD-10 codes for cause of death in 2001.

Thesis Design

This research project used a retrospective, longitudinal cohort study design. Raw data extracts of linked hospital and mortality records were provided for the analyses by the UHCE. Two types of records were used: 1) hospital records that contained AMI in any diagnostic field together with any associated death records, regardless of the cause of death, and 2) death records with AMI as the underlying cause of death, without any corresponding linked hospital records for AMI.

Study Population

The study population were residents of England (based on country of residence recorded in HES and ONS records). Individuals who had experienced an AMI event (see definition below) between 1 April 1998 and 31 March 2008 were included. In total, 1,025,228 AMIs occurred among 942,479 individuals. This was the main study cohort from which different sub-cohorts were derived and investigated to answer specific research questions. Hospital and death records that contained invalid sex, age, or dates of admission, discharge or death were excluded from the analyses (<0.1% of all records).

[c] ICD-10 specific software is provided by the National Center for Health Statistics in the USA.

Definitions of key variables

An **AMI event** was defined as either an emergency hospital admission with a main discharge diagnosis of AMI (ICD-10 codes I21 or I22) and a length of stay of more than two days for someone discharged alive, or a sudden death with AMI coded as the underlying cause of death on the death certificate. The two-day criterion for hospital stay was applied to avoid counting suspected AMIs in patients who were discharged home when AMI was not confirmed. For AMI events that were identified from hospital records, any subsequent hospital or death records that were present in the dataset within 30 days following the admission date were considered to relate to the same AMI. All subsequent hospital admissions or a death from AMI that occurred more than 30 days after the initial admission date were considered to be new events. Therefore, one individual could contribute multiple events during the course of the study. **Sudden AMI death** refers to an AMI event identified from a death record with AMI coded as the underlying cause of death for which there is no linked hospital admission for AMI in the previous 30 days. For each person, the first occurrence of a hospital admission for AMI or a death due to AMI in the dataset was recorded as the **index AMI event** on the admission date or death, as applicable.

Length of stay was defined as the total number of days that a patient spent in hospital care during their admission. An **admission** was defined as a continuous period of hospital care for AMI. One admission could be represented by one or more hospital records. If the difference between the discharge date of one hospital record and the admission date of the next hospital record for the same patient was one day or less, the records were considered to represent transfers between consultants and/or hospital providers and were treated as part of the same period of continuous hospital care for AMI.

AMI events were further categorised as fatal or non-fatal. **Fatal AMI** was defined as a sudden AMI death or a hospitalised AMI that had a death record within 30 days of a hospital admission for AMI, irrespective of the cause or place of death. The time to death was calculated by computing the time difference in days between the date of hospital admission for AMI and the date of death, as recorded on the death certificate. For sudden AMI deaths, time to death was set as being equal to zero days.

Definitions of other variables

Comorbidity was defined as any condition listed as a secondary diagnosis alongside the primary discharge diagnosis of AMI in the index admission or in any subsequent admission within 30 days of the date of AMI. For risk adjustments in the statistical analyses, comorbidities were divided into the following groups based on information in the literature[49, 71, 137, 149, 189, 191-195] about the most common comorbidities in AMI patients (ICD-10 codes): 1) cancer (C00-C97); 2) diabetes (E10-E14); 3) respiratory disease (J00-J99); 4) renal disease (N17-N19); and 5) selected cardiovascular diseases (CVD) (cerebrovascular disease (G45, I60-69); hypertension (I10-I15); non-AMI CHD (I20, I23-I25); arrhythmia (I28-I29); heart failure (I50); peripheral vascular disease (I70-I74)).

Procedures were defined as those coronary revascularisation procedures recorded in any operative field in the hospital records for a patient within 30 days of the date of AMI. In HES, procedures are coded according the 4th revision of the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS). Two coronary revascularisation procedures were included in the analyses (OPCS-4 codes): coronary artery bypass graft (CABG) (K40-46) and percutaneous transluminal coronary angioplasty (PTCA) (K49-50 and K75).

Deprivation category was defined as a quintile of the score of Index of Multiple Deprivation (IMD 2004) for lower super output areas or SOAs (each SOA covers a population of about 1,500 people, for a total of 34,378 SOAs in England). IMD score is a weighted composite measure of overall deprivation, derived from a model of multiple socioeconomic deprivation domains describing a particular geographic area, which include: income, employment, health and disability, skills, barriers to housing and services, living environment, and crime.[298] All records in the dataset were ordered and then grouped into quintiles based on the patients' IMD score (derived from postcode of residence of each patient), as recorded in the original HES data field. Higher IMD scores indicate higher levels of deprivation.

Government Office Region (GOR) was defined as a geographic location of residence within England, in the official Regions stipulated by the government, based on the predefined ONS borders. The GOR code, derived from the residential postal code, was obtained from hospital and mortality records. From 1998 to 2007, the following nine GORs were used for England: North East, North West, Yorkshire, East Midlands, West Midlands, East of England, London, South East and South West.

Statistical Analyses

Details regarding statistical analyses can be found in the methods section of each respective chapter. Throughout the thesis, differences in the distributions of key variables were examined using *t* tests of statistical significance for continuous variables and chi-square tests for categorical variables. Significance was accepted at the $p < 0.05$ level; all tests were two-tailed. All analyses were performed using STATA version 11 (Stata Corporation, College Station, Texas, USA).

Dataset preparation for analysis

The raw extract of linked hospital and mortality statistics produced for this thesis was not sufficient, without further exploration, for answering the specified research questions chosen for this thesis. The structure of the records reflected the fact that they had not been designed for research. Extensive data exploration, reorganisation, and preparation for analyses was undertaken. A series of separate studies was conducted to investigate the dataset's characteristics and to define key variables. These studies explored aspects of the data that were important for the analysis and interpretation of the results, and focussed on how to define cases of AMI, how to handle hospital transfers, and the method of grouping records that belonged to the same AMI event. These are now described.

Case ascertainment of AMI

There are several ways to identify and define a case of AMI. These include choices about: 1) ICD diagnosis code (ICD-10 codes I21, new AMI, or I22, subsequent AMI, or both), 2) ICD code position in a hospital record (main diagnosis or secondary diagnosis), 3) ICD code position on a death certificate (underlying cause of death or contributory cause of death), 4) admission type (emergency, elective, or any admission) in a hospital record, 5) length of hospital stay, and 6) AMI history (first or recurrent event).

1. ICD-10 diagnostic code

In the ICD-10 classification system, there are two codes for AMI: I21 for "acute myocardial infarction" and I22 for "subsequent myocardial infarction." In the HES data used for this thesis, the diagnostic code I21 was recorded in 86% of the records and code I22 in 14% of the records. Demographic characteristics of patients admitted for the two

diagnoses were similar. Of the individuals with the hospital records with a main diagnosis of I22, who also had subsequent records with a main discharge diagnosis of AMI, 8.6% of these subsequent records had the main diagnosis recorded as I21, erroneously identifying these cases as first AMI occurrences. Moreover, code I22 is almost never recorded as the underlying cause of death on death certificates, limiting the use of mortality data as the source of information differentiating first and recurrent AMI events. This analysis showed that the use of ICD-10 codes to differentiate first and recurrent events would be unreliable. Therefore, both I21 and I22 codes were included to identify all AMI records. Further analyses were then performed to categorise events into first and recurrent (see section 4 below).

Three-digit ICD diagnostic codes have additional decimal sub-codes, further increasing the complexity and diversity of diagnoses. Due to differences in training, interpretation, and daily practices among hospital providers, physicians, and coders, routine data analyses are likely to be more accurate, albeit less precise, if based on broader three-digit codes.[273, 274] In this thesis, only three-digit (I21 and I22) codes for AMI were used.

2. Diagnostic code position on a hospital record

Hospital records in HES have several diagnostic fields (seven before April 2002, 14 before April 2007, and 20 afterwards). The main discharge diagnostic field represents the main reason for care during a particular hospitalisation episode and secondary diagnostic fields can be used to identify other conditions that are relevant to the period of care. Secondary diagnoses may include complications that arose during the stay, pre-existing chronic comorbidities, or major past events, such as a previous heart attack or stroke. A decision needed to be made about whether to include records that have AMI mentioned only in the main diagnostic field or those with AMI recorded in any diagnostic field. In

the case of acute life-threatening emergencies such as AMI, which usually constitute the reason for admission, the use of the main diagnostic field alone is likely to be sufficient. To investigate this, all records with AMI recorded in any diagnostic field were examined. It was recorded in the primary diagnostic field for 81.9% of records and in a secondary diagnostic field for 18.5% of records. Of the latter, 98% did not have AMI also recorded in the primary diagnostic field. There is thus little overlap in coding of AMI, with only 0.45% of all AMI records having the diagnosis of AMI recorded in both primary and secondary diagnostic fields. Given the acute nature of AMI, records with a diagnosis of AMI appearing only in secondary diagnostic field were excluded in the dataset used for this thesis since they are very likely to be for patients with a history of AMI admitted to hospital for another condition. If a patient experienced an AMI while in hospital, such an acute event would generate another FCE for AMI care by a cardiology team or an ONS death certificate if the patient died suddenly. Therefore, a new AMI event that occurred during a hospital stay would have been captured by a separate record in the dataset.

3. Diagnostic code position on a death certificate

Death certificates have multiple fields to code conditions that have contributed to death. A decision had to be made about whether only to include death records with AMI certified as the underlying cause of death only or to include all death records with AMI recorded in any field. It was therefore necessary to explore the distribution of AMI diagnosis as the underlying or a contributing cause of death. In the ONS mortality dataset used for this thesis, 94% of death records had AMI as the underlying cause of death and 6% had AMI only as the contributing cause of death. While some death certificates with AMI coded as a contributory cause of death could have been true cases of AMI deaths, it is unlikely because the ICD selection and modification rules for coding of death

certificates, used by the ONS, favour specific causes over more general causes (e.g. AMI over CHD). In this thesis, only the underlying cause of death was used in the analyses of sudden deaths without a matching hospital record for AMI.

4. Admission type in hospital records

Hospital records differentiate between a number of admission types, such as emergency, elective, and transfer. With respect to the AMI records used for this thesis, emergency admission was by far the most common type of admission, accounting for 94% of hospital records. While emergency admissions are likely to be true cases of AMI, elective admissions usually refer to patients admitted for a follow-up diagnostic angiogram or a revascularisation procedure. Transfers, which are often emergencies if the main diagnosis is AMI, generally include patients transferred between different NHS institutions and are likely to be driven by the availability of specialist consultants and/or surgical facilities.

Inclusion of emergency admissions only may underestimate the true number of hospital care episodes for AMI, while inclusion of any type of admission may lead to an overestimation of new cases of AMI. In general, admission type is a well-coded field in HES and true instances of new and life-threatening AMIs are very unlikely to be coded as elective admissions. Therefore, a decision was made to include emergency admissions and transfers.

Another important consideration was whether to include patients who were admitted to hospital for an operative procedure or for another condition but subsequently experienced an AMI during hospitalisation, resulting in a new hospital record for AMI with method of admission coded as “emergency.” In the dataset used for this thesis, 9.3% of hospitalised AMI events (or 6.5% of all AMI events, including sudden deaths) actually occurred during the course of a hospital stay that began with admission for another condition. In an

effort to account for all AMI cases that have occurred in the country, AMI events that occurred in patients who were already in hospital were included in the analyses.

5. Length of hospital stay

A number of previous studies from other countries have excluded AMI patients who stayed in hospital for less than a specified number of days (usually one to three) and were discharged alive.[48, 82, 173, 206, 269, 287, 288] The length of stay exclusion criterion has been applied in these studies to avoid counting suspected AMIs in patients who were discharged home when AMI was not confirmed. Current American College of Cardiology/American Heart Association guidelines recommend that hospital care for patients with NSTEMI[d] requires them to be in hospital for at least 48 hours[299] and for patients with STEMI,[e] the recommended stay is longer.[300]

Since the main diagnostic field in a hospital record represents the primary reason for admission, the presence of AMI diagnosis is likely to indicate the actual occurrence of admission for AMI, but it may not necessarily be for a new or acute episode of CHD. Shorter hospital admissions with AMI recorded as the main diagnosis may be for suspected or misdiagnosed AMI cases or follow-up admissions for coronary procedures. Furthermore, diagnostic accuracy for AMI has been shown to be significantly higher for longer hospital admissions, with a PPV of 91% for stays over two days compared with a PPV of 48% for stays of two days or less.[261] In the thesis dataset, 6.4% of all hospital admissions for AMI had a length of stay of two days or less and it was decided to exclude these records from the analyses.

[d] Non-ST elevation AMI, a less severe form of AMI

[e] ST-elevation AMI, a more severe form of AMI

6. AMI history

Individuals can experience more than one AMI event. The first record in a linked hospital and mortality dataset with a diagnosis of AMI does not necessarily represent the true first occurrence of an AMI event, if the first event took place before the data became available in the linked format. Therefore, it is inevitable that a certain proportion of "first" index AMI cases, as identified in this dataset, were actually recurrent AMIs. Erroneous inclusion of prevalent cases with previous clinically recognised AMI prior to the study observation period in the calculation of disease incidence has been described as the "prevalent pool effect."[268] For individual-level analysis of AMI occurrence to be conducted, first and recurrent AMIs for an individual needed to be identified and appropriately classified.

Identification of first-ever events using routine data that are not linked to another clinical database usually requires a disease-free clearance period to avoid overestimation of incident events caused by counting recurrent cases as new events. It was necessary to decide about the optimal number of disease-free years of data needed in order to classify an AMI as first or recurrent. This decision is somewhat arbitrary and is mostly dependent on the time frame for which data are available. It is usually necessary to decide on a trade off between having some degree of uncertainty about prior admissions and having a longer period of follow-up time for identifying outcomes after the event of interest occurs. It has been estimated that most (around 90% or more) of previous AMIs or acute strokes occur within five years of the index event.[237, 268, 301, 302] However, different clearance periods to identify first-ever AMI cases have been used in the past, ranging from one to 16 years, with the most common time interval of four to seven years of no

AMI history: one year;[48, 108] three years;[159, 171] four years;[10, 15, 78, 206] five years; [27, 49, 65, 109, 131] seven years;[35, 83, 110, 162] 10 years;[132] 14 years; [301] and 16 years.[94]

For identification of first-ever events in the thesis dataset, the number and the percentage of cases that would be identified as first-ever and recurrent for different clearance periods were investigated. Using a nine-year clearance period of no recorded AMI (the maximum period available) and the estimated proportion of recurrent events in 2007, calculated to be 14.4%, as the standard, prevalence pooling over shorter clearance periods was investigated by calculating the ratio of first-ever cases to total cases for all years for the period 1998-2007 (Table 4). The estimated proportion of recurrent AMI events identified in 2007 for clearance periods of five, two and zero years (i.e. only linkage within the index year) were reduced to 11.7%, 8.4% and 4.3%.

Table 4. Acute myocardial infarction (AMI) cases estimated as first or recurrent, based on different lengths of clearance period, 2007, England.

Clearance period of no history of prior AMI (years)	**All AMI cases in 2007** (n=88,311)			
	Estimated first AMIs, n	Estimated recurrent AMIs, n	Recurrent AMIs estimated as first AMIs	Estimated % recurrent AMIs
0 (index year, 2007)	84,545	3,766	8,958	4.3
1	82,420	5,891	6,833	6.7
2	80,894	7,417	5,307	8.4
3	79,737	8,574	4,150	9.7
4	78,755	9,556	3,168	10.8
5	77,950	10,361	2,363	11.7
6	77,220	11,091	1,633	12.6
7	76,510	11,801	923	13.4
8	75,803	12,508	216	14.2
9*	75,587	12,724	0	14.4

Notes: Cases occurring in 2007 without any history of prior AMI event since April 1st, 1998 were assumed to be true incident cases. However, it is inevitable that some of them were recurrent cases themselves (after an AMI that pre-dated the dataset) and thus the presented bias may be slightly inflated.

**Since data for 1998 is only available for nine months (1 April – 31 December), a 9-year clearance period stands for a 8.75-year clearance period.*

To get an overall impression of the occurrence pattern of successive AMIs over time, recurrent index AMIs in 2007 were tabulated by time since the date of admission for prior AMI (Table 5). This retrospective analysis revealed that, of the individuals who experienced a prior AMI within nine years before the index event in 2007, 30% had experienced it in 2007, 17% one year before, 12% two years before, 9% three years before and only 1.7% nine years before. Cumulatively, of those individuals whose index AMI in 2007 was a recurrent event and who had a record of a prior AMI in the last nine years, 81% had the prior AMI within five years of 2007. Thus, the percentage of "false positive" first-ever AMIs, i.e. people identified as "first" who have had an AMI more than nine years before 2007, is likely to be small. The same retrospective analysis was performed by age group and the findings for each were similar to the overall results.

Table 5. Distribution of recurrent acute myocardial infarction (AMI) cases in 2007, based on the year of occurrence of previous AMI, England.

No. of years prior to 2007 when last AMI occurred	No. of recurrent AMIs in 2007	%	Cumulative %
0 (index year, 2007)	3,766	30	
1	2,125	17	46
2	1,526	12	58
3	1,157	9.1	67
4	982	7.7	75
5	805	6.3	81
6	730	5.7	87
7	710	5.6	93
8	707	5.6	98
9*	216	1.7	100
Total	12,724	100	

**Since data for 1998 is only available for nine months (1 April – 31 December), a 9-year clearance period stands for a 8.75-year period.*

Overall, the dataset shows that a substantial proportion (about one in six) of AMI events within a given year are in fact recurrent cases with a history of previous hospitalisation(s) for AMI. This highlights the need for a clearance period when hospital data are used to identify first-ever cases. For the estimation of true incidence, the longer the clearance period, the more reliable are the estimates. In this thesis, incidence was estimated for 2007 (Chapter 7), the latest complete year of data available, using a clearance period of nine years, the longest period for which data could be retrospectively analysed. In Chapter 5, however, a clearance period of five years was used instead, to allow for long-term follow up after the AMI.

Inter-hospital transfers and grouping hospital records into admissions

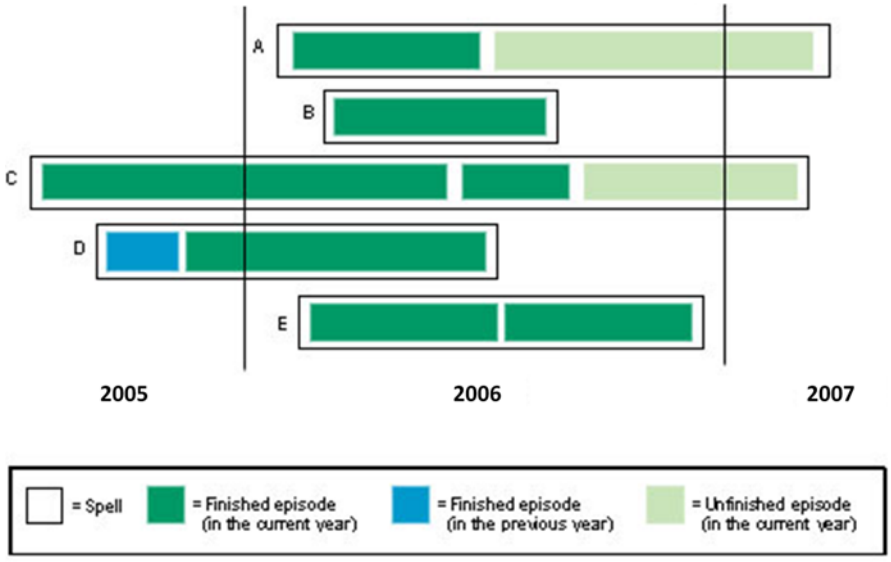
To identify distinct AMI events, several nuances regarding the way hospital records are compiled need careful consideration. In HES, every change in consultant or hospital provider generates a new record (FCE, as described above), even though the patient remains under continuous hospital care. Consequently, raw HES records are not appropriate to identify new AMI events: transfers between consultants or providers result in double-counting of patients and cause an overestimation of the hospital incidence rate of AMI and an underestimation of in-hospital mortality rate.[303] In addition, failing to account for transfers influences the calculation of the total length of stay under hospital care, in turn affecting the number of cases that are excluded from the analysis.

To avoid double-counting of patients and AMIs, it is important to define, identify, and account for transfers between consultants and hospital providers. Failure to do so may result in erroneous trends and conclusions. For example, in response to a report highlighting rising hospitalisations for AMI as a warning sign of a new CHD epidemic in

New Zealand,[304] Chan et al. showed that even though total hospitalisations increased by 8% per year, it was driven by an increase in hospital transfers, readmissions, and changes in diagnostic criteria, rather than changes in the underlying AMI incidence.[237]

To combine individual records into admissions, hospital records belonging to the same period of hospital stay were grouped together. An admission is a constructed field that represents a continuous in-patient period of hospital care under the NHS-run or NHS-funded care, irrespective of consultant change or transfer between hospital providers. Each new admission may therefore have several associated hospital records. Figure 1 illustrates the relationship between FCEs and admissions (termed spells in the Figure). Further, each new AMI event could be represented by more than one hospital admission if several separate hospital admissions took place within 30 days of the index admission.

Figure 1. Illustration of episodes and hospital admissions (spells) in Hospital Episode Statistics.



Adapted from HESOnline: How do you spell that? http://www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=1072 (Accessed August 2011)

In brief, once all of FCE records belonging to an individual patient were identified and grouped, some were combined together into one admission record to represent a continuous period of patient care for AMI within the NHS. To achieve this, all FCE records for each individual were sorted in chronological order by admission date and the correct episode (FCE) sequence number. Adjacent records were then combined into one admission if the following were true:

1. Patient identification number is the same;
2. Dates of admission and discharge are valid; and
3. The difference between discharge date of one record and admission date of next record is less than or equal to one day.

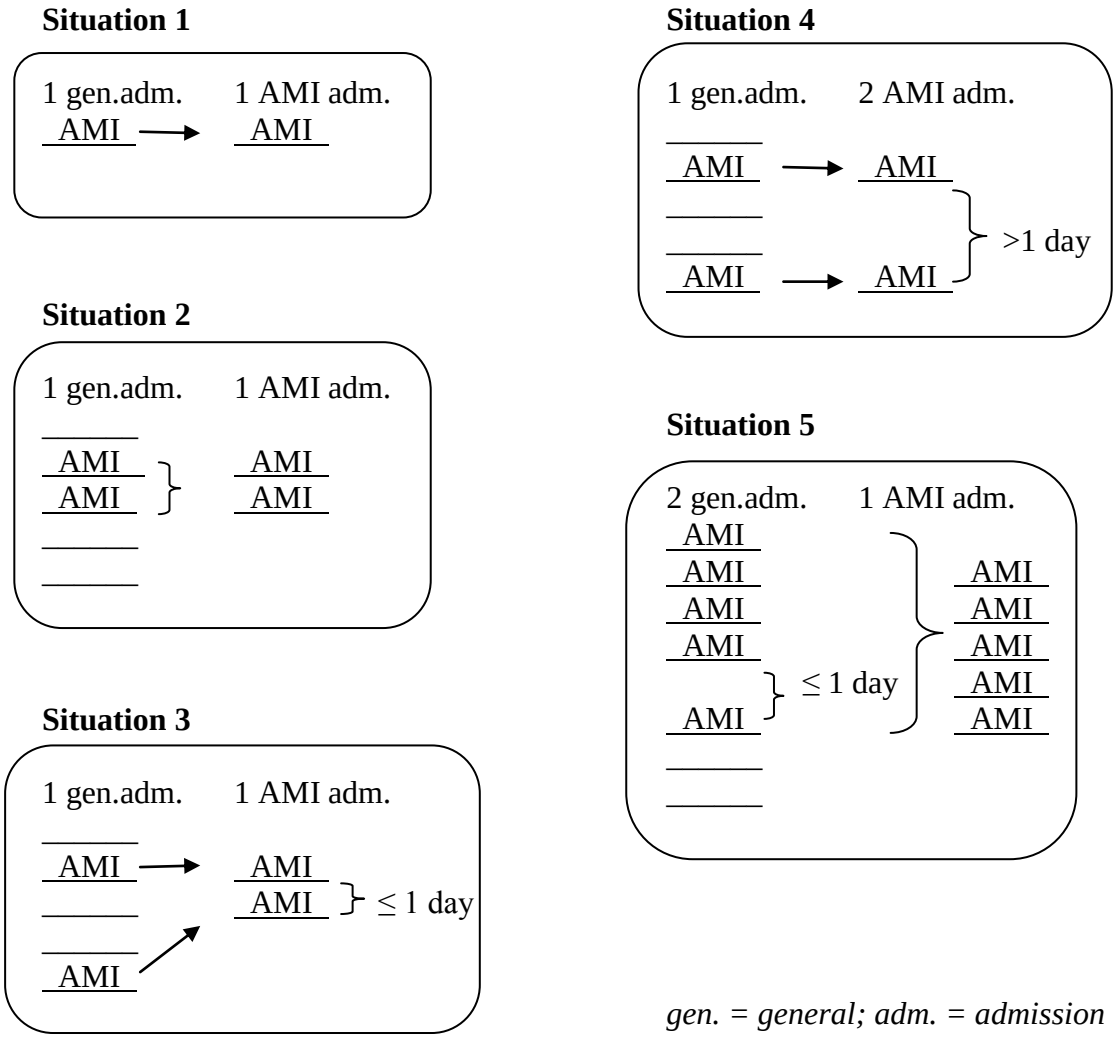
There is another nuance that needs consideration in the construction of admissions. During one hospital stay, a patient can have a series of FCEs, and not all would necessarily have the same primary diagnosis – it depends if the patient had more than one medical problem, suffered from a complication, or had to undergo a surgical procedure during their hospital stay, among other possibilities. Depending on the research questions, a study of a single condition could be based on all hospital records for a particular patient or solely on hospital records that have the condition of interest in the main diagnostic field. Grouping hospital records into admissions can therefore be done in two ways: 1) a continuous hospital stay including all contributing records irrespective of the main diagnoses (general admissions; the current structure of HES) or 2) a continuous hospital stay including all and only contributing records that have the diagnosis of interest (disease-specific admissions). The resultant constructed admission will be different depending on the approach and this decision has to be made early in the

research process. In this thesis, the second approach was used and AMI admissions were generated from grouping only those hospital records for an individual that had the main diagnosis of AMI. To illustrate, Figure 2 shows how AMI-specific admissions were constructed for this thesis from the HES general admissions.

In summary, the general steps that were followed to prepare HES data for analysis were:

1. Obtaining an extract of hospital records with the diagnosis of AMI;
2. Grouping records into continuous periods of hospital stay for AMI (i.e. generating AMI-specific admissions); and
3. Grouping AMI-specific admissions into distinct AMI events.

Figure 2. Construction of AMI-specific admissions from HES general admissions.



gen. = general; adm. = admission

Solid line represents one hospital record, or FCE. "AMI" above the solid line indicates the main diagnosis of AMI and a blank indicates another main diagnosis. In each diagram, the left column shows the current structure of general admissions in HES and the right column shows AMI-specific admissions constructed for this thesis.

Other technical considerations

Before definitive analyses could take place, it was necessary to perform extensive data cleaning. In particular, key variables were examined in detail for accuracy and any errors were corrected before proceeding with data analysis. In this thesis, these variables were:

1. Admission date
2. Date of discharge
3. Date of death
4. Date of birth
5. Sex
6. Age

There were some inconsistencies in the recording of key data fields that was not expected to change in a set of records belonging to the same person, such as their sex, date of birth, and date of death. In such cases, the modal value[f] of the variable was calculated and assigned to all of the patient's records. Regarding time-changing key variables, such as country of residence, deprivation category, and comorbidities, the same approach was used, but the calculation of modal value was performed for shorter time frames. If some records had a missing or invalid age, the correct age was calculated by subtracting the admission date from the date of birth, in years.

The process of grouping hospital records was not necessarily straightforward. Negative time intervals between subsequent records were uncommon, but occurred – they were a result of transfers within one hospital provider or valid, but incorrectly coded discharge or admission dates. It was therefore possible for some records to partially overlap or become embedded in others. Such records were examined in detail and dates adjusted based on episode order and dates of previous/preceding records.

[f] In the case of an equal split in the occurrences of two (or more) different values of a variable, one value was chosen.

Conclusion

Fundamentally, the issues that arise when using routinely collected administrative data for research purposes reduce to the relative balance between a large and representative sample size, unselected and population-based cohort, data availability, and low cost, weighted against any potential weaknesses in the structure and quality of data. Routine national hospital and mortality statistics are comprehensive sources of population-level data on disease occurrence and healthcare service use in England, allowing for a wide range of research questions to be answered. Notwithstanding the benefits, the array of analytical challenges and problematic aspects inherent to routine administrative datasets should not be underestimated. However, with thorough data cleaning and exploration, accompanied by realistic and relevant research objectives, clear case definitions, appropriate methodology and cautious interpretation, linked hospital and mortality data offer great potential for research and can be used to make valuable contributions to knowledge about the epidemiology of AMI (and other conditions).

CHAPTER 3: TRENDS IN AMI EVENT RATES, 1999-2007

This chapter provides estimates of acute myocardial infarction event rates in England from 1999 to 2007 by sex, age, and Government Office Region. Rates of occurrence of all identifiable AMI events – hospitalisations for AMI and sudden AMI deaths – are reported. Differences between men and women and different age groups are discussed.

Introduction

Although changes over time in AMI mortality and case fatality have been extensively researched, less is known about the trends in the occurrence of new AMI events, both fatal and non-fatal. The event rate is more difficult to study: analyses of occurrence of events are more complex, and fewer datasets are available that would be large enough and include all the necessary information. Existing studies that have examined event rate of new AMIs and incidence of first-ever AMIs over time have reported general declines in many developed countries,[3, 10, 14, 24, 69, 70] including the UK.[68, 73, 74]

However, the current estimates of trends in AMI event rate for the UK are based on relatively small studies,[68, 73, 74] which may not necessarily be representative of the whole population. Further, because of their small size, stratification is problematic and these studies do not generally provide information by population sub-groups. At the moment, it is unknown whether, and how, any changes in AMI occurrence over the past decade in England as a whole differ between men and women, different age groups, different geographic regions, and how changes in hospitalised AMI events compare with changes

in sudden AMI deaths. This information is important for describing and quantifying the changing epidemiology of AMI in England, planning health care services and setting public health policies.

The objectives of this chapter are:

1. To investigate trends in population-based overall AMI event rates in England from 1999 to 2007, by sex, age, and Government Office Region (GOR);
2. To report trends in population-based hospitalised AMI event and sudden AMI death rates from 1999 to 2007 by sex and age; and
3. To compare changes in event rates between sexes, age groups, and GOR.

Methods

Study population

Residents of England who had an AMI event between 1 January 1999 and 31 December 2007 were included. The same definitions of AMI event, sudden AMI death, hospital admission, fatal and non-fatal AMI, and Government Office Region as described in Chapter 2 (Methods) were used. For this chapter, AMI events were not classified into first or recurrent because the limited time period covered by the data did not allow for the use of a clearance period to distinguish between them within each year.

Statistical analyses

The event rate was defined as the rate of occurrence of new AMI events. The event rate was examined for all AMIs and separately for hospitalised AMIs and sudden AMI deaths.

All rates were calculated per 100,000 population of England by sex, age group, and Government Office Region using the mid-year population estimates published by the Office for National Statistics.[19] Rates were directly age-standardised to the European Standard Population. The 95% confidence intervals were estimated assuming that the observed number of events followed a Poisson distribution.

Time trends were estimated using log-linear Poisson regression of age-standardised as well as age- and sex-specific rates, with calendar year as an independent variable. The average annual percentage change in event rates was calculated from the beta coefficient for the calendar year in the regression models, using $-100*[1-\exp(\beta)]$ as an approximation. Overall percentage changes between 1999 and 2007 were expressed as relative, rather than absolute, changes from 100%, according to the following formula: overall decline from 1999 to 2007 = – (1-(rate in 2007/rate in 1999))*100.

Results

Study cohort

Between 1 January 1999 and 31 December 2007, a total of 914,763 AMI events occurred among 842,835 individuals. Table 6 shows the characteristics of all AMIs during the study period. Of all the events, 61% occurred in men; 41% were fatal; 30% were sudden AMI deaths; and 74% occurred in individuals aged 65 and older. Women were significantly older than men at both hospital admission for AMI (76 versus 68 years, $p<0.001$) and sudden AMI death (80 versus 73 years, $p<0.001$). The percentage of all events that were sudden AMI deaths was slightly higher in women than men (32% versus 28%, $p<0.001$).

Table 6. Baseline characteristics of acute myocardial infarction (AMI) events by sex, 1999-2007, England.

Characteristics	Total AMIs	Men			Women		
		All AMIs	Fatal AMIs		All AMIs	Fatal AMIs	
	n	n	n	% all AMIs	n	n	% all AMIs
Total	914,763	554,916	211,447	38	359,847	166,459	46
Type of event							
Hospital admission	643,656	398,599	55,130	14	245,057	51,669	21
Sudden AMI death	271,107	156,317	156,317	(100)	114,790	156,317	(100)
Age (years)							
Mean	72.3	69.2	73.9	-	77.1	80.3	-
Median	74	71	76	-	79	82	-
0-29	1,035	792	170	22	243	74	31
30-54	99,555	82,242	14,354	18	17,313	3,261	19
55-64	139,760	107,359	26,976	25	32,401	8,081	25
65-74	221,532	147,087	54,679	37	74,445	27,301	37
75-84	289,754	156,267	78,492	50	133,487	65,873	49
85+	163,127	61,169	36,776	60	101,958	61,869	61
Government Office Region							
East England	97,747	60,932	21,701	36	36,815	16,465	45
East Midlands	83,728	51,454	18,266	36	32,274	13,610	42
London	84,860	51,618	20,969	41	33,242	16,777	51
North East	60,599	35,194	12,301	35	25,405	10,316	41
North West	151,684	90,068	34,685	39	61,616	28,179	46
South East	130,646	79,466	30,134	38	51,180	24,506	48
South West	98,697	59,975	23,403	39	38,722	18,474	48
West Midlands	98,652	61,442	24,100	39	37,210	17,851	48
Yorkshire	107,403	64,347	25,727	40	43,056	20,140	47

Trends in AMI event rates

Table 7 shows the age-standardised annual sex-specific rates of occurrence for all AMI events. There was a general decline in the event rate for both men and women. From 1999 to 2007, the age-standardised overall AMI event rate per 100,000 population fell from 254 (95% CI: 252-256) to 174 (95% CI: 173-176) in men and from 105 (95% CI:

104-106) to 74 (95% CI: 73-75) in women. Higher event rates were observed in men compared with women in all age groups at each year over the study period.

Table 7. Age-standardised overall event rates for acute myocardial infarction (AMI) by year and sex, 1999-2007, England.

Year	Men				Women			
	Total AMI cases, n	Event rate (per 100,000) rate	95% CI		Total AMI cases, n	Event rate (per 100,000) rate	95% CI	
1999	68,880	254	252	256	44,325	105	104	106
2000	65,814	240	238	241	42,167	99	98	100
2001	64,030	229	227	231	40,733	94	93	95
2002	64,414	227	225	228	41,638	94	94	95
2003	63,026	218	217	220	41,493	92	92	93
2004	61,594	211	209	212	40,119	89	88	89
2005	58,210	195	194	197	38,434	84	83	85
2006	55,328	183	182	185	36,247	78	77	79
2007	53,620	174	173	176	34,691	74	73	75

Table 8 shows age-specific and overall trends in rates for men and women. A declining event rate was seen in all age groups and for both sexes. Comparing 1999 with 2007, overall event rates fell by 31% in men and by 30% in women. The age-standardised average annual change was -4.4% (95% CI: -6.0 to -2.7) in men and -3.9% (95% CI: -6.4 to -1.3) in women. For age-specific trends, the greatest overall declines between 1999 and 2007 in AMI event rates occurred in men and women aged 65-74 years (39.8% and 41.6%, respectively) and the smallest overall declines occurred in men and women aged 85 years and older (10.5% and 6.9%, respectively).

Table 8. Average annual changes in the overall acute myocardial infarction event rates by age and sex, 1999-2007, England.

Age group (years)	Event rate (per 100,000)		Overall change	Average annual change			
	1999	2007	(%)	%	95% CI		p-value
Men							
30-54	13	10	-24	-3.3	-10.4	4.4	0.393
55-64	55	35	-36	-5.3	-8.9	-1.6	0.005
65-74	104	63	-40	-5.9	-8.5	-3.2	<0.001
75-84	174	120	-31	-4.2	-6.1	-2.2	<0.001
85+	241	216	-11	-0.8	-2.4	0.8	0.320
All ages	254	174	-31	-4.4	-6.0	-2.7	<0.001
Women							
30-54	2	2	-12	-1.2	-16.4	16.7	0.884
55-64	17	10	-39	-6.3	-12.7	0.6	0.074
65-74	47	28	-42	-6.0	-9.8	-2.0	0.004
75-84	98	69	-29	-3.7	-6.3	-1.0	0.007
85+	163	152	-7	-0.2	-2.1	1.8	0.873
All ages	105	74	-30	-3.9	-6.4	-1.3	0.004

Table 9 shows the event rates for hospitalised AMIs and sudden AMI deaths by year for men and women. Figure 3 and Figure 4 illustrate the changes in rates over time for men and women, respectively.

Table 9. Age-standardised event rates for hospitalised acute myocardial infarction (AMI) events and sudden AMI deaths by year and sex, 1999-2007, England.

Year	Men				Women			
	Total AMI cases, n	Event rate (per 100,000)			Total AMI cases, n	Event rate (per 100,000)		
		Rate	95% CI			Rate	95% CI	
Hospitalised AMIs								
1999	45,640	172	170	173	26,518	68	67	69
2000	44,563	166	164	167	26,287	66	66	67
2001	44,961	164	162	165	26,684	65	64	66
2002	46,180	165	164	167	28,197	67	66	68
2003	45,665	161	159	162	28,558	67	66	67
2004	45,696	158	157	160	28,700	66	65	67
2005	43,378	148	146	149	27,930	63	62	64
2006	41,622	140	139	141	26,531	60	59	60
2007	40,894	135	134	136	25,652	57	56	57
Sudden AMI deaths								
1999	23,240	82	81	83	17,807	37	37	38
2000	21,251	74	73	75	15,880	33	32	33
2001	19,069	65	64	66	14,049	29	28	29
2002	18,234	62	61	62	13,441	27	27	28
2003	17,361	58	57	59	12,935	26	25	26
2004	15,898	52	51	53	11,419	23	22	23
2005	14,832	48	47	48	10,504	21	20	21
2006	13,706	43	42	44	9,716	19	18	19
2007	12,726	39	39	40	9,039	17	17	17

Figure 3. Age-standardised acute myocardial infarction (AMI) event rates in men, 1999-2007, England.

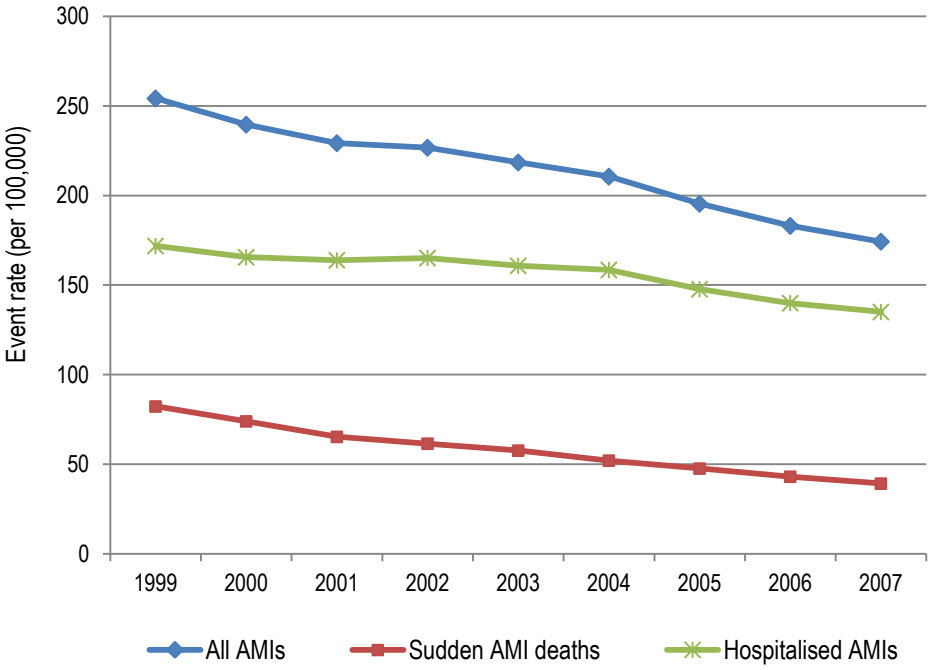
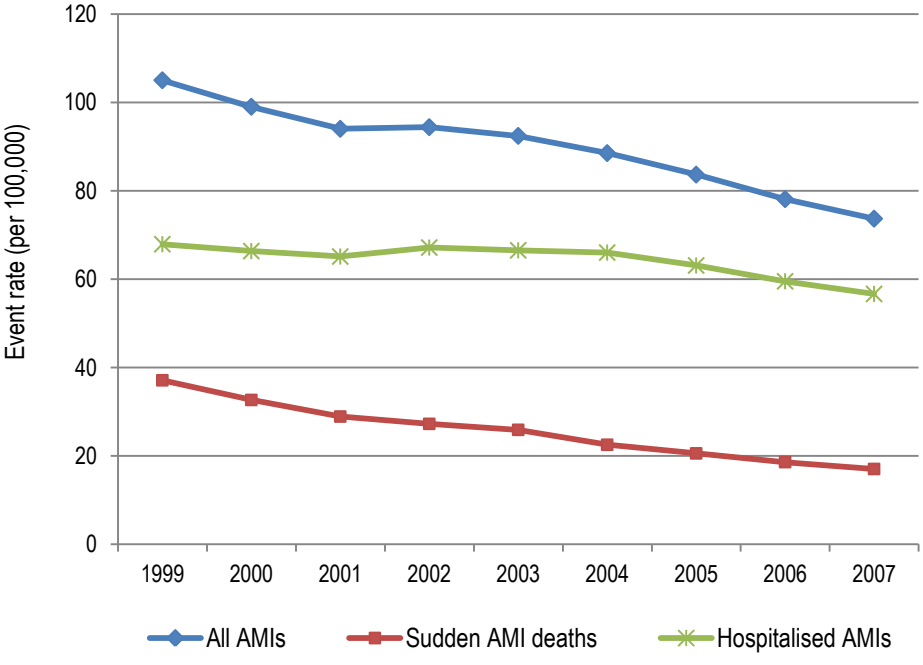


Figure 4. Age-standardised acute myocardial infarction (AMI) event rates in women, 1999-2007, England.



The decline in AMI event rates was observed for both hospitalised AMI events and sudden AMI deaths, albeit at different rates. Table 10 shows age-specific and all-ages trends for hospitalised AMI event rates for men and women. Between 1999 and 2007, the event rates decreased in most age groups, but almost all the changes were not significant. However, there was a significant increase in hospitalised AMI occurrence in the age group of 85 years and older: 3.9% (95% CI: 1.7-6.2) in men and 4.9% (95% CI: 2.2-7.7) in women. The age-standardised hospitalised AMI event rate per 100,000 population declined in men by 21.4% from 172 (95% CI: 170-173) to 135 (95% CI: 134-136) and in women, it declined by 16.6% from 68 (95% CI: 67-69) to 57 (95% CI: 56-57). The age-standardised average annual changes in hospitalised AMI rates were -2.8% (95% CI: -4.7 to -0.8) in men and -1.7% (95% CI: -4.8 to 1.4) in women.

Table 11 shows age-specific and all-ages trends for sudden AMI death rates for men and women. Between 1999 and 2007, significant declines were observed for all age groups except for men aged 30-54 years and women aged 30-64 years. The average annual changes were smallest in the youngest and the oldest age groups and largest in the age group of 65-74 years: -10.1% (95% CI: -14.8 to -5.2) in men and -11.4% (95% CI: -18.5 to -3.6) in women. The age-standardised sudden AMI death rate per 100,000 population decreased in men by 52.3% from 82 (95% CI: 81-83) to 39 (95% CI: 39-40) and in women, it fell by 54.1% from 37 (95% CI: 37-38) to 17 (95% CI: 17-17). The age-standardised average annual changes in sudden AMI death rates were -8.6% (95% CI: -11.6 to -5.4) in men and -8.9% (95% CI: -13.4 to -4.1) in women.

Table 10. Average annual changes in the hospitalised acute myocardial infarction event rates by age and sex, 1999-2007, England.

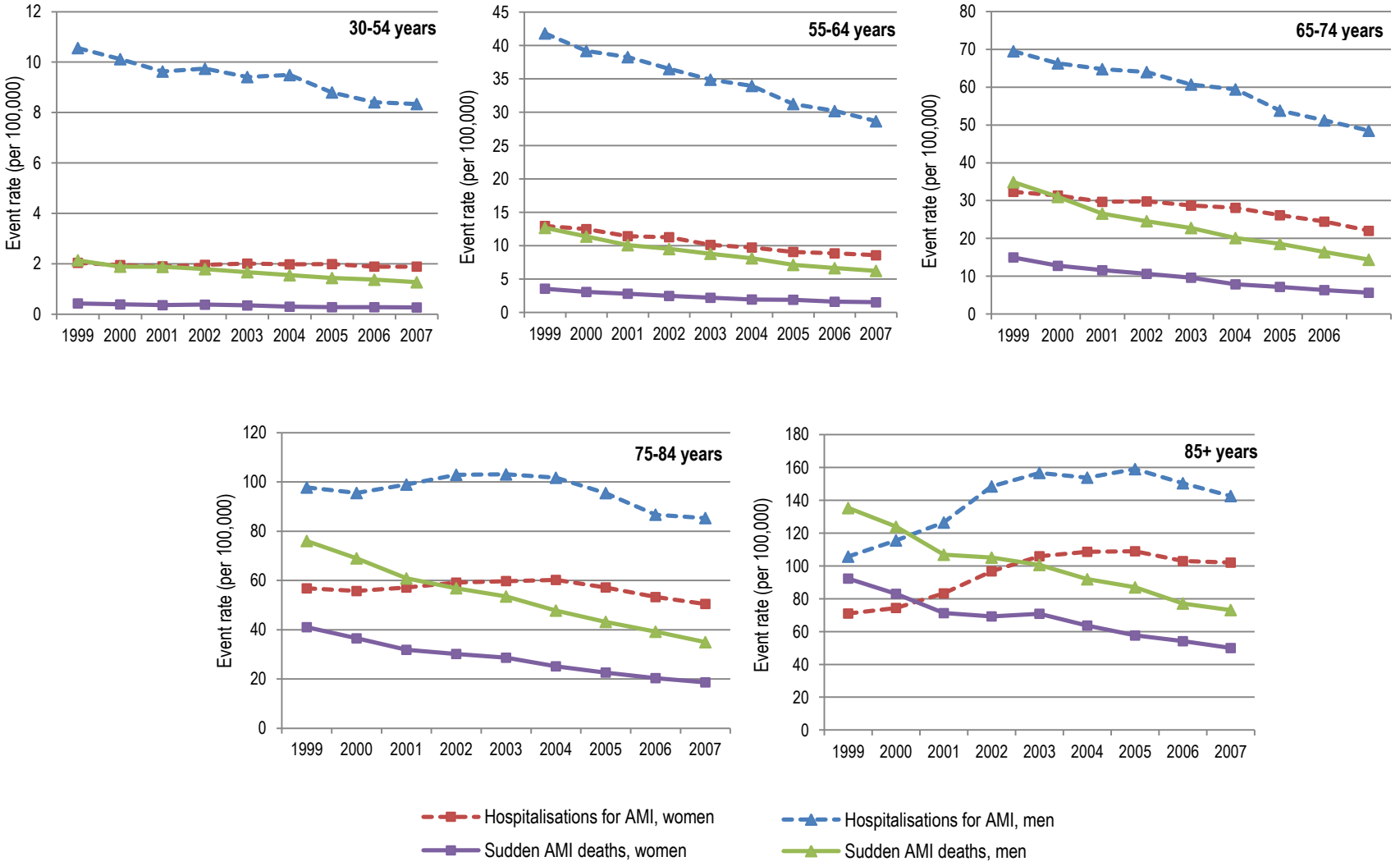
Age group (years)	Event rate (per 100,000)		Overall change	Average annual change			
	1999	2007	(%)	%	95% CI		p-value
Men							
30-54	11	8	-21	-2.8	-10.5	5.6	0.503
55-64	42	29	-32	-4.5	-8.5	-0.3	0.036
65-74	70	49	-30	-4.3	-7.4	-1.1	0.009
75-84	98	85	-13	-1.4	-4.0	1.1	0.268
85+	106	143	35	3.9	1.7	6.2	<0.001
All ages	172	135	-21	-2.8	-4.7	-0.8	0.006
Women							
30-54	2	2	-7	-0.5	-17.0	19.2	0.957
55-64	13	9	-34	-5.4	-12.5	2.4	0.167
65-74	32	22	-32	-4.1	-8.6	0.6	0.085
75-84	57	51	-11	-0.9	-4.2	2.5	0.589
85+	71	102	44	4.9	2.2	7.7	<0.001
All ages	68	57	-17	-1.7	-4.8	1.4	0.281

Table 11. Average annual changes in sudden death rates for acute myocardial infarction by age and sex, 1999-2007, England.

Age group (years)	Sudden death rate (per 100,000)		Overall change	Average annual change			
	1999	2007	(%)	%	95% CI		p-value
Men							
30-54	2	1	-41	-6.0	-22.9	14.5	0.539
55-64	13	6	-51	-8.5	-16.1	-0.3	0.042
65-74	35	14	-59	-10.1	-14.8	-5.2	<0.001
75-84	76	35	-54	-9.0	-12.1	-5.7	<0.001
85+	135	73	-46	-7.1	-9.5	-4.7	<0.001
All ages	82	39	-52	-8.6	-11.6	-5.4	<0.001
Women							
30-54	0	0	-37	-5.8	-39.3	46.0	0.789
55-64	4	2	-57	-10.2	-24.2	6.3	0.212
65-74	15	6	-62	-11.4	-18.5	-3.6	0.005
75-84	41	19	-55	-9.2	-13.5	-4.7	<0.001
85+	92	50	-46	-6.9	-9.7	-3.9	<0.001
All ages	37	17	-54	-8.9	-13.4	-4.1	<0.001

The graphs in Figure 5 illustrate changes over time in hospitalised AMI event rates and sudden AMI death rates by sex and age (one graph per age group). The graphs clearly show that both rates declined for men and women and across all age groups, with one exception: the rate of hospitalised AMI events in men and women aged 85 years and older has increased over the study period.

Figure 5. Age-specific acute myocardial infarction (AMI) event rates by sex and type of AMI event, 1999-2007, England.



Trends by Government Office Region

From 1999 to 2007, the age-standardised overall AMI event rate declined in all GORs (Figure 6 and Table 12). The absolute event rates remained generally higher in the north and lower in the south throughout the study period, but the differences in regional rates decreased over time, driven by the slightly higher annual rates of decline in the north. The greatest overall decrease in AMI event rate per 100,000 population occurred in the North East and the smallest overall decline occurred in the East Midlands. Comparing 1999 with 2007, overall AMI event rates fell by 44% in the North East and by 22% in the East Midlands; the age-standardised average annual changes were -6.4% (95% CI: -8.1 to -4.7) and -3.1% (95% CI: -5.2 to -1.0), respectively. However, the North East was an exception relative to other GORs, with a very sharp decline between 2003 and 2007.

Figure 6. Age-standardised overall acute myocardial infarction event rates by Government Office Region, 1999-2007, England.

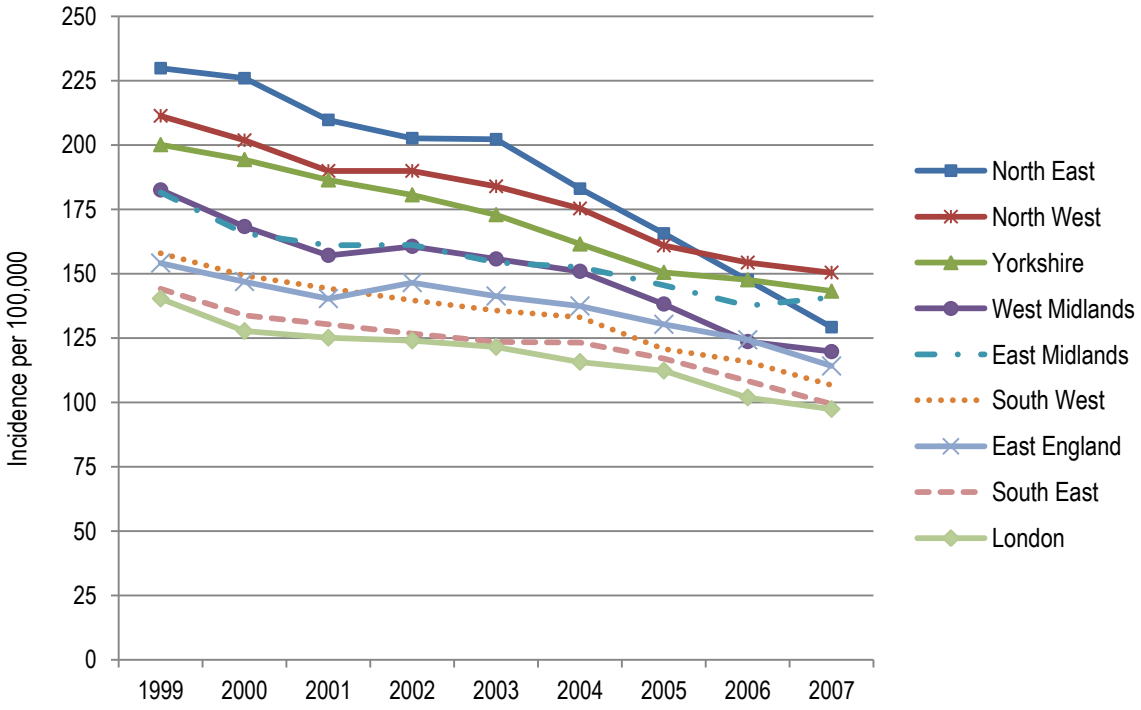


Table 12. Changes in the age-standardised overall acute myocardial infarction event rates by year and Government Office Region, 1999-2007, England.

Government	Event rate (per 100,000)									Overall	Average annual change			
Office Region	1999	2000	2001	2002	2003	2004	2005	2006	2007	decline (%)	%	95% CI		p-value
East England	154	147	140	147	141	137	130	124	114	26	-3.0	-5.0	-1.0	0.003
East Midlands	182	166	161	161	154	153	146	138	141	22	-3.1	-5.2	-1.0	0.005
London	140	128	125	124	122	116	112	102	97	31	-3.9	-6.1	-1.6	0.001
North East	230	226	210	203	202	183	166	148	129	44	-6.4	-8.1	-4.7	<0.001
North West	211	202	190	190	184	175	161	154	150	29	-4.2	-6.0	-2.3	<0.001
South East	144	134	130	127	124	123	117	108	99	31	-3.8	-6.0	-1.6	0.001
South West	158	149	144	140	136	133	121	116	107	32	-4.4	-6.5	-2.3	<0.001
West Midlands	183	168	157	161	156	151	138	124	120	34	-4.7	-6.6	-2.7	<0.001
Yorkshire	200	194	186	181	173	162	151	148	143	28	-4.4	-6.2	-2.5	<0.001

Discussion

This chapter reports on recent trends in AMI event rates between 1999 and 2007 in England. The rates declined for both sexes, almost all age groups, and all Government Office Regions. The age-standardised overall AMI event rate fell by around one third, while the hospitalised AMI event rate declined by around one fifth, and sudden AMI death rate fell by over half. Trends differed by age group: the greatest annual declines in overall event rate occurred in middle-aged individuals and the smallest declines occurred in the youngest and oldest individuals. The rate of occurrence of hospitalised AMI actually increased among men and women aged 85 years and older. Overall, these results suggest that there are fewer new AMI events in England each year, but relatively more are occurring among older individuals.

This study demonstrates that the decline in the AMI event rate in the UK, observed in previous decades,[5, 49, 73-75] has continued into the mid- to late 2000s. In accordance with previous research,[9, 15] the largest decreases in AMI occurrence were observed among middle-aged individuals. In contrast, the annual declines in event rate were slower and not statistically significant for men and women aged 30-54 years and 85 years and older. Similar findings of no improvement in incidence of AMI among men and women aged 35-54 years between 1996 and 2007 were recently reported for Australia.[305] For younger individuals, the rising rates of obesity and diabetes may be potential contributing factors to a leveling of event rate,[44, 202, 305, 306] while the shift in the first presentation of disease from middle age to older age groups is likely to contribute to the lack of significant decline, and in fact an increase, in the occurrence of AMI in the elderly.[38, 74, 176]

The estimates of the average annual change in the overall event rate are higher than those derived from The Health Information Network (THIN), a primary care database comprising patient data from general practices across the UK.[68] The THIN study reported that the average annual changes in incidence of first AMI in England were 3.1% for men and 2.8% for women for a period of time from 1996 to 2005, which are lower than 4.4% for men and 3.9% for women found in this study. The lower THIN estimates can be explained by the fact that they are produced for first AMI events only and come from a dataset that has a recognised weakness in under-recording of patient deaths.[68] Therefore, sudden AMI deaths were likely to have been underestimated. Furthermore, THIN relies on voluntary participation of general practices and represents only 3% of the UK population[68] and its generalisability can thus be questioned.

The British Regional Heart Study (BRHS) that examined changes in AMI incidence over 25 years from 1978 in a cohort of middle-aged men reported that the age-adjusted risk of AMI decreased by 3.8% per year, giving an overall decline of 62% over the time period of the study.[75] This rate of change is strikingly similar to the one reported in this study for men. BRHS attributed 46% of the decline in AMI incidence to improvements in cardiovascular risk factors, particularly reductions in smoking, mean systolic blood pressure, and mean non-HDL cholesterol levels.

While the exact contribution of changes in risk factors may not be the same for all ages and both sexes, it is very likely that the overall declining AMI event rates in England are driven, at least in part, by the improving cardiovascular risk factor profile of the underlying population. During the study period, national survey data for England indicate that the prevalence of the main cardiovascular risk factors has decreased between 1998

and 2007. Prevalence of smoking has declined from 27% to 21%,[g] prevalence of high systolic blood pressure (defined as pressure over 140mmHg) has decreased from 41% to 31% men and from 33% to 29% in women, and prevalence of individuals with raised total blood cholesterol levels (defined as total cholesterol concentration of ≥ 5.0mmol/L of blood) has also fallen, from 66% to 58% in men and from 67% to 61% in women.[61] In addition, more people were physically active, drinking less alcohol and consuming less saturated fat, sugars, and salt in 2007 compared with late 1990s.[61] Also, drug prescriptions for prevention and treatment of CHD have risen throughout the 2000s.[61, 141, 148] However, the prevalences of diabetes and obesity have increased,[61] and if these trends continue, the favourable developments in AMI event rate could be negatively affected.

The absolute event rates remained generally higher in the north of England and lower in the south of England during the study period. However, regional differences decreased over time, suggesting that while the north-to-south gradient in disease occurrence still persists, it has narrowed over the last decade. Declines in AMI occurrence were observed throughout England, implying that similar improvements can be achieved in reducing the number of new events even if the actual event rates differ between populations. The reasons for the rapid decline in AMI occurrence in the North East between 2003 and 2007 are unclear. This fall in event rate coincides with a period when there was an increase in the number of revascularisation procedures and a decrease in premature deaths from CHD in this region,[307] but it is not clear how changes in hospital treatment could have affected the rates of occurrence of new events. The fall in premature deaths is the more likely explanation, but more research on this is needed.

[g] In Great Britain

Conclusion

This study provides recent information on trends in AMI event rates in England between 1999 and 2007. The results indicate that the rates of occurrence of hospitalisations for AMI and sudden AMI deaths have declined for both sexes, almost all age groups, and all Government Office Regions. Middle-aged men and women experienced the greatest declines in all AMI event rates, while individuals aged 85 years and older experienced an increase in the hospitalised AMI event rate over the study period. The findings suggest a decreasing rate of AMI occurrence in England in general, but a possible shift of the disease towards older individuals.

CHAPTER 4: TRENDS IN AMI CASE FATALITY RATES, 1999-2007

This chapter provides estimates of 30-day case fatality rates for acute myocardial infarction in England from 1999 to 2007 by age, sex, and Government Office Region. Overall case fatality, hospitalised case fatality, and sudden AMI death rates are reported. Differences between men and women and different age groups are discussed.

Introduction

Short-term case fatality is a useful indicator of the severity of disease in a population, its progression, and, for people who survive long enough to reach medical care, the impact of treatment. A reduction in case fatality in patients hospitalised for AMI has been documented in many developed countries,[10, 14, 24, 108, 110, 117-119] including the UK,[49, 68, 121, 208, 308] since the late 1970s. However, fewer studies have been conducted of overall case fatality, which includes AMI deaths that occur without an admission to hospital. It is important to have both measures because while deaths following hospitalisations reflect, among other factors, the quality and effectiveness of medical treatment, sudden deaths serve as manifestations of disease progression and the effectiveness of preventive practices.

There is limited recent information on population-level national estimates of case fatality after AMI for England. Currently, it is unknown whether, and how, any changes in AMI case fatality over the past decade in England compare between men and women, different

age groups, different geographic regions, and for hospitalised individuals compared with all AMI cases, including sudden deaths.

The objectives of this chapter are to:

1. To investigate trends in population-based overall case fatality rates for AMI in England from 1999 to 2007, by sex, age, and Government Office Region (GOR);
2. To report trends in population-based hospitalised case fatality and sudden death rates for AMI in England from 1999 to 2007 by sex and age; and
3. To compare changes in case fatality rates between men and women, age groups, and GORs.

Methods

Study population

Residents of England who had an AMI event between 1 January 1999 and 31 December 2007 were included in the study. The same definitions of AMI event, sudden AMI death, hospital admission, fatal and non-fatal AMI, and Government Office Region as described in Chapter 2 (Methods) were used. For this chapter, AMI events were not classified into first or recurrent because the limited time period covered by the data did not allow for the use of a clearance period to distinguish between them within each year.

Statistical analyses

For each year, the overall 30-day case fatality rate (case fatality for brevity) was calculated using the total number of AMIs as the denominator, and all fatal AMIs as the numerator. The hospitalised 30-day case fatality rate was calculated using the total

number of hospitalised AMI cases as the denominator, and the number of deaths within 30 days of the admission date in the hospitalised population as the numerator. The sudden AMI death rate was calculated using the total number of AMIs as the denominator, and all fatal AMIs that were sudden deaths as the numerator, in each year. Case fatality and sudden death rates were directly age standardised using five-year age groups and the age distribution of the nine-year AMI event cohort as the standard population.

Time trends were estimated using a generalised linear model with binomial distribution and a log link function, with calendar year included as an independent variable. The average annual percentage change in case fatality was calculated from the beta coefficient for the calendar year in the regression models, using -100*[1-exp(β)] as an approximation. Overall percentage changes between 1999 and 2007 were expressed as relative, rather than absolute, changes from 100%, according to the following formula: overall decline from 1999 to 2007 = – (1-(rate in 2007/rate in 1999))*100.

Results

Study cohort

The same study cohort was used for this study as for the previous study on trends in event rate (Chapter 3). Between 1 January 1999 and 31 December 2007, there were a total of 377,906 fatal outcomes among 842,835 individuals who experienced 914,763 AMI events. Table 13 shows the characteristics of all AMIs over the study period. Of all fatal cases, 72% were sudden deaths without a formal hospital admission for AMI and the rest were deaths that occurred within 30 days of hospital admission for AMI.

Table 13. Baseline characteristics of acute myocardial infarction (AMI) events and deaths by sex, 1999-2007, England.

Characteristics	Total AMIs	Men			Women		
		All AMIs	Fatal AMIs		All AMIs	Fatal AMIs	
	n	n	n	% all AMIs	n	n	% all AMIs
Total	914,763	554,916	211,447	38	359,847	166,459	46
Type of event							
Hospital admission	643,656	398,599	55,130	14	245,057	51,669	21
Sudden AMI death	271,107	156,317	156,317	(100)	114,790	156,317	(100)
Age (years)							
Mean	72.3	69.2	73.9	-	77.1	80.3	-
Median	74	71	76	-	79	82	-
0-29	1,035	792	170	22	243	74	31
30-54	99,555	82,242	14,354	18	17,313	3,261	19
55-64	139,760	107,359	26,976	25	32,401	8,081	25
65-74	221,532	147,087	54,679	37	74,445	27,301	37
75-84	289,754	156,267	78,492	50	133,487	65,873	49
85+	163,127	61,169	36,776	60	101,958	61,869	61
Government Office Region							
East England	97,747	60,932	21,701	36	36,815	16,465	45
East Midlands	83,728	51,454	18,266	36	32,274	13,610	42
London	84,860	51,618	20,969	41	33,242	16,777	51
North East	60,599	35,194	12,301	35	25,405	10,316	41
North West	151,684	90,068	34,685	39	61,616	28,179	46
South East	130,646	79,466	30,134	38	51,180	24,506	48
South West	98,697	59,975	23,403	39	38,722	18,474	48
West Midlands	98,652	61,442	24,100	39	37,210	17,851	48
Yorkshire	107,403	64,347	25,727	40	43,056	20,140	47

Hospitalised case fatality consists of two components: deaths among patients who die within 30 days while still in hospital and deaths among patients who are discharged alive but die within 30 days in the community. In this study, the majority (around 90%) of 30-day deaths among hospitalised AMI patients occurred while patients were still in hospital. This can be explained by the fact that, if death occurs, it tends to occur fairly soon after the AMI event: around 60% of deaths in the hospitalised patient population occurred within five days and around 85% within 15 days of admission.

Trends in case fatality and sudden death rates

Table 14 shows age-standardised rates of overall and hospitalised case fatality and sudden death by year, for men and women. In each year, the overall case fatality rates were more than twice as high as hospitalised case fatality rates for both sexes. From 1999 to 2007, the age-standardised overall case fatality declined from 49% (95% CI: 49-50) to 35% (95% CI: 35-36) for men, and from 49% (95% CI: 49-50) to 34% (95% CI: 33-34) for women. The age-standardised case fatality among hospitalised patients declined from 21% (95% CI: 21-21) to 14% (95% CI: 14-15) for men, and from 23% (95% CI: 22-23) to 15% (95% CI: 15-15) for women. The age-standardised sudden AMI death rate declined from 38% (95% CI: 37-38) to 25% (95% CI: 25-25) for men, and from 36% (95% CI: 36-37) to 23% (95% CI: 23-23) for women. Figure 7 and Figure 8 illustrate the changes in these rates for men and women, respectively.

Table 15 shows changes in age-specific and all-age rates of overall and hospitalised case fatality and sudden death from 1999 to 2007, by sex. The overall declines and the annual rates of change were comparable between rates, but the reductions were smaller for the overall case fatality and greater for sudden death rate. For each rate, both overall and annual changes were slightly smaller for men than women. Comparing 1999 with 2007, relative declines for overall case fatality, hospitalised case fatality, and sudden AMI death rates in men were 29%, 32%, and 34%, respectively, and in women 31%, 35%, and 37%, respectively. Average annual changes in age-standardised rates for men were -4.1% (95% CI: -4.2 to -4.0), -4.6% (95% CI: -4.9 to -4.3), and -5.0% (95% CI: -5.1 to -4.8), respectively; in women, they were -4.7% (95% CI: -4.8 to -4.6), -4.8% (95% CI: -5.1 to -4.5), and -6.3% (95% CI: -6.5 to -6.2), respectively.

Table 14. Age-standardised rates of overall and hospitalised case fatality (%) and sudden deaths as a proportion of all events (%) for acute myocardial infarction by year and sex, 1999-2007, England.

Year	Men				Women			
	Total deaths, n	Rate			Total deaths, n	Rate		
		%	95% CI			%	95% CI	
Overall case fatality								
1999	30,247	49	49	50	24,191	49	49	50
2000	27,775	47	47	48	21,803	46	46	47
2001	25,526	44	43	44	20,051	44	44	45
2002	24,987	42	42	42	19,734	42	42	43
2003	23,783	41	40	41	19,112	41	40	41
2004	22,028	39	38	39	17,165	37	37	38
2005	20,443	37	37	38	16,133	37	36	37
2006	18,992	37	36	37	14,592	35	34	35
2007	17,666	35	35	36	13,678	34	33	34
Hospitalised case fatality								
1999	7,007	21	21	21	6,384	23	22	23
2000	6,524	20	20	20	5,923	21	20	21
2001	6,457	19	18	19	6,002	20	20	21
2002	6,753	18	18	19	6,293	20	19	20
2003	6,422	17	17	18	6,177	19	18	19
2004	6,130	17	16	17	5,746	17	17	18
2005	5,611	15	15	16	5,629	17	17	18
2006	5,286	15	15	16	4,876	15	15	16
2007	4,940	14	14	15	4,639	15	15	15
Sudden death rate								
1999	23,240	38	37	38	17,807	36	36	37
2000	21,251	36	36	37	15,880	34	33	34
2001	19,069	32	32	33	14,049	31	31	32
2002	18,234	30	30	31	13,441	29	29	29
2003	17,361	29	29	30	12,935	28	27	28
2004	15,898	27	27	28	11,419	25	25	26
2005	14,832	27	26	27	10,504	24	24	25
2006	13,706	26	26	26	9,716	24	23	24
2007	12,726	25	25	25	9,039	23	23	23

Figure 7. Age-standardised rates of overall case fatality, hospitalised case fatality, and sudden deaths as a proportion of all events (%) for acute myocardial infarction in men, 1999-2007, England.

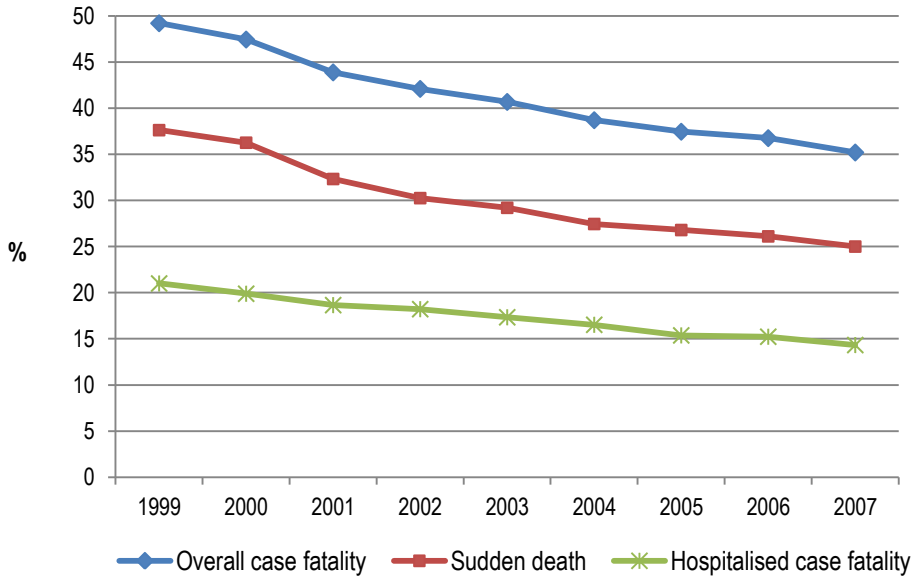
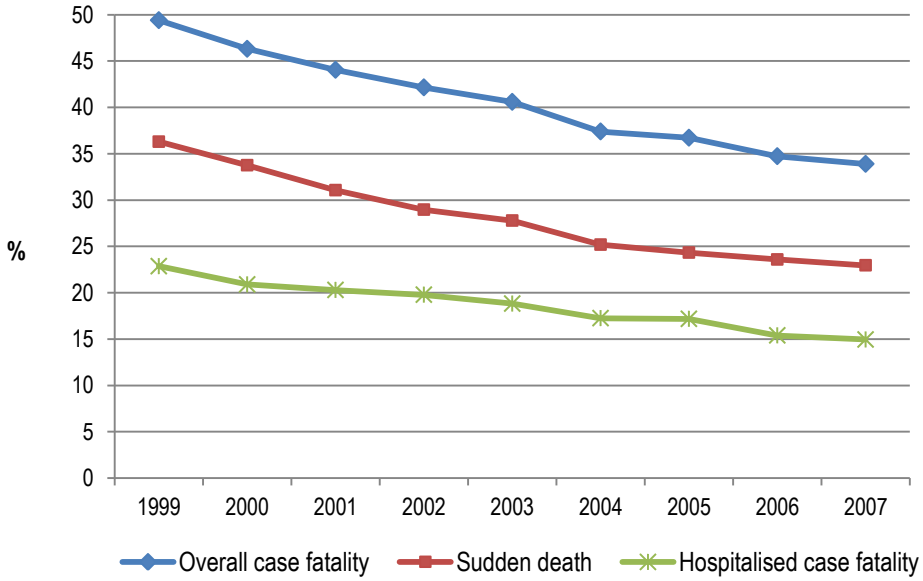


Figure 8. Age-standardised rates of overall case fatality, hospitalised case fatality, and sudden deaths as a proportion of all events (%) for acute myocardial infarction in women, 1999-2007, England.



Declines in rates were observed in all age groups and in both sexes. For overall and hospitalised case fatality, the greatest average annual declines occurred in those aged 65-74 years: for overall case fatality, they were -4.4% (95% CI: -4.6 to -4.1) for men and -5.2% (95% CI: -5.5 to -4.8) for women; for hospitalised case fatality, they were -5.5% (95% CI: -6.1 to -4.9) for men and -5.7% (95% CI: -6.5 to -5.0) for women. The declines in sudden AMI death rate increased with older age: the average annual change was -2.8% (95% CI: -3.5 to -2.2) for men aged 30-54 years and -6.6% (95% CI: -6.9 to -6.3) for men aged 85 years and older; the corresponding figures for women were -4.5% (95% CI: -5.9 to -3.2) and -7.0% (95% CI: -7.3 to -6.7).

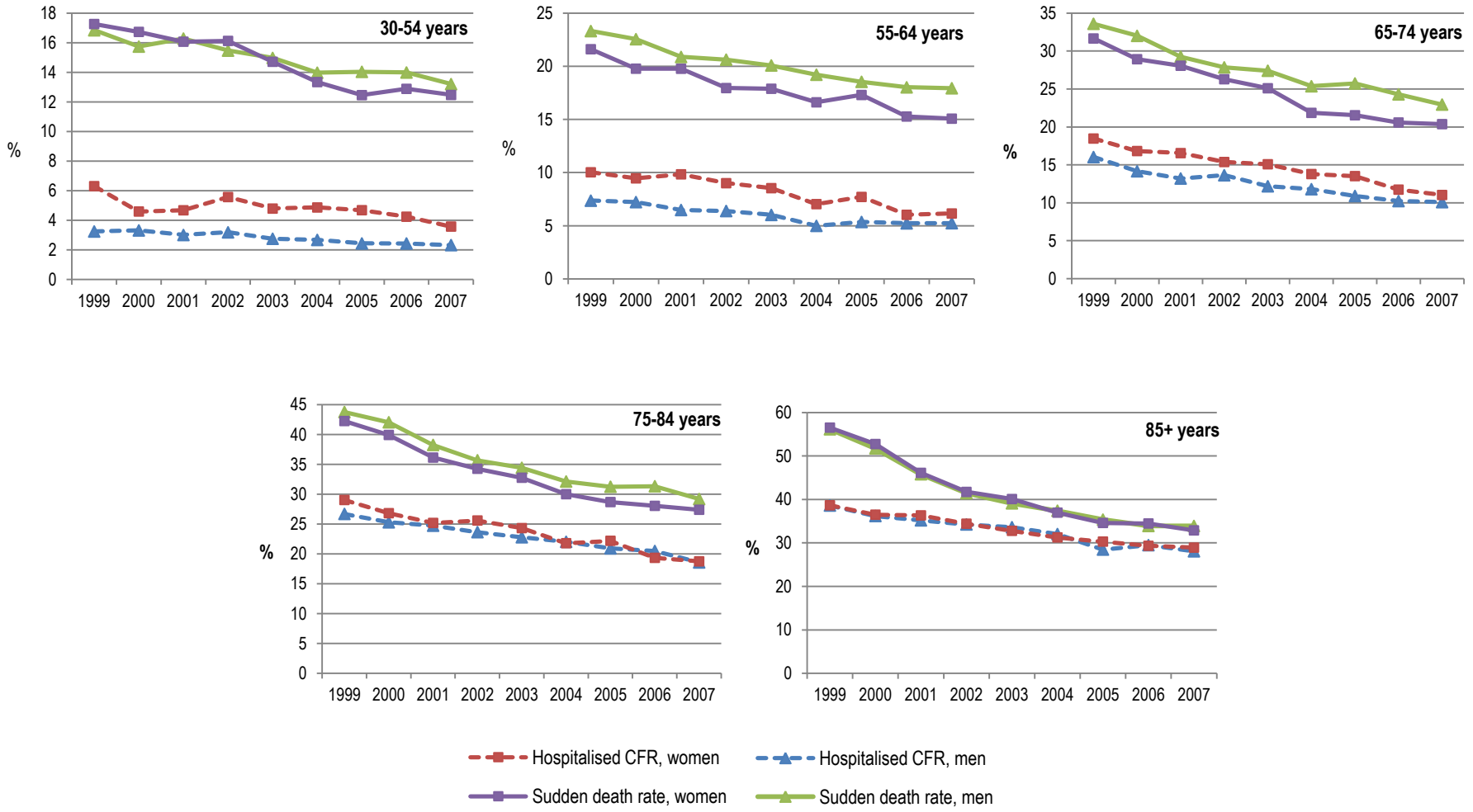
Table 15. Average annual changes in 30-day case fatality rates (CFR) and sudden death rate for acute myocardial infarction by age and sex, 1999-2007, England.

Age group (years)	1999		2007		Overall	Average annual change			
	Deaths	Rate, %	Deaths	Rate, %	decline, %	%	95% CI		p-value
Overall CFR									
Men									
30-55	2,042	20	1,237	15	-22	-3.0	-3.6	-2.5	<0.001
55-64	3,943	29	2,314	15	-23	-3.5	-3.9	-3.1	<0.001
65-74	8,918	44	3,888	22	-31	-4.4	-4.6	-4.1	<0.001
75-84	10,858	59	6,306	31	-28	-4.0	-4.2	-3.8	<0.001
85+	4,471	73	3,898	42	-28	-4.3	-4.5	-4.0	<0.001
All ages	30,247	49	17,666	35	-28	-4.1	-4.2	-4.0	<0.001
Women									
30-55	461	22	289	16	-31	-4.3	-5.5	-3.2	<0.001
55-64	1,259	29	629	20	-31	-4.5	-5.2	-3.8	<0.001
65-74	4,613	44	1,772	29	-34	-5.2	-5.5	-4.8	<0.001
75-84	9,715	59	4,956	41	-31	-4.6	-4.8	-4.4	<0.001
85+	8,132	73	6,021	52	-29	-4.4	-4.6	-4.2	<0.001
All ages	24,191	49	13,678	34	-31	-4.7	-4.8	-4.6	<0.001

Age group (years)	1999		2007		Overall	Average annual change			
	Deaths	Rate,%	Deaths	Rate,%	decline,%	%	95% CI		p-value
Hospitalised CFR									
Men									
30-55	282	3	164	2	-28	-4.6	-6.2	-3.0	<0.001
55-64	769	7	448	5	-29	-5.0	-5.9	-4.0	<0.001
65-74	2,146	16	984	10	-37	-5.5	-6.1	-4.9	<0.001
75-84	2,773	27	1,958	19	-30	-4.0	-4.5	-3.6	<0.001
85+	1,036	39	1,379	28	-27	-3.9	-4.5	-3.3	<0.001
All ages	7,007	21	4,940	14	-32	-4.6	-4.9	-4.3	<0.001
Women									
30-55	107	6	58	4	-43	-4.3	-7.0	-1.6	0.002
55-64	336	10	162	6	-39	-6.2	-7.7	-4.8	<0.001
65-74	1,315	18	534	11	-40	-5.7	-6.5	-5.0	<0.001
75-84	2,759	29	1,645	19	-35	-5.0	-5.5	-4.6	<0.001
85+	1,864	39	2,235	29	-25	-3.7	-4.2	-3.3	<0.001
All ages	6,384	23	4,639	15	-35	-4.8	-5.1	-4.5	<0.001
Sudden death rate									
Men									
30-55	1,760	17	1,073	13	-22	-2.8	-3.5	-2.2	<0.001
55-64	3,174	23	1,866	18	-23	-3.4	-3.8	-2.9	<0.001
65-74	6,772	34	2,904	23	-32	-4.5	-4.9	-4.2	<0.001
75-84	8,085	44	4,348	29	-33	-5.1	-5.3	-4.8	<0.001
85+	3,435	56	2,519	34	-40	-6.6	-6.9	-6.3	<0.001
All ages	23,240	38	12,726	25	-34	-5.0	-5.1	-4.8	<0.001
Women									
30-55	354	17	231	12	-28	-4.5	-5.9	-3.2	<0.001
55-64	923	22	467	15	-30	-4.2	-5.1	-3.3	<0.001
65-74	3,298	32	1,238	20	-36	-5.8	-6.3	-5.3	<0.001
75-84	6,956	42	3,311	27	-35	-5.7	-6.0	-5.4	<0.001
85+	6,268	57	3,786	33	-42	-7.0	-7.3	-6.7	<0.001
All ages	17,807	36	9,039	23	-37	-6.3	-6.5	-6.2	<0.001

Figure 9 shows trends in hospitalised case fatality and sudden death rates by sex and age (one graph per age group). The graphs show the greatest declines for hospitalised case fatality in middle-aged individuals and for sudden death rates, in the oldest individuals.

Figure 9. Age-specific rates of hospitalised case fatality (CFR,%) and sudden deaths as a proportion of all events (%) for acute myocardial infarction by sex, 1999-2007, England.



Trends by Government Office Region

From 1999 to 2007, the overall case fatality rate declined for all GORs (Table 16 and Figure 10). While the rates were generally similar between the GORs, the overall declines and the age-standardised average annual changes in case fatality were slightly greater in the south and slightly lower in the north. The greatest decline in case fatality occurred in the East England, from 44% (95% CI: 43-44) to 28% (95% CI: 27-28). The smallest decline occurred in the North East, from 40% (95% CI: 39-41) to 33 (95% CI: 31-34). Comparing 1999 with 2007, overall case fatality fell by 37% in the East England and by 19% in the North East; the average annual changes were -5.4% (95% CI: -5.7 to -5.2) and -2.9% (95% CI: -3.3 to -2.5), respectively.

Figure 10. Age-standardised overall case fatality rates for acute myocardial infarction by Government Office Region, 1999-2007, England.

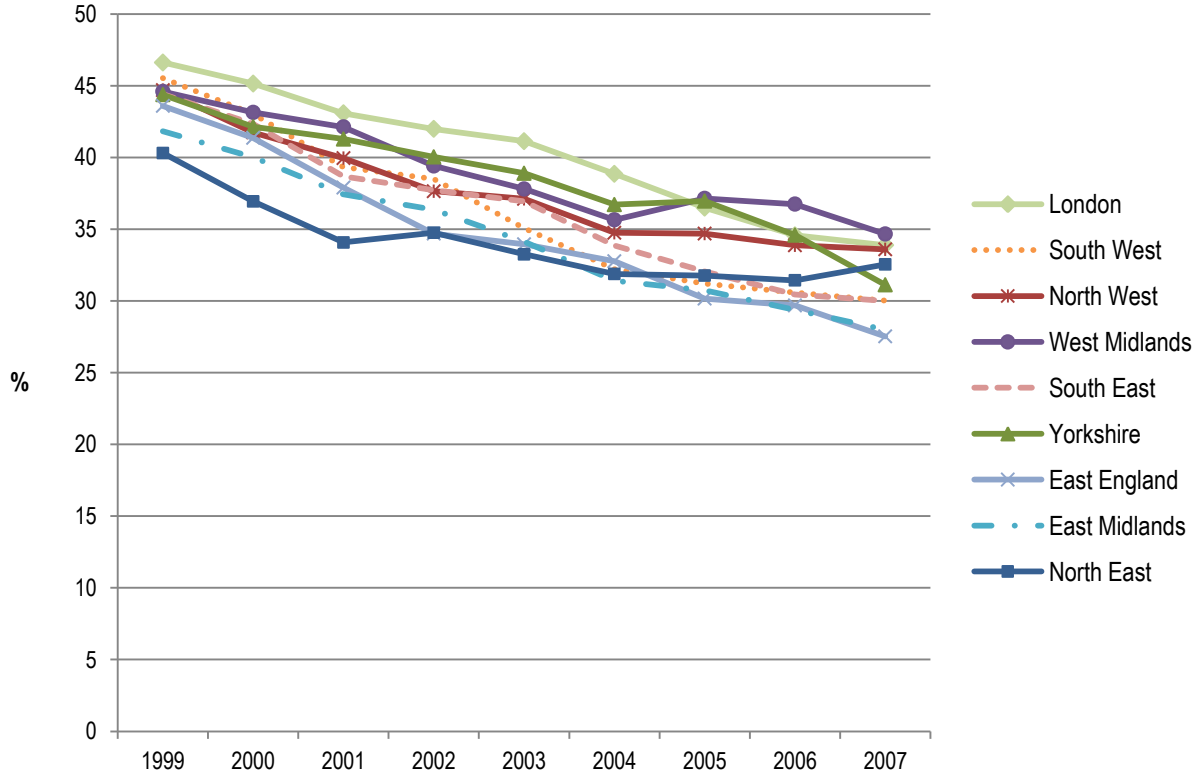


Table 16. Changes in the age-standardised overall case fatality rates for acute myocardial infarction by year and Government Office Region, 1999-2007, England.

Government Office Region	Case fatality rate (%)									Overall decline (%)	Average annual change			
	1999	2000	2001	2002	2003	2004	2005	2006	2007		%	95% CI		p-value
East England	44	41	38	35	34	33	30	30	28	37	-5.4	-5.7	-5.2	<0.001
East Midlands	42	40	37	36	34	31	31	29	28	33	-5.0	-5.3	-4.7	<0.001
London	47	45	43	42	41	39	36	35	34	27	-4.0	-4.3	-3.7	<0.001
North East	40	37	34	35	33	32	32	31	33	19	-2.9	-3.3	-2.5	<0.001
North West	45	42	40	38	37	35	35	34	34	25	-3.6	-3.8	-3.4	<0.001
South East	44	42	39	38	37	34	32	30	30	32	-5.0	-5.2	-4.8	<0.001
South West	46	43	39	38	35	32	31	31	30	34	-5.4	-5.7	-5.2	<0.001
West Midlands	45	43	42	39	38	36	37	37	35	22	-3.1	-3.4	-2.8	<0.001
Yorkshire	44	42	41	40	39	37	37	35	31	30	-3.7	-4.0	-3.5	<0.001

Discussion

This chapter reports on recent trends in AMI case fatality and sudden death rates between 1999 and 2007 in England. All measures of fatality declined for both sexes, all age groups, and all Government Office Regions. Overall case fatality, hospitalised case fatality, and sudden AMI death rates all declined by around one third. Trends differed by age group: for overall and hospitalised case fatality, the greatest declines occurred in middle-aged individuals, while the proportion of all AMIs that were sudden deaths increased with older age and was greatest for those aged 85 years and older. Overall, there was an improvement in short-term prognosis after AMI in England over the last decade, with more people surviving to reach hospital after the onset of the event and with fewer AMI events leading to death within 30 days.

The results show that the decline in 30-day case fatality for AMI in the UK, observed in previous decades,[5, 49, 73-75, 121] has continued well into the 2000s. Declines were observed for all examined population sub-groups and for both overall and hospitalised case fatality. The findings in this chapter provide evidence for England of a steady decline in both hospitalised and overall case fatality that has been observed in other countries since the 1980s, including the US,[24, 114-116] Canada,[43, 117] Denmark,[94] Finland,[10] Norway,[110] Sweden,[14, 119] and Switzerland.[120]

There were no sex differences in the rates of hospital admissions for AMI or sudden AMI deaths for men and women aged 75 years and older. However, in those aged under 75 years, hospitalised case fatality was slightly higher for women than men and sudden AMI death rate was slightly higher for men than women. These patterns did not change over the study period, suggesting that while both sexes have benefited from improved

prognosis after AMI, fundamental differences in fatal outcomes still exist between younger men and women.

Declines in case fatality also differed by age group. For individuals hospitalised for AMI, prognosis has improved the most for middle-aged patients, suggesting that medical treatment and intervention have been the most effective in this group. The decreasing proportion of all AMIs that manifested as sudden deaths indicates that, compared with 1999, more individuals survived long enough to receive hospital care for AMI in 2007, particularly among the elderly population. This suggests better response time and faster treatment by the ambulance and emergency room staff.

Traditionally, the declines in event rate are seen to reflect improvement in primary prevention, while declines in case fatality are generally attributed to successful pre-hospital and in-hospital treatment.[91] However, this view is over-simplistic and does not accurately account for the fact that primary prevention through better control of risk factors also has a beneficial impact on the probability of fatality after AMI by shifting the distribution of AMIs to less severe forms.[125] Therefore, in addition to improvements in treatment and care, another possible explanation for improving case fatality and the decline in sudden deaths is that AMIs may be becoming less severe, which in turn would lead to better survival. Recent studies in the US demonstrated a decreasing severity of AMI over the past two decades.[72, 122-124] Thus, the observed beneficial trends in case fatality are likely a result of not only improving treatment, but rather a combination of successful primary *and* secondary preventive measures.

In England, the prevalence of the main cardiovascular risk factors (smoking, high blood cholesterol, high blood pressure) has declined over the period of the study, while coronary revascularisation procedures (particularly PCI) and drug prescriptions for

prevention and treatment of CHD have increased.[61, 141, 148] Further, the introduction of the National Service Framework for CHD in England in 2000,[247] a strategic document that set standards for CHD prevention, diagnosis, treatment, and service delivery, may have also played a role in the improving outcomes of AMI patients over the last decade. However, the impact of the Framework remains to be elucidated.

Overall, the changes in outcomes after AMI cannot be explained by one specific factor and reflect changes in the progression of disease, health status and risk factor profile of the population, quality and effectiveness of care, access to procedures, and use of pharmaceutical and operative interventions, among others.[48, 61] The change in the diagnostic criteria for AMI in 2000, which included the introduction of the use of more sensitive biochemical markers for detection of damage to myocardium,[89] has been shown not to have affected trends in hospitalised case fatality.[94, 102, 104]

Regional trends indicate that short-term prognosis after an AMI has been improving in all parts of England, albeit at slightly different rates, varying from a fall of about a fifth to a fall of over a third between 1999 and 2007. The observed faster overall declines and average annual changes in the south could reflect greater improvements in population risk profile as well as better access to acute care, better response times, and faster adoption of effective treatments. The fact that the North East experienced the smallest decline is puzzling; a recent report from the North East Public Health Observatory stated that premature deaths from CHD have fallen and revascularisations have risen since 2003. Further investigation is needed to clarify the reasons behind regional differences.

Conclusion

This chapter provides recent information on trends in AMI case fatality rates in England between 1999 and 2007. Overall case fatality, hospitalised case fatality, and sudden AMI

death rates have declined in both sexes, all age groups and in all Government Office Regions. The findings suggest that short-term prognosis after AMI has improved overall and particularly for the middle-aged individuals, and that a higher percentage of people with AMI survived long enough to reach hospital in recent years than in earlier years.

CHAPTER 5: EXPLAINING TRENDS IN AMI MORTALITY, 1999-2007

This chapter provides estimates of mortality rates for acute myocardial infarction for all England and by Government Office Region between 1999 and 2007. The contributions of changes in AMI event rates and case fatality rates to the declining trends in AMI mortality are examined by age, sex, and geographic region. Comparisons are drawn with other studies in the UK and elsewhere. Implications of the results for public health policy and the relative importance of primary and secondary prevention are discussed.

Introduction

Declines have been observed in population-based mortality rates from coronary heart disease (CHD) and acute myocardial infarction (AMI) in many developed countries, including England, since the 1970s.[37, 61] The drivers behind the declining rates have been the subject of intensive research. For any given condition, the mortality rate in a population is a function of the event rate and case fatality rate. The most notable study that investigated the reasons behind the decline in CHD mortality is the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Study, which examined trends in AMI mortality rates, event rates, and one-month case fatality in men and women aged 35-64 years from 38 populations in 21 countries over 10 years, from 1985-87 to 1995-97.[29] The MONICA study found that, between the mid-1980s and mid-1990s, two thirds of the decline in CHD mortality in

individuals aged under 65 years could be attributed to the decline in coronary event rate and one third to the decline in case fatality.[3]

Studies from the MONICA centres also showed that the relative contributions of changes in event rate and case fatality to the decline in CHD mortality vary by region and country.[12, 24, 309] The MONICA populations in the United Kingdom were Glasgow and Belfast – there was no English population. The relative contributions of AMI event rate and case fatality to the decline in AMI mortality have not been studied in England.

The objectives of this chapter are:

1. To report population-based AMI mortality rates for England from 1999 to 2007 by age, sex, and Government Office Region (GOR);
2. To examine the relative contribution of changes in event rate and case fatality to changes in mortality rates; and
3. To investigate whether the relative contributions of event rate and case fatality to changes in mortality differ by age, sex and GOR.

Methods

Study population

Residents of England who had died with AMI recorded as the underlying cause of death between 1 January 1999 and 31 December 2007 were included in the study. The same definitions of AMI event, sudden AMI death, and Government Office Region as described in Chapter 2 (Methods) were used. For this chapter, AMI events were not classified into first or recurrent.

Statistical analyses

The total population-based mortality rate was defined as the annual rate of death with AMI recorded as the underlying cause of death. Mortality rates were calculated per 100,000 population of England by age group and sex, using the mid-year population estimates published by the Office for National Statistics.[19] Rates were directly age-standardised to the European Standard Population. The 95% confidence intervals were estimated assuming that the observed number of events followed a Poisson distribution.

Time trends were estimated using log-linear Poisson regression with calendar year as an independent variable. The average annual percentage change in mortality rate was calculated from the beta coefficient for the calendar year in the regression models, using -100*[1-exp(β)] as an approximation. Overall percentage changes in mortality rates were expressed as relative, rather than absolute, change from 100%, according to the following formula: overall decline from 1999 to 2007 = – (1-(rate in 2007/rate in 1999))*100.

The relative contribution of event and case fatality rates to the decline in AMI mortality was calculated using the same method as in the MONICA study.[3] In essence, the average annual change in the mortality rate is the sum of the average annual changes in event and case fatality rates, expressed as percentages.

This is based on the formula that

$$M = E * C$$

where M = mortality rate, E = event rate, and C = case fatality rate in a given year.

To convert to rates, we must differentiate by time (t). Using the standard equation for differentiation of products, we have:

$$\frac{dM}{dt} = E * \frac{dC}{dt} + C * \frac{dE}{dt}$$

Or, substituting, x' for dx/dt:

$$M' = E * C' + C * E'$$

where M', E' and C' stand for the average annual change for each rate in absolute terms. Let ΔM = M'/M, ΔE = E'/E, ΔC = C'/C, i.e. the percentage changes in mortality, event rate and case fatality over a given time period. Then,

$$\Delta M = \frac{M'}{M} = \frac{E * C' + C * E'}{M}$$

$$= \frac{E * C'}{E * C} + \frac{C * E'}{E * C}$$

$$= \frac{C'}{C} + \frac{E'}{E}$$

$$= \Delta C + \Delta E$$

It is important to note that mortality rates include only deaths certified as being due to AMI, while case fatality rates include deaths from any cause within 30 days of AMI. Consequently, ΔM does not exactly equal to the sum of ΔC and ΔE. For this reason, both estimates for the average annual rate of decline in mortality are presented – those based on mortality statistics and those based on average annual changes in event and case fatality rates.

New diagnostic criteria for AMI, which rely on the use of more sensitive biochemical markers of damage to myocardium for detection of AMI, were introduced in 2000 by the European Society of Cardiology and the American College of Cardiology.[89] An additional analysis on a subset of the data was performed, covering the years of 2003 to 2007, to examine changes in rates after the new criteria were likely to have been mostly

integrated into clinical practice. Further, the introduction of the new criteria was found to affect older patients to a greater extent than younger patients.[93, 94, 310] For this reason, rates for those aged under 75 years are also reported separately.

In addition, the proportion of total mortality decline that was due to a decline in sudden deaths was calculated as follows, according to the approach used in the MONICA centre in Finland: 100 x (Ms/Mt), where Ms=(sudden death rate in 1999 – sudden death rate in 2007) and Mt=(total mortality rate in 1999 – total mortality rate in 2007).[36]

Results

Trends in AMI mortality

Between 1 January 1999 and 31 December 2007 in England, 198,894 men and 155,598 women died with AMI recorded as the underlying cause of death, giving a total of 354,492 AMI deaths. Table 17 and Figure 11 show the annual age-standardised AMI mortality rates by sex. From 1999 to 2007, the age-standardised AMI mortality rate per 100,000 population decreased from 101 (95% CI: 100-102) to 50 (95% CI: 49-51) for men, and from 48 (95% CI: 47-48) to 23 (95% CI: 23-24) for women. Comparing 1999 with 2007, mortality rates fell by 51% for men and by 52% for women.

Table 17. Total age-standardised mortality rates for acute myocardial infarction (AMI) by year and sex, 1999-2007, England.

Year	Men				Women			
	Total AMI deaths, n	Mortality rate (per 100,000) Rate	95% CI		Total AMI deaths, n	Mortality rate (per 100,000) Rate	95% CI	
1999	28,742	101	100	102	22,878	48	47	48
2000	26,531	92	91	93	20,727	43	42	43
2001	24,155	82	81	83	18,903	39	38	39
2002	23,567	79	78	80	18,593	37	37	38
2003	22,389	74	73	75	17,823	35	35	36
2004	20,572	67	66	68	15,931	31	31	32
2005	19,044	61	60	61	14,816	29	28	29
2006	17,578	55	54	56	13,399	25	25	26
2007	16,316	50	49	51	12,528	23	23	24

Figure 11. Total age-standardised mortality rates for acute myocardial infarction by year and sex, 1999-2007, England.

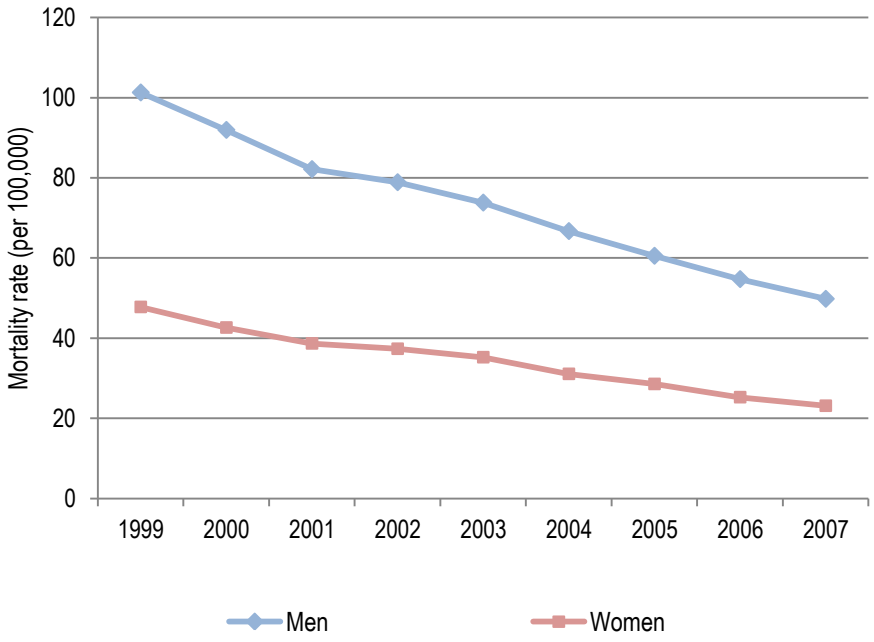


Table 18 shows trends in the event rate, case fatality, and mortality rate from 1999 to 2007 for all ages, by age group, and by sex. Results for the overall declines and average annual changes in event rate and case fatality, which can be found in the first and second vertical sections of the table, are from Chapters 3 and 4, respectively; they were included in the table for completeness.

Estimates of the annual trends in mortality rate by age and sex are shown in the third vertical section of Table 18. Declining mortality was seen in all age groups and for both sexes. The greatest rates of decline (around 10% per year) occurred in men and women aged 55-74 years – about twice as high as the lowest rates of decline (around 5% per year), observed for individuals aged 85 years and older. The average annual change was -8.1% (95% CI: -10.8 to -5.3) in men and -8.4% (95% CI: -12.3 to -4.3) in women.

Determinants of AMI mortality trends in England

The relative contributions of changes in AMI event rate and case fatality to the change in AMI mortality rate between 1999 and 2007 are summarised in the last vertical section of Table 18 and in Figure 12. In men, the contribution of changes in the event rate to the decline in mortality was higher for all age groups except for individuals aged 85 years and over. In women, the change in event rate played a larger role than the change in case fatality for those aged 55-74 years. For all ages, about half of the decline in total mortality could be attributed to a decline in event rate (52% in men, 45% in women) and half to a decline in case fatality rate (48% in men, 55% in women). A similar pattern was observed for individuals aged under 75 years, with about half of the decline in mortality being driven by a decline in AMI event rate (56% in men, 51% in women) and half by a decline in case fatality (44% in men, 49% in women).

Table 18. Trends in event rate, case fatality, and mortality for acute myocardial infarction by sex and age, 1999-2007, England.

Age group (years)	Event rate (per 100,000)[1]				Case fatality rate (%)[2]				Mortality rate (per 100,000)					Contribution to mortality decline[4]	
	1999	2007	Overall decline, %	Annual trend, %	1999	2007	Overall change, %	Annual trend, %	1999	2007	Overall decline, %	Annual trend, %	Estimated trend,[3] %	Event rate, %	Case fatality rate, %
Men															
30-54	13	10	-24	-3.3*	20	15	-22	-3.0	2	1	-41	-6.1*	-6.3	52	48
55-64	55	35	-36	-5.3	29	15	-23	-3.5	15	7	-51	-8.7	-8.9	60	40
65-74	104	63	-40	-5.9	44	22	-31	-4.4	43	18	-59	-10.2	-10.3	58	42
75-84	174	120	-31	-4.2	59	31	-28	-4.0	97	46	-52	-8.4	-8.1	51	49
85+	241	216	-10	-0.8*	73	42	-28	-4.3	167	101	-39	-5.5	-5.1	16	84
Under 75	178	117	-34	-5.0	34	25	-27	-3.9	56	26	-54	-9.1	-8.9	56	44
All ages	254	174	-31	-4.4	49	35	-29	-4.1	101	50	-51	-8.1	-8.5	52	48
Women															
30-54	3	2	-12	-1.2*	23	16	-31	-4.3	0	0	-38	-5.6*	-5.6	22	78
55-64	17	10	-39	-6.3*	30	20	-31	-4.5	5	2	-58	-10.5*	-10.8	58	42
65-74	47	28	-42	-6.0	44	29	-34	-5.2	20	7	-63	-11.2	-11.2	54	46
75-84	98	69	-29	-3.7	59	41	-31	-4.6	54	25	-53	-8.6	-8.3	45	55
85+	163	152	-7	-0.2*	73	52	-29	-4.4	114	73	-36	-5.0	-4.6	4	96
Under 75	59	38	-36	-5.2	35	24	-33	-5.0	20	8	-59	-10.3	-10.2	51	49
All ages	105	74	-30	-3.9	49	34	-31	-4.7	48	23	-52	-8.4	-8.5	45	55

**Indicates statistical non-significance, i.e. p>0.05*

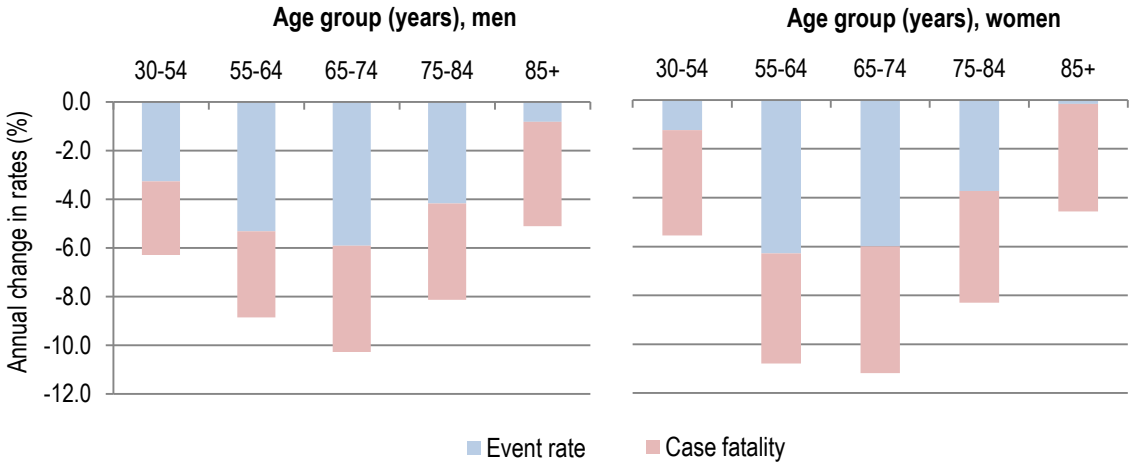
[1]*Taken from Chapter 3*

[2]*Taken from Chapter 4*

[3]*Based on average annual changes in event rate and case fatality*

[4]*Based on the estimated trend in mortality*

Figure 12. Contribution of average annual changes in event rate and case fatality to the changes in mortality for acute myocardial infarction by sex, 1999-2007, England.



Restricting analyses to data from 2003 to 2007, i.e. after the period of introduction and integration of the new diagnostic criteria into clinical practice, showed that mortality and event rates declined faster and case fatality declined slower during that period. The age-standardised average annual changes for mortality, event rate, and case fatality were -9.3% (95% CI: -16.3 to -1.8), -5.7% (95% CI: -9.8 to -1.5), and -3.3% (95% CI: -3.7 to -3.0) for men, and -10.0% (95% CI: -20.0 to -1.1), -5.5% (95% CI: -11.7 to -1.2), and -3.9% (95% CI: -4.3 to -3.6) for women. Changes in the event rate contributed around 60% (63% in men, 58% in women) and changes in case fatality about 40% (37% in men, 42% in women) to the decline in AMI mortality. In other words, the relative contribution of reductions in these two components to the decline in AMI mortality varied with time and was different for 1999-07 and 2003-07.

Separating the rate of sudden AMI deaths from the overall mortality rate for the entire study period from 1999 to 2007 shows that the majority of the total mortality decline was driven by the decline in sudden AMI deaths in all age groups and in both men and women (Table 19). In the oldest age group of individuals aged 85 years and older, declines in AMI mortality were driven entirely by the declines in sudden death rates. In other words, most of the observed fall in deaths from AMI can be explained by a fall in sudden deaths that occurred without a formal record of hospital care for AMI.

Table 19. Total mortality rate and sudden death rate for acute myocardial infarction by sex and age, 1999-2007, England.

Age group (years)	Sudden AMI death rate per (100,000)			Overall mortality rate per (100,000)			% absolute mortality decline due to sudden deaths
	1999	2007	Absolute decline	1999	2007	Absolute decline	
Men							
30-54	2	1	1	2	1	1	89
55-64	13	6	7	15	7	8	83
65-74	35	14	21	43	18	24	81
75-84	76	35	41	97	46	51	81
85+	135	73	62	167	101	65	96
All ages	82	39	43	101	50	51	84
Women							
30-54	0	0.	0	0	0	0.	80
55-64	4	2	2	5	2	3	77
65-74	15	6	9	20	7	13	76
75-84	41	19	24	54	25	29	78
85+	92	50	43	114	73	41	100
All ages	37	17	21	48	23	25	82

Trends in AMI mortality by Government Office Region

From 1999 to 2007, the AMI mortality rate declined by about half in all GORs and the gap between GORs has narrowed (Figure 13 and Table 20). The age-standardised average annual changes were higher in the south and lower in the north of England. The greatest overall decrease in AMI mortality rate per 100,000 population occurred in the South West from 69 (95% CI: 67-71) to 30 (95% CI: 29-31). The smallest overall decline occurred in the North West from 87 (95% CI: 85-89) to 47 (95% CI: 46-49). Comparing 1999 with 2007, overall AMI mortality fell by 57% in the South West and by 46% in the North West; the age-standardised average annual changes were -9.9% (95% CI: -13.3 to -6.5) and -7.6 (95% CI: -10.5 to -4.6), respectively.

Figure 13. Age-standardised mortality rates for acute myocardial infarction by year and Government Office Region, 1999-2007, England.

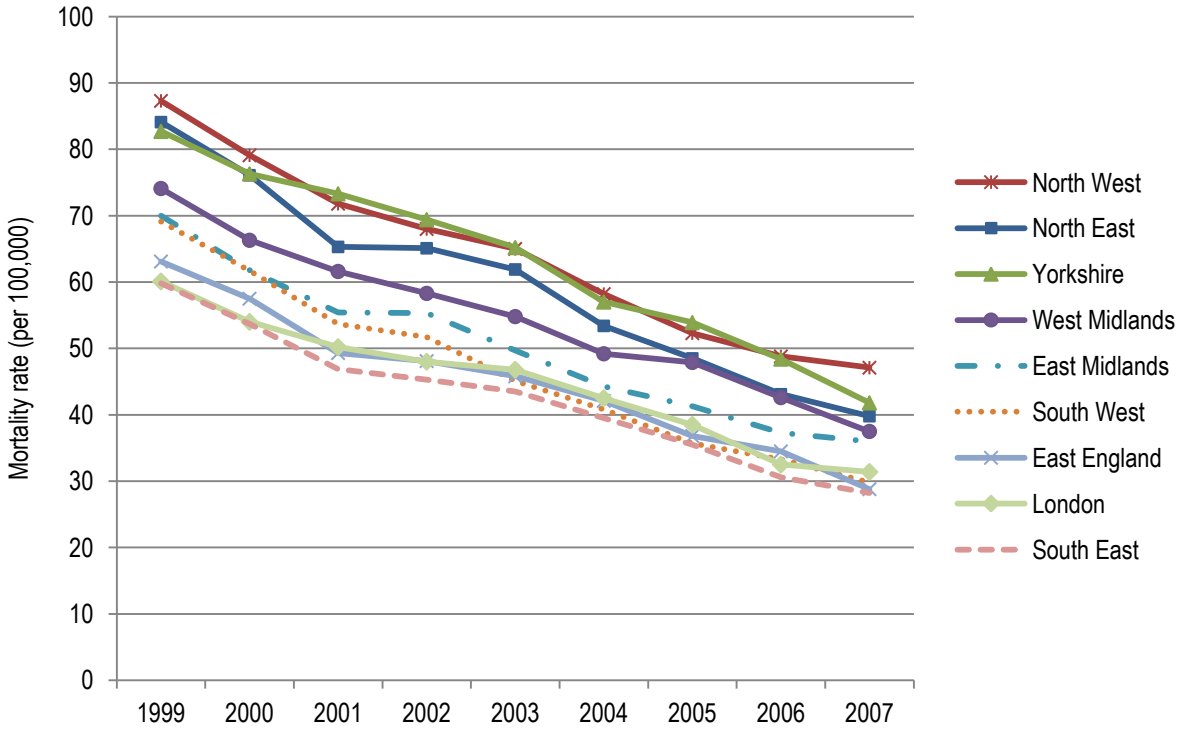


Table 20. Age-standardised mortality rates for acute myocardial infarction by year and Government Office Region, 1999-2007, England.

Government	Mortality rate (per 100,000)									Overall	Average annual change			
Office Region	1999	2000	2001	2002	2003	2004	2005	2006	2007	decline (%)	%	95% CI		p-value
East England	63	58	49	48	46	42	37	35	29	54	-8.0	-11.3	-4.6	<0.001
East Midlands	70	62	55	55	50	44	41	37	36	49	-8.5	-11.9	-4.9	<0.001
London	60	54	50	48	47	43	39	33	31	48	-7.5	-11.0	-3.9	<0.001
North East	84	76	65	65	62	53	49	43	40	53	-8.7	-11.7	-5.6	<0.001
North West	87	79	72	68	65	58	52	49	47	46	-7.6	-10.5	-4.6	<0.001
South East	60	54	47	45	44	40	36	31	28	53	-8.5	-12.0	-4.8	<0.001
South West	69	62	54	52	45	41	36	33	30	57	-9.9	-13.3	-6.5	<0.001
West Midlands	74	66	62	58	55	49	48	43	38	49	-7.5	-10.7	-4.2	<0.001
Yorkshire	83	76	73	69	65	57	54	48	42	50	-7.6	-10.6	-4.6	<0.001

Determinants of AMI mortality trends by Government Office Region

Table 21 summarises trends and average annual percentage changes from 1999 to 2007 for mortality rate, event rate, and case fatality by GOR. All three rates declined in all GORs over the study period. The relative contributions of event rates and case fatality to the change in AMI mortality rate are provided in the last column of Table 21 and illustrated in Figure 14 below; the GORs are ordered in the descending order of the relative contribution of event rate to declining mortality. The reduction in event rate differed between regions, ranging from 68% to 38%; generally, it played a bigger role in the north of England, whereas in the south of England, the reduction in case fatality was a bigger component.

Figure 14. Contribution of average annual changes in event rate and case fatality to the changes in mortality for acute myocardial infarction by Government Office Region, 1999-2007, England.

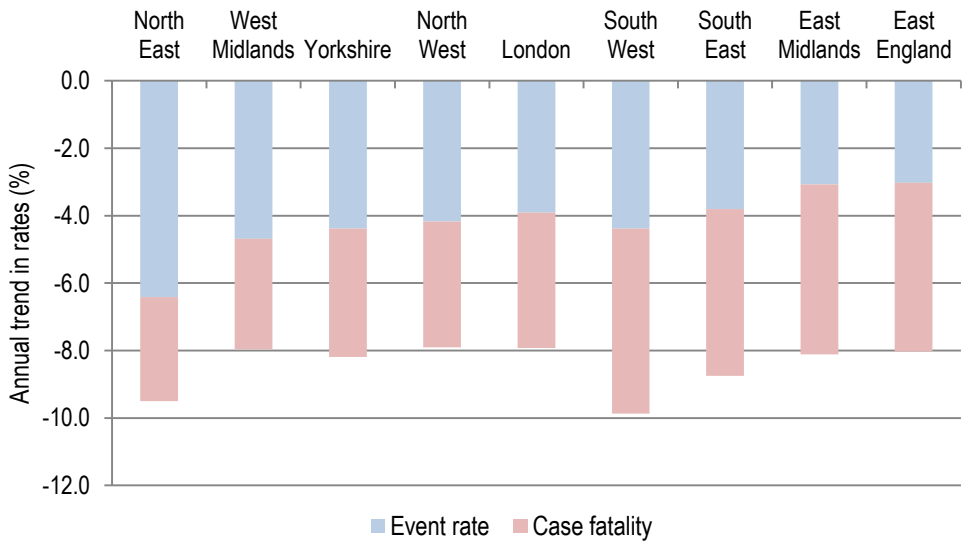


Table 21. Reduction in AMI mortality rate per 100,000 attributed to reduction in event rate (%) and overall case fatality (%) by Government Office Region, 1999-2007, England.

Government Office Region	Event rate (per 100,000)[1]				Case fatality rate (%)[2]				Mortality rate (per 100,000)					Contribution to mortality decline[4]	
	1999	2007	Overall decline, %	Annual trend, %	1999	2007	Overall change, %	Annual trend, %	1999	2007	Overall decline, %	Annual trend, %	Estimated trend,[3] %	Event rate, %	Case fatality rate, %
North East	230	129	44	-6.4	40	33	19	-3.1	84	40	53	-8.7	-9.5	68	32
West Midlands	183	120	34	-4.7	45	35	22	-3.3	74	38	49	-7.5	-8.0	59	41
Yorkshire	200	143	28	-4.4	44	31	30	-3.8	83	42	49	-7.6	-8.2	54	46
North West	211	150	29	-4.2	45	34	25	-3.7	87	47	46	-7.6	-7.9	53	47
London	140	97	31	-3.9	47	34	27	-4.0	60	31	48	-7.5	-7.9	49	51
South West	158	107	32	-4.4	46	30	34	-5.5	69	30	57	-9.9	-9.9	44	56
South East	144	99	31	-3.8	44	30	32	-4.9	60	28	53	-8.5	-8.8	44	56
East Midlands	182	141	22	-3.1	42	28	33	-5.0	70	36	49	-8.5	-8.1	38	62
East England	154	114	26	-3.0	44	28	37	-5.0	63	29	54	-8.0	-8.0	38	62

[1]Taken from Chapter 3

[2]Taken from Chapter 4

[3]Based on average annual changes in event rate and case fatality

[4]Based on the estimated trend in mortality

Discussion

This chapter reports on recent trends in AMI mortality rates between 1999 and 2007 in England. The results show that total age-standardised AMI mortality fell by approximately half. The relative contributions of event rate and case fatality reductions to the decline in AMI mortality differed by sex, age, and Government Office Region, with changes in case fatality playing a greater role for women, older individuals, and in the south-east region of the country. Overall, the average annual reductions were similar for event and case fatality rates, indicating that they contributed almost equally to the decline in mortality. In other words, compared to earlier years over the last decade, fewer AMIs occurred in the later years, and, of those AMIs that did occur, fewer were fatal.

Trends in AMI mortality

Between 1999 and 2007, AMI mortality rates declined by approximately 50% in both men and women in England as a whole as well as in all Government Office Regions. However, the rates of decline differed by age group. The results showed non-significant annual declines in AMI mortality in men and women aged 30-54 years. These findings support previous reports of a flattening and a possible reversal in CHD mortality rates in young adults in England and other developed countries towards the end of the 20th and the beginning of the 21st centuries,[36, 38, 44, 306, 311, 312] and reinforce the importance of monitoring and managing risk factors in this population.

The greatest decline in mortality occurred among individuals aged 65-74 years. These results are in agreement with a recently published study of trends in CHD deaths in the UK, which found the greatest declines in CHD mortality for the same age group.[311] However, that study did not include individuals aged 75 years and older and was thus

limited in scope. The results of the present study include individuals of all ages and provide further insight into mortality declines in different age groups. They show that while mortality declines were greatest in the middle-aged individuals, older people experienced less dramatic falls and the rate of decline in those aged 85 years and over was approximately the same as in those aged 30-54 years.

Declines in mortality were observed for all geographic regions, suggesting that comparable improvements can be achieved in all areas, even if the absolute rates are different. Similarly to trends in event rates shown in Chapter 3, the relative differences in absolute rates have decreased between GORs, indicating that the north-to-south gap in AMI mortality in England has narrowed during the 2000s.

Explaining the decline in AMI mortality

The findings that falling event rate and case fatality contributed approximately equally to the observed decline in AMI mortality contrast with the MONICA study's results, which reported that the decline in event rate accounted for two thirds of the total decline in mortality.[3] However, the MONICA findings were based on data from previous decades, did not include individuals aged older than 64 years, and did not cover England. Therefore, the MONICA results are unlikely to apply to more recent years, be representative of whole populations, or be directly applicable to England.

In this study, the relative contributions of event rate and case fatality differed by age: event rate played a bigger role in the middle-aged, while case fatality played a bigger role in the young and the very old. This can be explained by the fact that, while overall declines between 1999 and 2007 in case fatality rate did not differ much between age groups, the declines in event rate did. Event rate changes were lowest, as well as non-significant, in the 30-54 years and 85 years and over age groups. As a result, the relative

contribution of case fatality changes differed by age and was higher for younger and for older individuals.

Similar to other studies,[36, 313] it was found that the majority of fatal AMIs were sudden deaths. In this study, the fall in sudden AMI deaths was found to be the key driver behind the fall in total AMI mortality. Others have found that about half of individuals dying suddenly from CHD or AMI already have a history of symptomatic CHD.[32, 33, 36] It is reasonable to assume that this study's cohort also consisted of individuals with and without pre-existing CHD. Therefore, both primary prevention and secondary prevention would have contributed to the decline in sudden AMI death rate. In addition to reducing rates of sudden death, coronary prevention can reduce disease severity, and therefore may contribute to the decline in case fatality for individuals who survive long enough to receive hospital care for AMI. Furthermore, changes in fatal outcomes among hospitalised AMI patients also reflect, at least in part, the improvements in acute medical treatment during the study time period.

The dataset used in this study did not include clinical information on risk factors, comorbidities, prior disease history, or current and past drug prescriptions for the study cohort, and thus the questions about the specific elements of prevention and treatment and their relative importance could not be addressed. Other studies have shown that changes in both the main cardiovascular risk factors (smoking, high blood pressure, and high blood cholesterol) and coronary care (including drug therapy for treatment and prevention, thrombolysis, and revascularisation procedures) are associated with the declines in mortality.[24, 25, 50-52, 79]

Modelling studies have suggested that about half of CHD mortality decline is driven by risk factor reduction: 57% in the US between 1980 and 1990,[314] 44% in the US between

1980 and 2000,[8] 52% in New Zealand between 1982 and 1993,[59] 55% in Sweden between 1986 to 2002,[57] 48% in Canada between 1994 to 2005,[56] 51% in Spain between 1988 to 2005,[58] and 60% in Scotland between 1975 and 1994.[53] The modeling study conducted for England and Wales between 1981 and 2000 found that reductions in main cardiovascular risk factors (particularly smoking) contributed 58% to the decline in CHD mortality and medical treatment (particularly secondary prevention) contributed 42%.[54] Further modelling exercises for England and Wales comparing the relative benefits of primary and secondary prevention found that of the deaths avoided because of reductions in three major risk factors, 81% were in people without prior CHD, indicating that primary prevention is much more effective than secondary prevention in reducing CHD deaths.[315]

The regional analysis of mortality decline showed that the relative contribution of changes over time in event rate and case fatality to changes in mortality rate differed by Government Office Region. The event rate reductions accounted for more than half of the mortality decline in the north of England, while in the south, changes in case fatality accounted for more than half of the decline. These findings are in agreement with the regional variation found within and between countries in the MONICA study.[3] This study provides further evidence that the drivers behind declining mortality rates differ geographically and results specific to one region cannot be necessarily applied to other regions.

Furthermore, it was shown that the relative contribution of the determinants of the mortality decline for AMI differed by time period, as evidenced by different contribution of event rate and case fatality for 1999-07 compared with 2003-07. This finding emphasises the importance of continuous monitoring of trends in disease occurrence and

fatal outcomes in populations, especially during the time periods when changes in diagnostic criteria occur.

It is important to note that only deaths from AMI, and not all CHD, were examined. A similar analysis of determinants of trends in CHD mortality was not attempted because all new CHD events (other than AMI) could not be reliably identified using just hospitalisation and mortality data. Extrapolation of results presented here to all CHD should be made with caution. Age-standardised mortality rates from non-AMI CHD causes in England declined less than AMI mortality over the study period (data not shown). The precise reasons behind these trends merit further research but lie beyond the scope of this thesis.

Conclusion

This study reports trends in AMI mortality between 1999 and 2007 in England and examines the relative contribution of changes in event rate and case fatality to the observed decline in AMI mortality overall, by age, sex, and Government Office Region. The majority of AMI fatalities continue to be sudden deaths. Approximately half of the decline in AMI mortality can be attributed to a reduction in event rate and half to improved 30-day survival. However, the drivers behind declining mortality rates differ by sex, age, time period, and geographic region. The results also highlight groups, particularly the young and the very old, who experienced the least improvement in the occurrence of and mortality from AMI.

CHAPTER 6: HOSPITALISED AMI PATIENT POPULATION, 1999-2007

This chapter describes trends over time in characteristics of patients hospitalised for acute myocardial infarction (AMI), including age and prevalence of comorbidities, and their use of National Health Service resources, as quantified by the length of their hospital stay. Changes in the age distribution of AMI patients are discussed in detail. The association between length of stay and mortality within one month and one year of discharge from hospital is explored.

Introduction

Studies from a number of developed countries have reported that the hospitalised AMI patient population has been getting older over the last three decades.[43, 116, 119, 138, 175, 176] Older individuals tend to have more comorbidities, more in-hospital complications, longer hospital stays, and cost the health care service providers more.[240, 241] The older AMI patient population could have arisen from an ageing underlying population and/or from a shift in the occurrence of AMI to older ages. Recent trends in the characteristics of hospitalised AMI patients, particularly their age distribution and concurrent illnesses and in-hospital complications, have not been reported for England. If the AMI patient population is also getting older in England, it has important implications for the National Health Service (NHS) in relation to patient management, amount of care and staff resources, and therefore financial costs.

In parallel with the changes in age distribution, the mean length of stay for AMI patients has been falling across the developed world.[239, 240] The declining length of stay has raised

concerns about possible negative impacts on patients' health outcomes[115, 195, 243] as well as the possible displacement of short-term deaths following AMI from an in-hospital to a community setting.[144, 195] Mortality after discharge is one potential indicator of the effect of length of stay on health outcomes. Although a number of studies in other countries have reported no adverse effects of shorter stays on mortality following discharge from hospital,[101, 115, 240, 241, 243] it is unknown whether this is also true for England. With no standard guidelines for the optimal length of hospital stay for AMI, and with economic incentives to discharge patients as soon as possible, it is important to evaluate the association between length of stay and health outcomes in AMI patients in England.

The objectives of this chapter are:

1. To examine trends in the characteristics of AMI patients admitted to hospitals under NHS care in England between 1999 and 2007, including age distribution, comorbidity prevalence, and frequency of coronary revascularisation procedures;
2. To explore trends in mean length of hospital stay by sex, age, and year; and
3. To evaluate the association between length of stay mortality up to one year after discharge, examining deaths within 30 days and deaths within 31-365 days.

Methods

Study population

Residents of England who had a hospital record with AMI recorded in the main diagnostic field between 1 January 1999 and 31 December 2007 were included. The same definitions of AMI event, hospital admission, fatal and non-fatal AMI, comorbidities, and

coronary revascularisation procedures as described in Chapter 2 (Methods) were used for the analyses. For this chapter, AMI events were not classified into first or recurrent.

For each patient, the first occurrence of an AMI in the dataset was termed index AMI. For each AMI, the first hospital admission was termed index admission (some AMIs had more than one admission if admissions occurred within 30 days of the index admission).

Statistical analyses

Length of stay was defined as the total number of days for the index admission. Mean length of stay was calculated and presented in two ways. First, all index admissions were included, irrespective of the length of time spent in hospital. Second, only 99% of index admissions were included, after the top one percent with the longest length of stay was excluded. The second approach was applied because the distribution of the length of stay per admission was highly skewed to the right. Median lengths of stay are also reported.

Postdischarge mortality was defined as the proportion of hospitalised AMIs that resulted in death from any cause within 30 days or within 31- 365 days of the discharge date from the index admission for AMI. Only individuals who survived until discharge were included in the analysis. For postdischarge mortality between 31 and 365 days, only AMIs with a discharge date between 1999 and 2006 were included, to allow for a one year follow up. The association between the length of stay and postdischarge mortality was examined using univariate and multivariate logistic regression models. Multivariate models were run separately for men and women and were adjusted for age, coronary revascularisation procedures, and comorbidities.

Results

Baseline characteristics of the study cohort

Between 1 January 1999 and 31 December 2007, a total of 643,656 hospitalised AMI events occurred among 590,705 individuals. Table 22 shows the baseline characteristics of hospitalised AMIs for years 1999 and 2007 by sex. The percentage of women increased from 36.7% to 38.5% over the study period ($p<0.001$) – a small increase, although based on very large numbers. Between 1999 and 2007, the annual number of hospitalised AMIs and the hospitalisation rate per 100,000 population fell (see Chapter 3 for more details), while the mean length of hospital stay for AMI patients has slightly increased (see below). The mean age at admission, the overall age distribution of AMI patients, the prevalence of comorbidities, and the use of revascularisation procedures all changed over the study period. These changes are now examined.

Table 22 shows that AMI patient population has become older between 1999 and 2007, driven by a decline in AMI admissions among middle-aged individuals and a rise in admissions in older people. Figure 15 illustrates the age distribution of hospitalised AMI patients by year. In men, the relative proportion of all AMI admissions decreased between 1999 and 2007 for individuals aged less than 75 years and increased for individuals aged 75 years and older. The largest overall decline occurred in men 65-74 years (19%, $p<0.001$) and the largest overall increase occurred in men aged 85 years and older (104%, $p<0.001$). AMI admissions decreased for women aged less than 85 years and increased for women aged 85 years and older (66%, $p<0.001$). As in men, the largest fall occurred in women aged 65-74 years (30%, $p<0.001$). Overall, between 1999 and 2007, the proportion of hospitalised AMI patients who were aged 75 years and older increased from 29% to 38% in men and from 54% to 65% in women ($p<0.001$ for both).

Table 22. Baseline characteristics of hospitalised acute myocardial infarction events, 1999-2007, England.

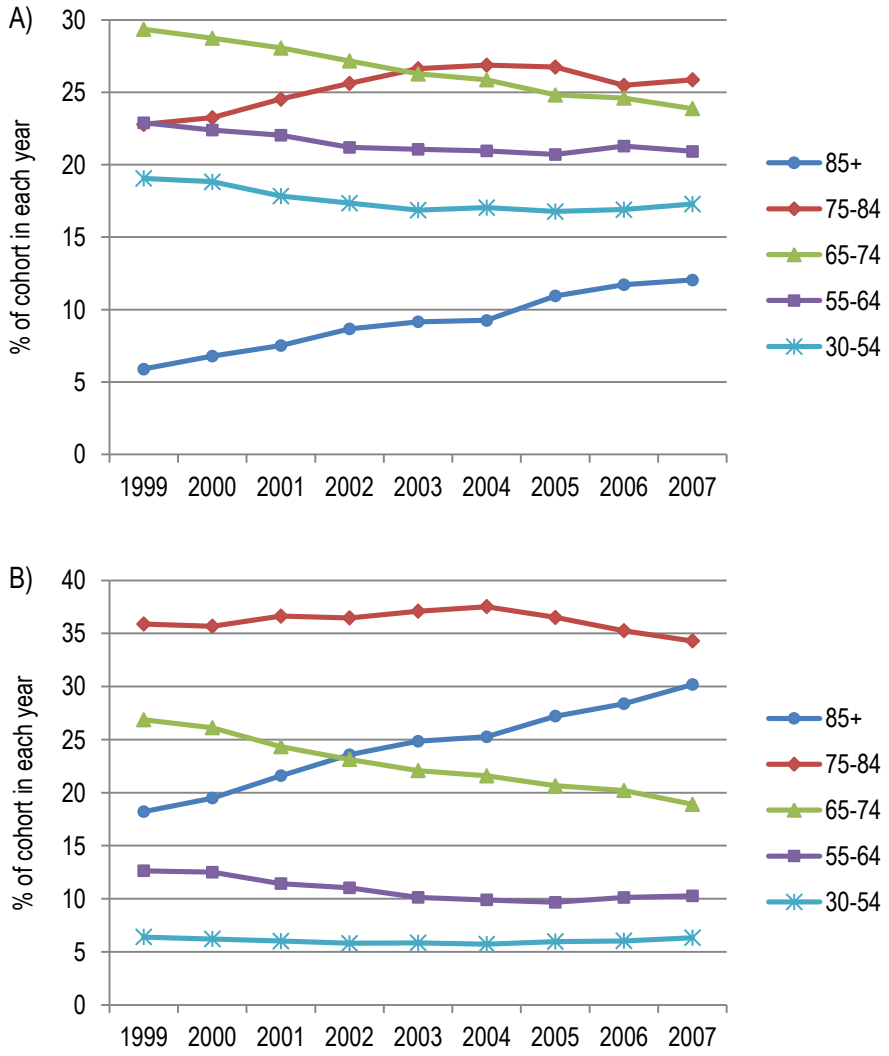
	Men			Women		
	1999	2007	Change (%)*	1999	2007	Change (%)*
Hospitalised AMIs						
Total, n	45,640	40,894	-10	26,518	25,652	-3
Hospitalisation rate/100,000**						
<75	132	95	-28	44	31	-29
All ages	172	135	-21	68	57	-17
Length of stay (days)						
Mean	7.9	8.8	12	9.4	10.7	14
Median	6	6	0	7	7	0
Age (years)						
Mean	66.3	68.4	3	74.0	76.6	4
Median	67	70	5	76	79	4
30-54, %	19.1	17.3	-9	6.4	6.3	-1
55-64, %	22.9	20.9	-9	12.6	10.3	-19
65-74, %	29.4	23.9	-19	26.9	18.9	-30
75-84, %	22.8	25.9	14	35.9	34.3	-4
85+, %	5.9	12.0	104	18.2	30.2	66
Comorbidity (%)						
Arrhythmia	8.4	14.6	74	10.3	20.3	98
Cancer	1.5	3.9	151	1.1	2.3	113
Cerebrovascular disease	2.5	3.3	31	3.3	4.3	30
Diabetes	12.3	19.8	61	13.9	20.8	50
Heart failure	13.2	17.2	30	18.4	23.4	27
Hypertension	16.3	41.9	156	20.6	49.4	140
Peripheral vascular disease	2.5	5.2	106	2.4	4.0	69
Renal disease	3.0	7.8	164	3.2	8.3	161
Respiratory disease	11.9	21.2	78	14.1	27.0	91
Coronary revascularisation procedures (%)						
CABG	0.2	1.2	417	0.1	0.6	417
PTCA	3.5	17.8	411	2.1	10.2	383

CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

** Overall relative percent change from 1999 to 2007 = – (1-(Value in 2007/Value in 1999))*100%*

***Taken from Chapter 3*

Figure 15. Age distribution of patients hospitalised for acute myocardial infarction as proportion (%) of the total number of admissions in A) men and B) women by age group, 1999-2007, England.



The prevalence of comorbidities was generally higher in older patients and in women, and increased over the study period. Relative percentage increases between 1999 and 2007 were observed for all conditions, both sexes, and all age groups. Using logistic regression models to assess the significance of the overall increase in the prevalence of each comorbidity has shown that all were significant, even after adjusting for age

($p<0.001$ for all). The magnitude of the overall increase for each comorbidity was broadly similar between men and women (Table 22). Particularly high increases (in relative percentage terms, comparing 1999 with 2007) were observed for hypertension, cancer, peripheral vascular disease and renal disease; however, the absolute prevalence of these conditions (except for hypertension) was relatively low compared with others. Age-specific stratification (Table 23) showed the prevalence of comorbidities generally increased in all age groups over time, but it increased more in older individuals.

Table 23. Prevalence (%) of comorbidities in patients hospitalised for acute myocardial infarction by age group, 1999-2007, England.

Comorbidity	30-54 years			55-64 years			65-74 years		
	1999	2007	% change*	1999	2007	% change	1999	2007	% change
Arrhythmia	2.8	3.5	27	5.1	7.1	41	9.0	14.6	63
Cancer	0.4	0.5	39	0.6	1.8	179	1.5	3.2	110
Cerebrovascular disease	0.8	0.7	-14	1.6	1.8	15	3.0	3.7	24
Diabetes	9.3	13.7	47	13.6	17.6	30	15.3	24.9	63
Heart failure	4.8	6.3	32	8.1	10.1	25	14.1	17.1	21
Hypertension	14.3	29.6	108	18.1	40.7	126	20.1	48.2	139
Peripheral vascular disease	1.1	1.9	76	2.0	3.5	78	3.0	5.7	93
Renal disease	0.8	1.5	82	1.4	2.6	86	2.7	6.6	144
Respiratory disease	6.0	10.7	78	9.3	15.4	66	14.0	23.7	69

	75-84 years			85+ years		
	1999	2007	% change	1999	2007	% change
Arrhythmia	13.2	23.1	75	14.7	27.6	87
Cancer	2.0	4.8	133	2.0	4.3	116
Cerebrovascular disease	3.9	5.2	33	4.4	5.0	14
Diabetes	13.2	23.9	81	9.4	15.9	70
Heart failure	22.3	24.9	12	26.3	31.8	21
Hypertension	19.0	50.8	168	14.1	45.9	227
Peripheral vascular disease	3.0	6.1	103	2.7	4.8	79
Renal disease	4.6	11.1	143	5.9	14.0	138
Respiratory disease	16.2	29.5	83	15.7	29.8	89

** Overall relative percent change from 1999 to 2007 = – (1-(Value in 2007/Value in 1999))*100%*

The percentage of hospitalised AMI admissions that also had a record of CABG or PTCA within 30 days of the index admission has grown dramatically from 1999 to 2007 (Table 22). The increases in both procedures and for both sexes (about four-fold over the study period) were statistically significant ($p<0.001$ for all). However, the use of procedures was different – about 15 times more patients underwent PTCA than CABG in 2007.

Length of stay

Length of hospital stay was examined separately for fatal and non-fatal AMIs. The distribution of the length of stay for index hospital admissions for AMI was strongly skewed to the right for both fatal and non-fatal events (Figure 16). This shows that a small proportion of patients had very long hospital stays, some for over 30 days (3.1% for men and 5.5% for women).

To illustrate the effect of very long hospital stays, Figure 17 shows the mean length of stay by year for all hospital admissions and for 99% of admissions (excluding the top one percent with the longest stays). The effect of excluding the top one percent was an average reduction in the mean length of stay of 0.6 days for men and 1.1 days for women. These represent reductions of 6.1% and 10.3%, respectively. Figure 17 also shows that while there was no large overall change between 1999 and 2007, the length of stay increased between 1999 and 2004, peaked in 2004 at 9.9 days for men and 11.7 days for women, and then declined to 8.8 days for men and 10.7 days for women by 2007. In every year, the mean length of stay was about two days longer in women than in men ($p<0.001$ for all years). The median length of stay did not change between 1999 and 2007, remaining at 6 days in men and 7 days in women.

Figure 16. Length of stay of index hospital admissions for A) fatal and B) non-fatal acute myocardial infarction events, 1999-2007, England.

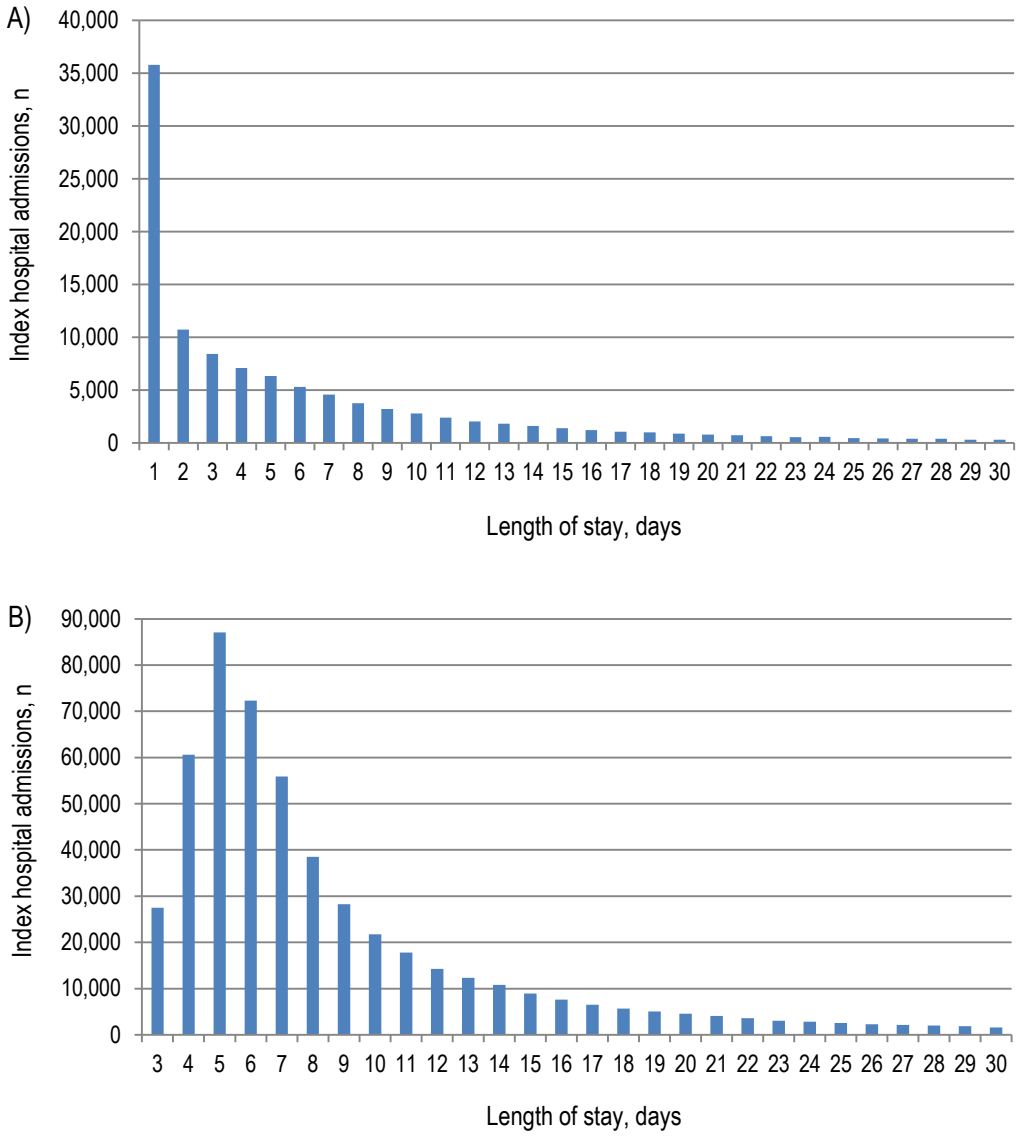
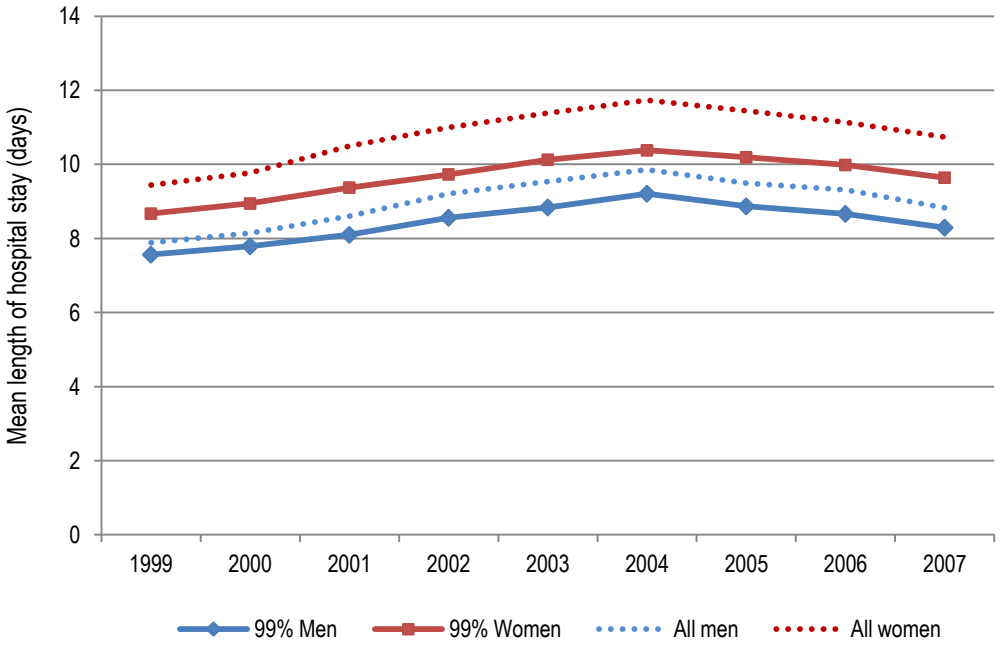


Figure 18 shows changes in the distribution of length of stay for index AMI admission by sex and year of admission. Hospital stays of 3-5 days have increased between 1999 and 2007 by 28% for men and 32% for women ($p<0.001$), while stays of 6-8 days have fallen by 37% for men and 32% for women ($p<0.001$). The proportion of stays that lasted 9-14 days slightly increased in men and slightly decreased in women. Stays of 15 days and over increased until 2004 and decreased afterwards.

Figure 17. Mean length of hospital stay for acute myocardial infarction by sex and year of admission, all and 99%* of admissions, 1999-2007, England.



*99% excludes the top one percent of admissions with the longest stays

Figure 18. Distribution of length of hospital stay for acute myocardial infarction by sex and year of admission, 1999-2007, England.

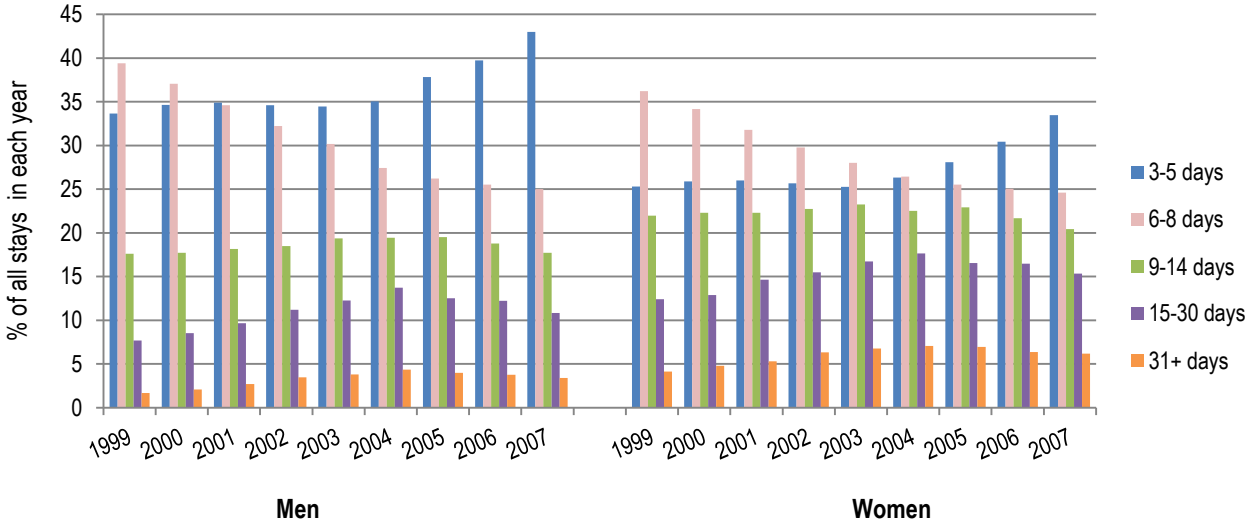
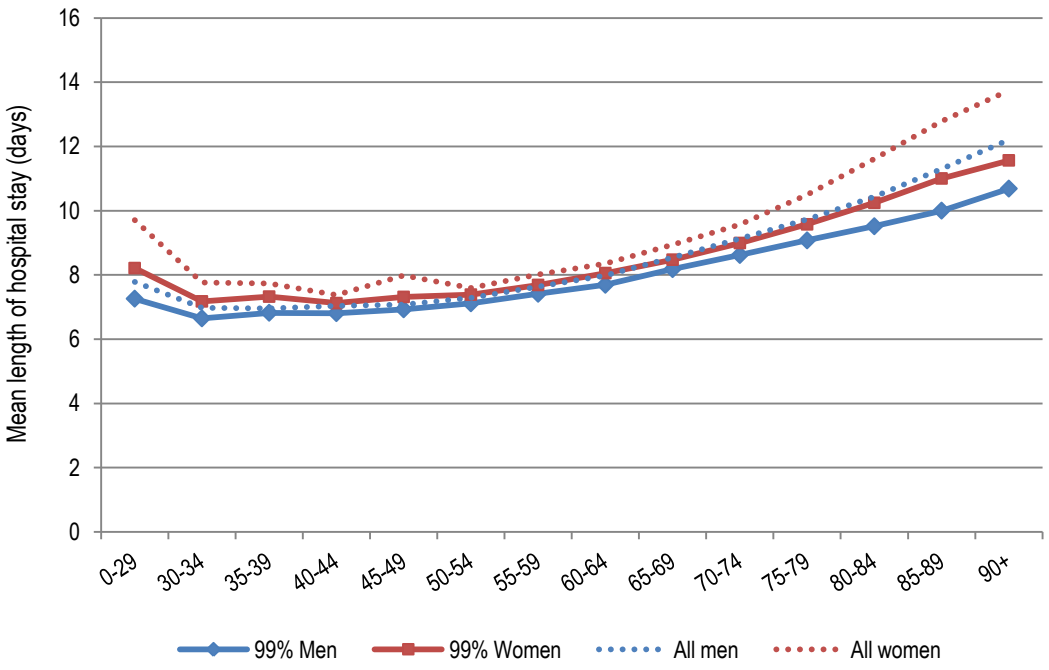


Figure 19 shows the change in the mean length of stay for index AMI admission by age group, for all admissions and 99% of admissions (excluding the top one percent with longest stays). For all admissions, the mean length of stay was higher in women than men in each age group. For men, it was lowest for those aged 30-44 years at 7.0 days and increased to 12.2 days for men aged 90 years and older. For women, the mean length of stay was lowest in the 40-44 years age group at 7.4 days and increased to its highest at 13.7 days for women aged 90 years and older. The median length of stay increased from 5 and 6 days in men and women aged 30-34 years, respectively, to 7 days in men and 8 days in women aged 85 years and older.

Figure 19. Mean length of hospital stay for acute myocardial infarction by age group and year of admission, all and 99%* of admissions, 1999-2007, England.



99% excludes the top one percent of admissions with the longest stays

Length of stay and 30-day postdischarge mortality

The association between the length of stay and postdischarge mortality was examined for those patients who survived to discharge from index hospital admission for AMI. Table 24 shows crude 30-day postdischarge mortality rates as well as unadjusted and adjusted odds ratios for death within 30 days of discharge, by length of stay. The reference category was 6-8 day length of stay because it contained the median for both men and women. Crude mortality rates and unadjusted odds ratios were lowest for the shortest stay of 3-5 days, and increased with longer hospital stays. The unadjusted risk of dying within 30 days of hospital discharge was about four times higher for the longest stays of 31 days or more compared with the reference category of 6-8 days for both sexes.

Adjusting for age, coronary revascularisation procedures, and comorbidities attenuated these differences, but the risk of dying within 30 days of discharge still increased with increasing length of stay and was highest for the longest stays in both men (OR=2.20, 95% CI: 2.02-2.40) and women (OR=2.14, 95% CI: 1.97-2.34). However, the risk of dying was not significantly different from the median for short lengths of stay (3-5 days) for both men (OR=0.95, 95% CI: 0.89-1.01) and women (OR=1.03, 95% CI: 0.95-1.11).

Table 24. Mortality within 30 days of discharge date from index admission for acute myocardial infarction (AMI) by sex and length of stay, 1999-2007, England.

Length of stay (days)	AMIs, n	Deaths, n	Crude death rate (%)	Model 1			Model 2			Model 3		
				OR*	95% CI		OR**	95% CI		OR***	95% CI	
Men												
3-5	123,203	2,199	1.78	0.79	0.74	0.84	0.84	0.79	0.89	0.95	0.89	1.01
6-8	108,807	2,450	2.25	Ref.			Ref.			Ref.		
9-14	62,360	2,321	3.72	1.68	1.58	1.78	1.42	1.34	1.51	1.34	1.26	1.42
15-30	35,151	1,967	5.60	2.57	2.42	2.73	1.89	1.77	2.01	1.71	1.61	1.82
31+	9,709	848	8.73	4.15	3.83	4.50	2.57	2.36	2.81	2.20	2.02	2.40
Women												
3-5	49,902	1,303	2.61	0.91	0.85	0.98	0.94	0.87	1.01	1.03	0.95	1.11
6-8	58,328	1,664	2.85	Ref.			Ref.			Ref.		
9-14	42,983	1,827	4.25	1.51	1.41	1.62	1.39	1.30	1.49	1.27	1.19	1.36
15-30	28,283	1,786	6.31	2.30	2.14	2.46	1.92	1.79	2.06	1.64	1.53	1.76
31+	10,469	980	9.36	3.52	3.24	3.82	2.73	2.50	2.97	2.14	1.97	2.34

OR=odds ratio

**Unadjusted; **Adjusted for comorbidities only; ***Adjusted for age, coronary revascularisation procedures, and comorbidities*

Length of stay and 31-365 day postdischarge mortality

Table 25 shows crude postdischarge mortality rates as well as unadjusted and adjusted odds ratios for dying between 31 and 365 days of discharge, according to the length of stay for the index AMI admission. Crude mortality rates and unadjusted odds ratios were lowest for the shortest stays, but increased with increasing length of stay. Adjustment for age, coronary revascularisation procedures, and comorbidities attenuated these differences, but the risk of dying between 31 and 365 days of discharge still increased with increasing length of stay and was almost twice as high for the longest stays compared with the reference category in both men (OR=1.79, 95% CI: 1.68-1.91) and

women (OR=1.75, 95% CI: 1.64-1.85). The risk of dying following shorter lengths of stay (3-5 days) was slightly lower than the reference category for both men (OR=0.87, 95% CI: 0.84-0.90) and women (OR=0.91, 95% CI: 0.87-0.95).

Table 25. Mortality within 31-365 days of discharge date from index admission for acute myocardial infarction (AMI) by sex and length of stay, 1999-2006, England.

Length of stay (days)	AMIs, n	Deaths, n	Crude death rate (%)	Model 1			Model 2			Model 3		
				OR*	95% CI		OR**	95% CI		OR***	95% CI	
Men												
3-5	107,961	6,063	5.62	0.70	0.68	0.72	0.75	0.72	0.77	0.87	0.84	0.90
6-8	99,860	7,833	7.8	Ref.			Ref.			Ref.		
9-14	56,242	6,877	12.2	1.64	1.58	1.69	1.39	1.34	1.44	1.29	1.24	1.33
15-30	31,582	5,131	16.3	2.28	2.19	2.37	1.68	1.62	1.75	1.51	1.45	1.58
31+	8,654	1,945	22.5	3.41	3.22	3.60	2.16	2.03	2.30	1.79	1.68	1.91
Women												
3-5	43,113	3,629	8.4	0.79	0.76	0.83	0.82	0.78	0.85	0.91	0.87	0.95
6-8	53,093	5,520	10.4	Ref.			Ref.			Ref.		
9-14	38,791	5,890	15.2	1.54	1.48	1.61	1.42	1.37	1.48	1.27	1.22	1.32
15-30	25,253	5,080	20.1	2.17	2.08	2.26	1.84	1.76	1.92	1.52	1.45	1.59
31+	9,290	2,374	25.6	2.96	2.80	3.12	2.38	2.24	2.52	1.75	1.64	1.85

OR=odds ratio

**Unadjusted; **Adjusted for comorbidities only; ***Adjusted for age, coronary revascularisation procedures, and comorbidities*

Discussion

This study reports the changing characteristics of individuals hospitalised for AMI, trends in length of hospital stay for AMI, and the association between length of stay and postdischarge mortality between 1999 and 2007. Of all AMI hospitalisations in 2007, over one third for men and around two thirds for women were in individuals aged 75 years and older. Compared with 1999, patients admitted to hospital for AMI in 2007 were older and presented with more comorbidities; more patients underwent revascularisation procedures within 30 days of admission. On average, AMI patients spent about one week in hospital. Generally, the length of stay was longer for women than men and for older than younger patients. Shorter lengths of stay were not associated with a higher mortality within 30 days or one year after discharge date from the index AMI hospital admission.

Age distribution

This study confirms earlier reports from several countries of an increasingly elderly AMI patient population.[43, 71, 114, 116, 119, 138, 173, 175, 176] Amongst English AMI patients in 2007, 62% of men were aged 65 years and older, and 38% were aged 75 years and older; for women, the corresponding figures were 83% and 65%. These findings are comparable to those of others. According to the US National Hospital Discharge Survey for 2003-05, 64% of AMI patients were aged 65 years and older and 42% were aged 75 years and over.[114] The corresponding figures for Canada in 2004, based on the national Hospital Morbidity Database, were 63% and 41%, respectively.[43] An older patient cohort is likely to include more individuals with complex clinical profiles who may be more difficult to treat.[237] The increasing availability of cardiologic treatments for AMI calls for further research on their impact in older individuals.

An older AMI patient population has probably arisen both from an increasingly elderly total population in England and from a rise, over time, in the rate of occurrence of AMI events among older individuals. As life expectancy in England increases, the ageing population brings changes to the demographic composition of AMI patients as well. In Chapter 3, it was reported that age-specific hospitalised event rates in men and women aged under 85 years decreased over the study period, while age-specific rates in those aged 85 years and over increased. In other words, fewer younger people and more older people were experiencing heart attacks. These results suggest that a real demographic transition in the epidemiology of AMI is occurring in England, and AMI is increasingly becoming a disease of old age, especially in women. This shift in the occurrence of disease towards the elderly is likely to be a consequence of effective prevention strategies and risk factor control in the middle-aged population.[176] It also emphasises the importance of including the elderly in epidemiological studies of AMI for completeness (many previous studies have used age cut-offs of 65 or 75 years).

Comorbidities

In addition to the increasing age at admission over time, others have found that the demographic characteristics of AMI patients have changed to include more women and more patients with pre-existing comorbidities.[71, 114, 116, 171, 175, 195, 227, 316] In this chapter, there were very clear increases in the prevalence of all examined comorbidities for both sexes and all age groups between 1999 and 2007. In any given year, prevalence of comorbidities was higher for women and older individuals. These results concur with reports from other countries: for example, in the US National Hospital Discharge Survey, the prevalence of hypertension and diabetes among AMI patients increased by 234% and 59%, respectively, between 1979-81 and 2003-05.[114] In Spain, comorbidities significantly increased for both fatal and non-fatal hospitalised AMI cases between 2003 and 2009.[317]

A UK study that examined changes over time in the patient population undergoing coronary revascularisation procedures between 1995 and 2004 in Leicestershire also found a significant increase in comorbidities recorded on hospital records.[316]

However, none of the above studies reported changes in comorbidity by age group. Given the increasingly older patient population, increased overall prevalence of comorbidities is expected. The advantage of the present study is that it shows that prevalence of comorbidities generally increased in all age groups. Factors that could have contributed to the higher recorded comorbidity prevalence include better diagnostic tools, changes in coding practices for hospital records, increasing number of secondary diagnostic fields available on hospital records, and, possibly, a real change in the patient health profile.[71] The particularly high increases that can be seen for recorded hypertension across all age groups are likely a result of better coding of secondary diagnoses, a shift in the definition of hypertension towards lower thresholds, as well as increasing availability and prescription of antihypertensive drugs. However, further research is required to elucidate the factors driving the observed rise in recorded comorbidities.

Revascularisation procedures

The National Service Framework for CHD, introduced by the Department of Health in 2000, acknowledged that the UK had low revascularisation rates compared with other countries and noted that there was considerable scope for improvement.[247] As shown in the findings of this chapter, there has been an increase during the 2000s in the proportion of AMI patients who have undergone a revascularisation procedure in England, particularly PTCA. The observed rising revascularisation rates over the last decade reflect changing clinical guidelines, wider availability of the procedures, mounting scientific evidence on their safety and efficacy, and technological advances.[316, 318, 319] Globally,

increases in the use of PTCA and CABG for AMI patients have also been reported in Canada,[134] Australia,[143] and the US[50, 114] since the 1980s.

Length of stay

The trends in length of stay reported in this study are closely aligned with the UK figures published by the Organisation for Economic Co-operation and Development Health Data database.[239] Both sources show an increasing trend up until 2004 and a decreasing trend afterward. For comparison, Figure 20 shows mean lengths of stay for AMI patients for some other countries from the OECD database. As in the UK, there was a peak in the mean length of stay in 2004 in Ireland, followed by a decline. Figure 20 also shows that, unlike the UK and Ireland, many other developed countries experienced a consistent decline in mean lengths of stay during the time period of this study. Declines have also been occurring in the previous years as well. Studies from the US and Europe have reported consistent declines in length of stay since the 1980s.[78, 114, 115, 138, 195, 241]

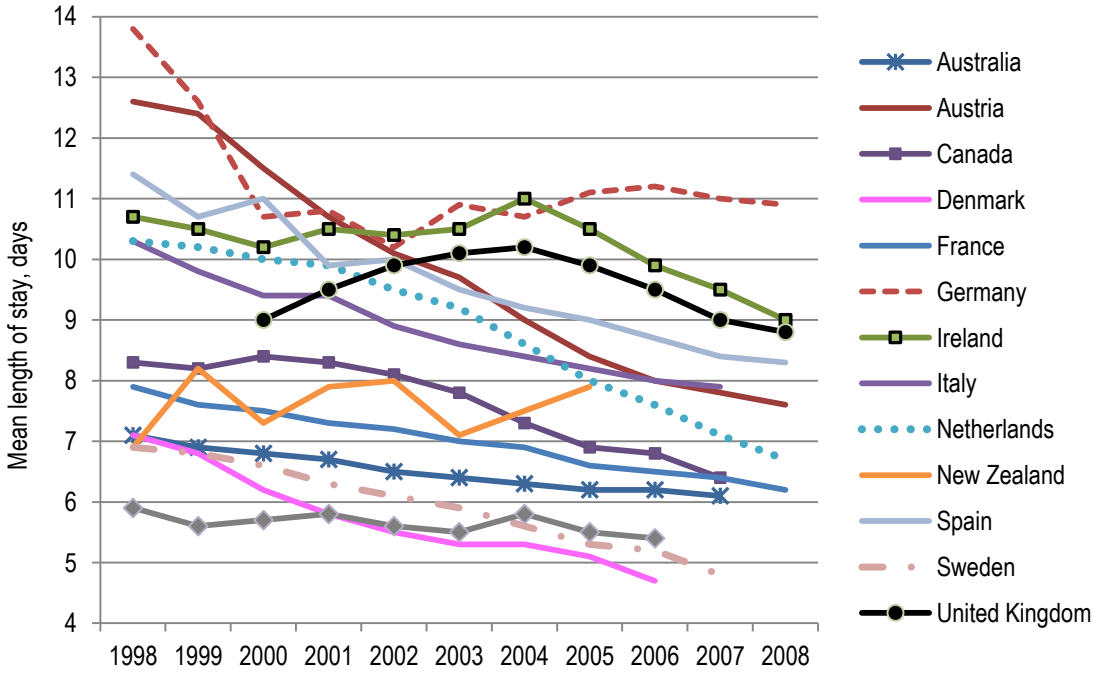
Length of stay and postdischarge mortality

Results of the examination of the effect of length of stay on 30-day and 31-365 day postdischarge mortality suggest that lengths of stay shorter than the median stay of 6-8 days may not be associated with increased mortality after discharge in the short-term or long-term. However, more research using English data and including clinical information is needed, with adjustment for severity of AMI, because length of stay is associated with the severity of the condition. Findings from non-UK studies that adjusted for clinical characteristics of AMI events showed that shorter hospital stays do not translate into higher mortality after discharge.[101, 115, 240, 241, 243] For example, data from the Worcester Heart Attack Study, a population-based study that reported postdischarge mortality by length of stay, similarly showed that the likelihood of dying after hospital discharge was

not significantly different for lengths of stay shorter than the median stay of 5-6.9 days (OR=1.28, 95% CI 0.87-1.89 for stays of 3-4.9 days).[241] The lack of a negative effect of shorter hospital stays on subsequent mortality has been attributed to improvements in the availability and use of effective treatments, such as coronary reperfusion and revascularisation procedures; changing approaches to AMI management, including early mobilisation and home care; and financial pressures to cut costs.[115, 241-243]

The results of this study also suggest that longer lengths of stay may be associated with a higher risk of both short-term and long-term postdischarge mortality. Others have found that longer stays had an adverse effect on 90-day and one-year mortality following hospitalisation for AMI.[101, 240, 241] Higher postdischarge mortality associated with lengths of hospital stay longer than a week is likely a reflection of an older and/or a sicker group of patients who had unrecorded comorbidities on admission and/or in-hospital complications that required additional treatment and medical care (and hence required longer in-patient stays).[243]

Figure 20. Mean length of stay in hospital by patients admitted for acute myocardial infarction by country, 1998-2008.



Data source: Organisation for Economic Co-operation and Development Health Data database, 2009.

Conclusion

This study shows that, between 1999 and 2007, the AMI patient population in England became increasingly elderly, presented to hospital with more comorbidities, and underwent more coronary revascularisation procedures. The mean length of hospital stay for AMI patients was approximately one week. Shorter lengths of stay were not associated with increased mortality within 30 days or within one year of discharge from hospital. However, older and more medically complex patients, who are also discharged earlier, may be at increased risk of other adverse outcomes, emphasising the importance of appropriate long-term care.

CHAPTER 7: AMI INCIDENCE AND CASE FATALITY IN 2007

This chapter provides recent population-based estimates of incidence and short-term (30-day) case fatality rates for acute myocardial infarction (AMI) in England in 2007. Results are provided by age group, sex, Government Office Region, and type of AMI event, distinguishing between first and recurrent AMI. The effects of prognostic factors on case fatality are investigated and include age, sex, deprivation category, and history of a previous AMI. Geographic variation in AMI incidence and case fatality is explored by Government Office Region. Socioeconomic inequalities in case fatality are explored by comparing deprivation categories.

Introduction

There are few recent population-based UK studies of AMI that reported incidence estimates.[5, 26, 28, 29, 67, 85] These studies were local rather than national (three come from Oxfordshire), did not necessarily include all age groups or report results distinguishing between first AMI and reinfarction, and dated to the 1990s and early 2000s. As such, published recent national population-based data on AMI incidence and case fatality in England are limited, making the current burden of disease, and clinical prognosis, difficult to quantify. Further, while regional differences in CHD occurrence have been observed throughout England, particularly the higher mortality rate from AMI in the north compared with the south,[61-63] geographic differences in AMI incidence and case fatality have not been well quantified on a population-based national level.

Finally, while socioeconomic differences in AMI mortality and occurrence are well established,[210, 219, 220, 223, 233, 320] there are conflicting findings on the association between socioeconomic deprivation and case fatality. Some studies found that after adjusting for baseline characteristics, higher socioeconomic deprivation was associated with higher mortality[220-223, 229-231] but others did not.[121, 219, 233, 234] Deprivation gradient for short-term case fatality has been recently reported in Scotland,[83] but no up-to-date population-based representative data are available for England. Also, the sample size of many studies that examined the association between deprivation and case fatality after AMI did not allow stratification by age, and thus limited information is available on differences in case fatality by deprivation for different age groups.

The objectives of this chapter are:

1. To report population-based rates of occurrence of first and recurrent AMI in England in 2007 by age, sex, and Government Office Region (GOR);
2. To present short-term (30-day) AMI case fatality rates in England in 2007 by type of AMI, age, sex, GOR, and deprivation category;
3. To compare AMI incidence and case fatality rates between first and recurrent AMI, men and women, age groups, GORs, and deprivation categories; and
4. To explore the effects on fatality of age, sex, deprivation, and prior AMI.

Methods

Study population

Residents of England who had an AMI event between 1 January 2007 and 31 December 2007 were included in the study. For this chapter, the definitions of AMI event, hospital

admission, fatal and non-fatal AMI, deprivation, comorbidities, revascularisation procedures, and Government Office Regions are the same as in Chapter 2 (Methods).

For each person, the first occurrence of an AMI in 2007 was flagged as the index event. To classify the index AMI event in 2007 as first or recurrent AMI, a nine-year clinical history (defined as a previous hospital record with AMI as primary or secondary diagnosis) was used from the hospital admission linked file (see Chapter 2, section on AMI history for more details). If the index AMI event in 2007 occurred in an individual with no clinical history of AMI during the previous nine years, it was categorised as a first AMI, as a proxy for true first AMI. Otherwise, the index event was categorised as recurrent AMI, or reinfarction. (Distinguishing between first and recurrent AMI allowed for a more comprehensive and detailed epidemiological analysis of sub-groups.)

Statistical analyses

Incidence and recurrence were defined as the rates of occurrence of first and recurrent AMI, respectively. The event rate was defined as the rate of occurrence of all AMI, including first and recurrent AMI. All rates of occurrence were calculated per 100,000 population of England by age group and sex, using the mid-year population estimates published by the Office for National Statistics.[19] Rates were directly age-standardised to the European Standard Population. The 95% confidence intervals were estimated assuming that the observed number of events followed a Poisson distribution.

Hospitalised 30-day case fatality was calculated using the total number of hospitalised AMIs in 2007 as the denominator, and the number of fatal AMIs within 30 days of admission to hospital in 2007 as the numerator. Overall 30-day case fatality was calculated using the total number of AMIs in 2007 (hospital admission or sudden death)

as the denominator, and the number of all fatal AMIs in 2007 as the numerator. Rates were directly age standardised using five-year age groups and the age distribution of the entire nine-year AMI event cohort as the standard population.

Multiple logistic regression analysis, yielding odds ratios (ORs), was used to quantify the effects of sex, age, deprivation category, and history of a previous AMI on 30-day case fatality, after adjusting for the other factors. Risk ratios were calculated for overall and hospitalised case fatality rates in each age group to compare the ratio of the most deprived to the least deprived category. The effect of treatment and comorbidities on case fatality was not analysed because this information was only available for hospitalised AMI cases, and if these factors were included in the calculation of hospitalised case fatality, then it would not be directly comparable to the overall case fatality.

Results

Study cohort

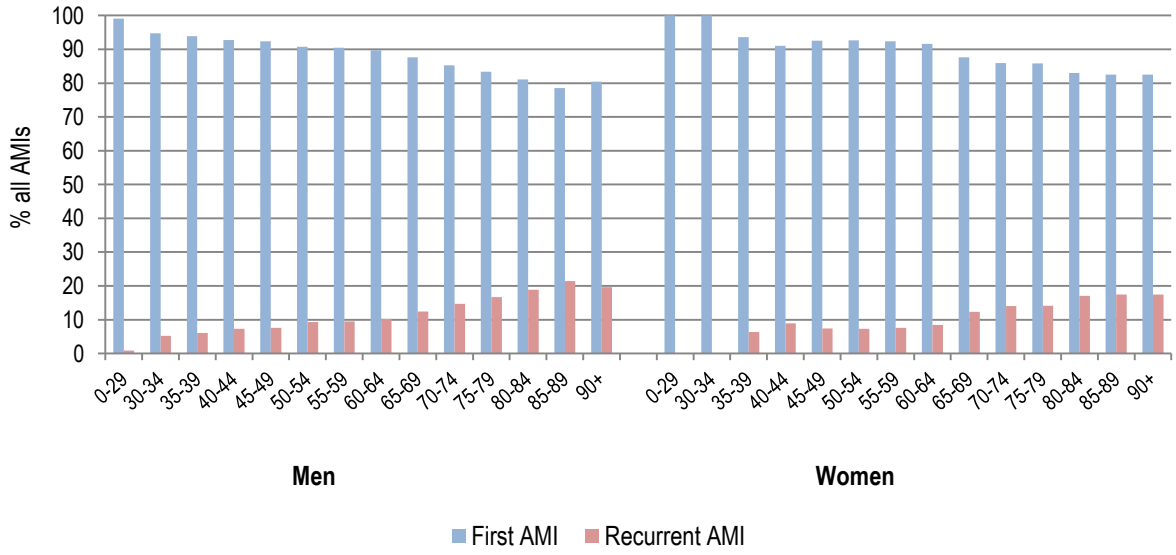
Between 1 January and 31 December 2007, a total of 88,311 AMI events occurred among 85,612 individuals. Table 26 shows the characteristics of all AMI cases in 2007 by type of AMI. Of all the events, 86% were first AMIs; 61% occurred in men; 36% were fatal; and 73% occurred in people aged 65 years and over. Women were significantly older than men at both hospital admission for AMI (77 versus 68 years, $p<0.001$) and sudden AMI death (81 versus 74 years, $p<0.001$). The percentage of all events that were sudden AMI deaths was similar for first and recurrent AMI (25% and 24%, respectively, $p=0.12$). The mean ages at first and recurrent AMI were 72 and 76 years, respectively ($p<0.001$). The percentage of all events that were reinfarctions was slightly higher for women than

men (14.7% versus 14.2%, p=0.026) and increased with older age in both sexes, from less than 1% for the youngest age group to about 20% for the oldest age group (test for trend p<0.001) (Figure 21).

Table 26. Characteristics of all, first, and recurrent acute myocardial infarction (AMI) events, 2007, England.

Characteristic	All AMIs	First AMIs			Recurrent AMIs		
		All	Fatal		All	Fatal	
	n	n	n	% all cases	n	n	% all cases
Total	88,311	75,587	26,735	35	12,724	4,609	36
Type of event							
Hospital admission	66,546	56,887	8,035	14	9,659	1,544	16
Sudden AMI death	21,765	18,700	18,700	(100)	3,065	3,065	(100)
Sex							
Male	53,620	46,008	14,960	33	7,612	2,706	36
Female	34,691	29,579	11,775	40	5,112	1,903	37
Age (years)							
Mean	72.8	72.2	77.3	-	76.4	79.2	-
Median	75	75	80	-	79	81	-
0-29	171	170	34	20	1	0	0
30-54	9,979	9,184	1,406	15	795	120	11
55-64	13,498	12,214	2,602	21	1,284	341	76
65-74	18,724	16,188	4,865	30	2,536	795	33
75-84	26,994	22,446	9,522	42	4,548	1,740	33
85+	18,945	15,385	8,306	54	3,560	1,613	43
Deprivation							
Least deprived, 1	18,233	15,909	5,407	34	2,324	873	38
2	18,155	15,699	5,397	34	2,456	913	37
3	17,471	14,876	5,334	36	2,595	910	35
4	17,289	14,705	5,288	36	2,584	940	36
Most deprived, 5	16,882	14,192	5,253	37	2,690	938	35

Figure 21. Proportion (%) of all acute myocardial infarctions (AMIs) by type of event, sex and age, 2007, England.



Rates of occurrence of AMI events

All AMIs, all England

The overall annual age-standardised event rate of all AMI events (including first and recurrent) per 100,000 population was 174 (95% CI: 173-176) in men and 74 (95% CI: 73-75) in women.

Recurrent AMIs, all England

The annual age-standardised AMI recurrence rate per 100,000 population was 23 (95% CI: 23-24) in men and 10 (95% CI: 10-10) in women. Because of low numbers, the recurrence rate of AMI was not investigated further.

First AMIs, all England

In 2007, there were 75,587 first AMI events in England. Table 27 shows incidence rates of first AMI by age and sex. The age-standardised incidence of first AMI per 100,000 population was 151 (95% CI: 150-152) in men and 64 (95% CI: 63-65) in women. The incidence of first AMI increased with older age for both men and women (Figure 22). In men, the incidence rate per 100,000 population rose from 11 (95% CI: 9-13) for those aged 30-34 years to 1,988 (95% CI: 1,900-2,081) for those aged 90 years and older; in women, it increased from 2 (95% CI: 2-3) to 1,467 (95% CI: 1,422-1,514) in the corresponding age groups.

Figure 22. Overall incidence rates of first acute myocardial infarction by age and sex, 2007, England.

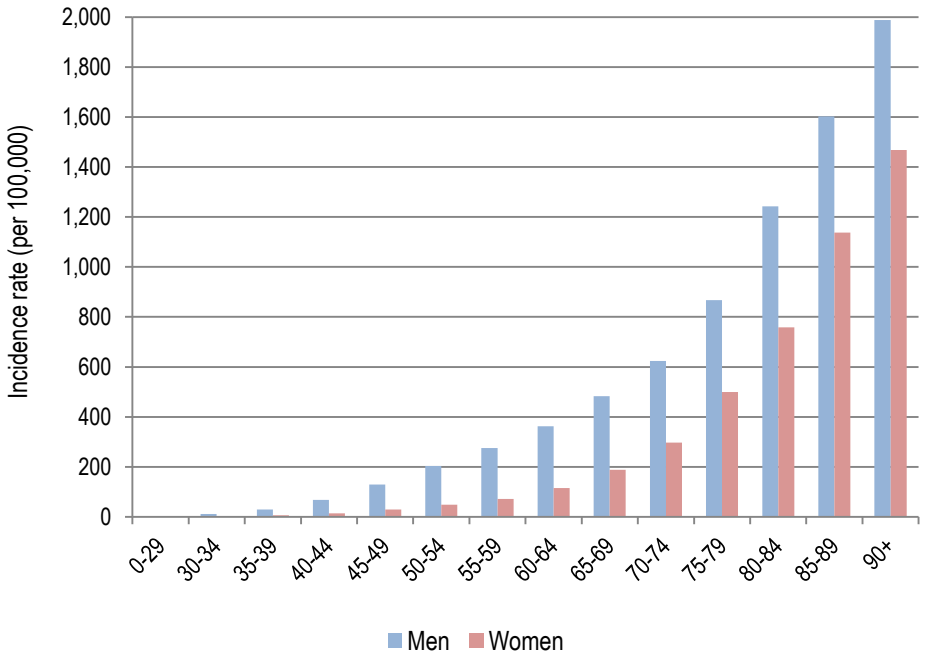
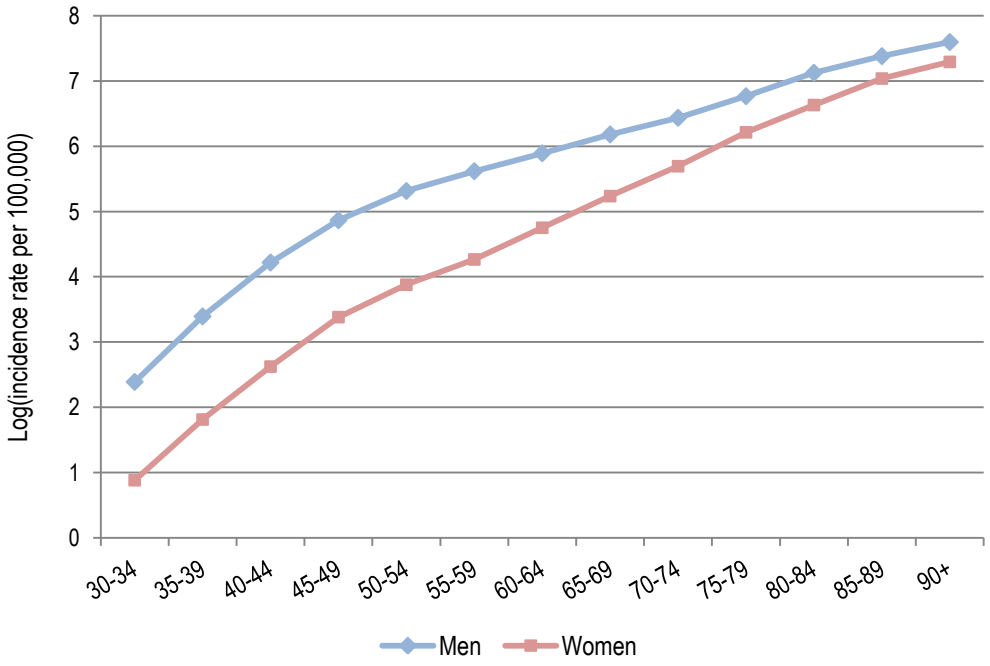


Table 27. Population-based incidence rates of first acute myocardial infarction (AMI) by sex and age, 2007, England.

Sex	Age	First AMIs, n			Incidence rate per 100,000		
		Hospital admissions	Sudden deaths	Total first AMIs	Hospital admissions	Sudden deaths	Overall
Men	0-29	93	16	109	1	0	1
	30-34	145	36	181	9	2	11
	35-39	483	84	567	25	4	30
	40-44	1,162	175	1,337	59	9	68
	45-49	2,013	263	2,276	115	10	130
	50-54	2,688	420	3,108	176	28	203
	55-59	3,555	675	4,230	231	44	275
	60-64	4,167	971	5,138	294	69	362
	65-69	4,125	1,074	5,199	383	100	483
	70-74	4,304	1,422	5,726	468	155	623
	75-79	4,476	1,799	6,275	619	249	867
	80-84	4,111	1,872	5,983	854	389	1,243
	85-89	2,677	1,353	4,030	1,064	538	1,602
	90+	1,145	704	1,849	1,231	757	1,988
	All ages	35,144	10,864	46,008	117	34	151
Women	0-29	55	6	61	1	0	1
	30-34	33	7	40	2	0	2
	35-39	95	23	118	5	1	6
	40-44	238	37	275	12	2	14
	45-49	471	55	526	26	3	29
	50-54	660	96	756	42	6	48
	55-59	975	153	1,128	62	10	71
	60-64	1,444	274	1,718	97	18	116
	65-69	1,775	398	2,173	153	34	188
	70-74	2,409	681	3,090	231	65	297
	75-79	3,422	1,187	4,609	370	129	499
	80-84	3,918	1,661	5,579	532	226	758
	85-89	3,729	1,815	5,544	765	372	1,137
	90+	2,519	1,443	3,962	933	534	1,467
	All ages	21,743	7,836	29,579	49	15	64

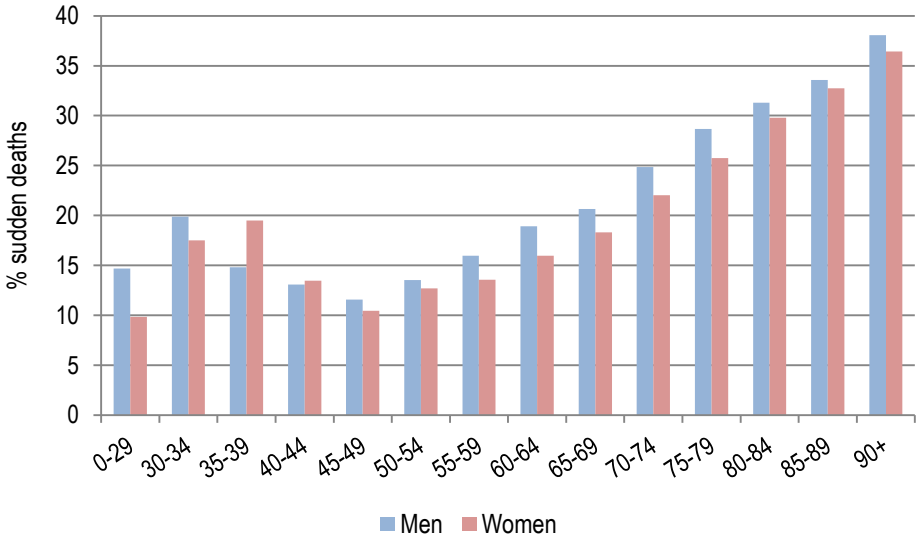
In all age groups, the incidence rate was higher for men than women. However, the difference between men and women in their age-specific rates decreased markedly with increasingly older age. Figure 23 illustrates the closing gap in AMI incidence rate between increasingly older men and women. The incidence rate ratio (RR) of first AMI in men compared with women was highest for the 40-44 years age group (RR=4.93, 95% CI: 4.33-5.61) and declined to its lowest for the 90 years and over age group (RR=1.35, 95% CI: 1.28-1.43). In other words, the incidence rate per 100,000 was about five times higher for men than women aged 40-44 years (68 compared with 14) but only 35% higher for men than women aged 90 years and older (1,988 compared with 1,467) (Table 27).

Figure 23. Age-specific population-based incidence rates of first acute myocardial infarction on a logarithmic scale by sex, 2007, England.



Amongst first AMI events, the proportion of sudden deaths varied between men and women and between age groups for those aged under 45 years. However, for individuals aged 45 years and over, the proportion of first AMIs that were sudden deaths increased with older age and was consistently slightly higher for men than women (Figure 24).

Figure 24. Proportion of sudden deaths amongst first acute myocardial infarction events by sex, 2007, England.



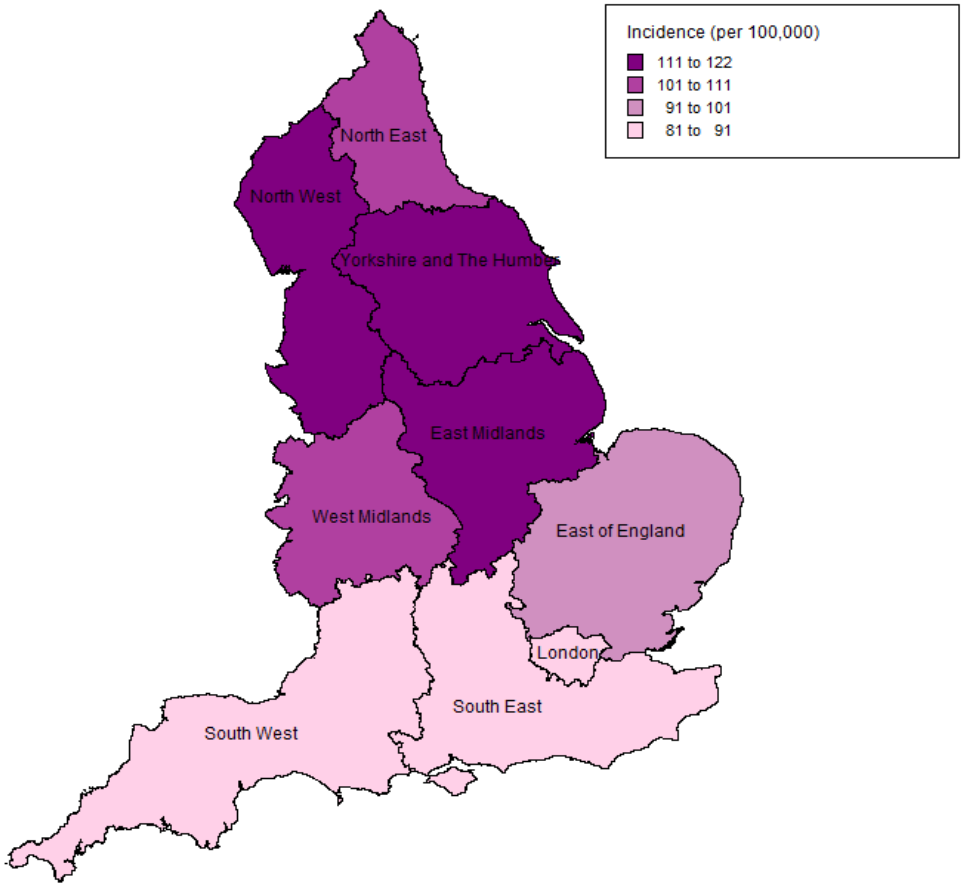
First AMI, by Government Office Region

Incidence rates for first AMI were not uniform across England, demonstrating a clear north-to-south gradient (Figure 25). When analysed by GOR, the incidence rate per 100,000 population was lowest in London, at 81 (95% CI: 79-83), and highest in the North West, at 122 (95% CI: 120-125) (Table 28). The age-standardised incidence rate in the North West was 50% higher than the rate in London (RR=1.51; 95% CI: 1.14-1.99).

Table 28. Overall incidence of first acute myocardial infarction and incidence rate ratios by Government Office Region, 2007, England.

Government	Incidence rate			Rate ratio		
Office Region	Rate	95% CI		Ratio	95% CI	
London	81	79	83	Ref.		
South East	84	82	86	1.04	0.76	1.41
South West	90	88	93	1.11	0.82	1.50
East England	96	94	98	1.19	0.88	1.59
West Midlands	102	99	104	1.26	0.94	1.69
North East	104	100	107	1.28	0.96	1.72
East Midlands	114	112	117	1.41	1.06	1.87
Yorkshire	117	115	120	1.44	1.09	1.92
North West	122	120	125	1.51	1.14	1.99

Figure 25. Overall incidence of first acute myocardial infarction by Government Office Region, 2007, England.



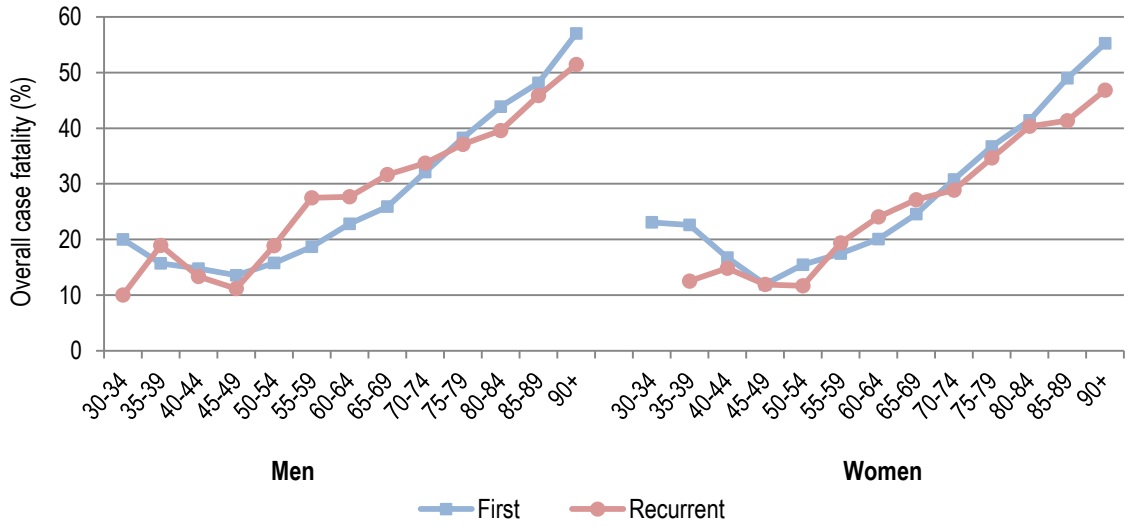
Overall case fatality

All AMI, all England

Of 31,344 fatal AMIs in 2007, 69% were sudden AMI deaths. The percentage of sudden AMI deaths was higher for men than women (72% versus 66%, p<0.001) and higher for first AMIs than reinfarctions (70% versus 67%, p<0.001). Individuals who died suddenly from AMI without hospitalisation for AMI were, on average, five years older than patients hospitalised for AMI (77 versus 72 years, p<0.001).

Figure 26 shows overall 30-day case fatality by age group, sex, and type of AMI. For both men and women, the overall case fatality was lowest for those aged 45-49 years and increased to its highest for those aged 90 years and older. Rates were slightly higher for reinfarctions in middle-aged men and women, and slightly higher for first AMIs in older individuals. Age-adjusted overall case fatality rates for men and women, respectively, were 34% (95% CI: 34-34) and 33% (95% CI: 32-33) for first AMI and 34% (95% CI: 33-35) and 31% (95% CI: 30-32) for recurrent AMI.

Figure 26. Overall 30-day case fatality by age, sex, and type of AMI, 2007, England.



Multivariate logistic regression was used to investigate the effects of age, sex, deprivation category, and history of a previous AMI event on overall 30-day case fatality (Table 29, first column). Age was the strongest predictor of death within 30 days of an AMI (e.g. comparing the age group of 85 years and older with the age group of 30-54 years: OR=6.60, 95% CI: 6.20-7.04). Men fared slightly worse than women (OR=1.06, 95% CI: 1.03-1.09). Individuals in the most deprived quintile were at higher risk than those in the least deprived quintile (OR=1.31, 95% CI: 1.25-1.37).

First AMI, all England

Multivariate logistic regression analysis of only first events yielded similar results to the analysis of all events (Table 29, comparing second column with first column).

Recurrent AMI, all England

The analysis of only recurrent AMI events showed no effect of deprivation category, a weaker effect of age, and a stronger effect of male sex on overall case fatality compared with all AMIs (Table 29, comparing third column with first column).

First AMI, by Government Office Region

Overall 30-day age-standardised case fatality for first AMI was broadly similar between GORs, and no clear geographic pattern was observed (Table 30 and Figure 27). However, there were still some differences between the regions, with the overall case fatality being lowest in the East Midlands at 28% (95% CI: 27-29) and highest in the West Midlands at 35% (95% CI: 34-36). The difference between these two regions was statistically significant, with the risk ratio of 1.25 (95% CI: 1.20-1.31) in the West Midlands compared with the East Midlands.

Table 29. Overall 30-day case fatality rates (CFR) for all, first, and recurrent acute myocardial infarction (AMI) events, and hospitalised 30-day CFR for all AMI events: results of logistic regression analysis, 2007, England.

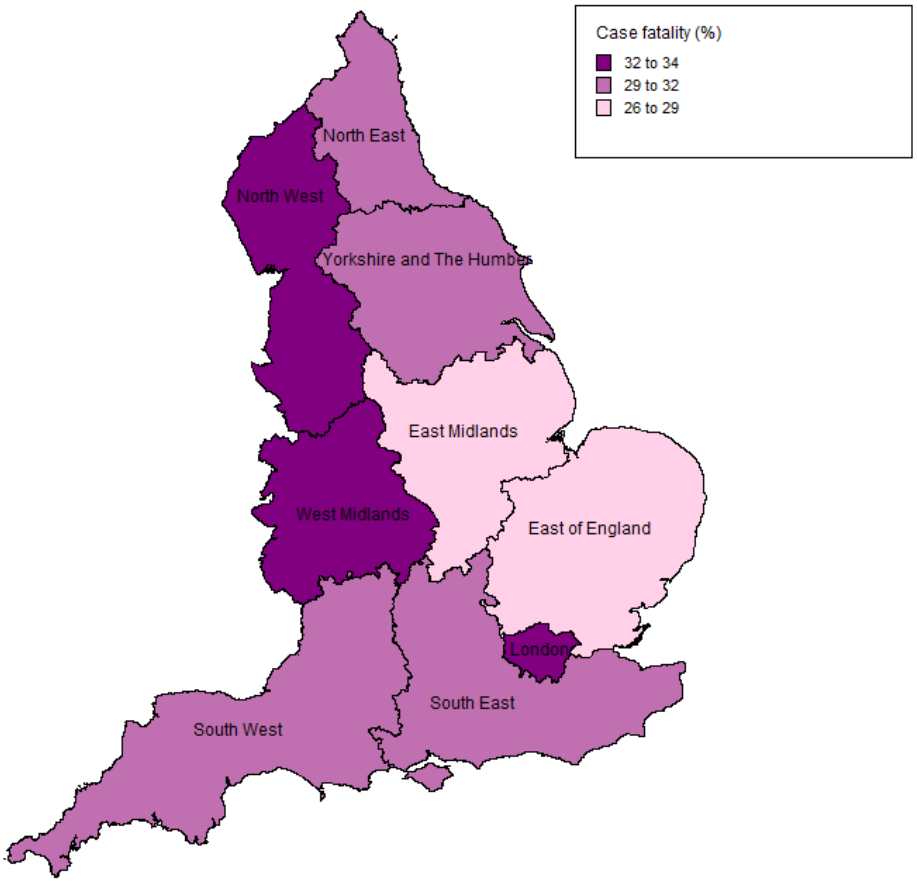
Factor	Overall CFR, all AMIs (n=87,913)			Overall CFR, first AMIs (n=75,265)			Overall CFR, recurrent AMIs (n=12,648)			Hospitalised CFR, all AMIs (n=66,211)		
	OR*	95% CI		OR*	95% CI		OR*	95% CI		OR*	95% CI	
Age (years)												
30-54	Ref.			Ref.			Ref.			Ref.		
55-64	1.58	1.48	1.70	1.54	1.43	1.65	2.04	1.62	2.57	2.25	1.93	2.64
65-74	2.49	2.34	2.66	2.45	2.30	2.62	2.63	2.12	3.26	4.52	3.91	5.23
75-84	4.21	3.96	4.47	4.28	4.02	4.56	3.60	2.93	4.43	8.95	7.78	10.3
85+	6.60	6.20	7.04	6.92	6.47	7.40	4.94	4.01	6.10	15.7	13.6	18.1
Sex												
Women	Ref.			Ref.			Ref.			Ref.		
Men	1.06	1.03	1.09	1.05	1.02	1.08	1.13	1.04	1.22	0.95	0.91	1.00
Deprivation category												
Least deprived, 1	Ref.			Ref.			Ref.			Ref.		
2	1.03	0.99	1.08	1.03	0.99	1.09	1.00	0.89	1.13	1.03	0.96	1.10
3	1.10	1.05	1.15	1.12	1.07	1.18	0.93	0.83	1.05	1.09	1.02	1.17
4	1.20	1.14	1.25	1.21	1.16	1.27	1.04	0.92	1.17	1.17	1.09	1.26
Most deprived, 5	1.31	1.25	1.37	1.36	1.30	1.43	1.03	0.91	1.16	1.21	1.13	1.30
History												
No history of AMI	Ref.			-	-	-	-	-	-	Ref.		
Previous AMI	0.86	0.82	0.90	-	-	-	-	-	-	0.90	0.84	0.96

**OR=odds ratio; adjusted for all other factors shown*

Table 30. Overall 30-day age-standardised case fatality rate from first acute myocardial infarction events by Government Office Region, 2007, England.

Government	Case fatality rate			Risk ratio		
Office Region	%	95% CI		Ratio	95% CI	
East Midlands	28	27	29	Ref.		
East England	28	27	29	1.01	0.96	1.05
South West	30	29	31	1.08	1.04	1.13
South East	30	30	31	1.09	1.05	1.14
Yorkshire	31	30	32	1.13	1.08	1.17
North East	33	32	34	1.19	1.13	1.25
London	34	33	35	1.23	1.18	1.28
North West	34	34	35	1.23	1.18	1.28
West Midlands	35	34	36	1.25	1.20	1.31

Figure 27. Overall 30-day age-standardised case fatality from first acute myocardial infarction events by Government Office Region, 2007, England.



Recurrent AMI, by Government Office Region

Overall 30-day age-standardised case fatality for recurrent AMI was also broadly similar between GORs, similarly exhibiting no clear geographic pattern. Overall case fatality was lowest in the East of England at 27% (95% CI: 25-30) and highest in the West Midlands at 35% (95% CI: 32-37) (Table 31). The difference between these two Regions was statistically significant, with the risk ratio of 1.27 (95% CI: 1.14-1.41) in the West Midlands compared with the East Midlands.

Table 31. Overall 30-day age-standardised case fatality rate from recurrent acute myocardial infarction events by Government Office Region, 2007, England.

Government	Case fatality rate			Risk ratio		
Office Region	%	95% CI		Ratio	95% CI	
East England	27	25	30	Ref.		
South East	28	26	31	1.04	0.94	1.15
South West	30	27	32	1.09	0.98	1.20
Yorkshire	30	28	33	1.11	1.00	1.23
East Midlands	31	29	32	1.12	1.02	1.23
North East	31	28	34	1.13	1.00	1.27
North West	31	29	33	1.14	1.03	1.26
London	32	29	35	1.18	1.05	1.32
West Midlands	35	32	37	1.27	1.14	1.41

Hospitalised case fatality

All AMI, all England

The last column in Table 29 shows the results of multivariate logistic regression analysis for 30-day case fatality for individuals admitted to hospital for AMI. Age was a strong predictor of death (e.g. comparing the over 85 years age group with the 30-54 years age group: OR=15.7, 95% CI: 13.6-18.1). Men were at a slightly lower risk of dying within 30 days than women (OR=0.95, 95% CI: 0.91-1.00). The independent effects of deprivation and history of previous AMI were similar to those found for the overall case fatality (Table 29, comparing last column with first column).

Within each age group, hospitalised case fatality rates were about half the overall rates. For men, the age-standardised hospitalised 30-day case fatality rate was 15% (95% CI: 14-15) for first AMI and 14% (95% CI: 13-15) for recurrent AMI. For women, it was 15% (95% CI: 15-16) and 14% (95% CI: 13-15), respectively.

Socioeconomic inequalities in case fatality

There were no differences in the socioeconomic gradient in case fatality between men and women, and the results are thus presented for both sexes. There was a socioeconomic gradient in case fatality across deprivation categories for first AMI, but not recurrent AMI, for both overall and hospitalised case fatality (Table 32, Figure 28, and Figure 29). For first events, the individuals in the most deprived category had about a 20% higher relative risk (RR) of dying within 30 days of experiencing an AMI compared with the individuals in the least deprived category, for all cases (RR=1.22, 95% CI: 1.18-1.25) and hospitalised cases (RR=1.21, 95% CI: 1.13-1.29) (Table 32).

Table 32. Age-standardised overall 30-day case fatality rates and risk ratios by deprivation category and type of acute myocardial infarction (AMI), 2007, England.

Deprivation quintile	Case fatality rate (CFR)						Risk ratio (RR)					
	First AMIs			Recurrent AMIs			First AMIs			Recurrent AMIs		
	CFR (%)	95% CI		CFR (%)	95% CI		RR	95% CI		RR	95% CI	
Overall CFR												
Least deprived, 1	29	28	30	31	29	33	Ref.			Ref.		
2	30	29	30	30	28	32	1.03	1.00	1.06	0.97	0.90	1.04
3	32	31	32	28	27	30	1.09	1.06	1.13	0.92	0.86	1.00
4	33	32	34	31	29	33	1.15	1.11	1.18	1.01	0.94	1.09
Most deprived, 5	35	34	36	31	29	32	1.22	1.18	1.25	1.00	0.93	1.08
Hospitalised CFR												
Least deprived, 1	12	11	12	12	11	12	Ref.			Ref.		
2	12	11	12	12	11	12	1.02	0.96	1.09	0.98	0.85	1.13
3	13	12	14	12	12	14	1.12	1.05	1.19	0.95	0.82	1.10
4	14	13	14	13	13	14	1.19	1.11	1.26	1.08	0.93	1.24
Most deprived, 5	14	13	15	13	13	15	1.21	1.13	1.29	1.06	0.92	1.23

Figure 28. Age-standardised overall case fatality rates by deprivation category and type of acute myocardial infarction, 2007, England.

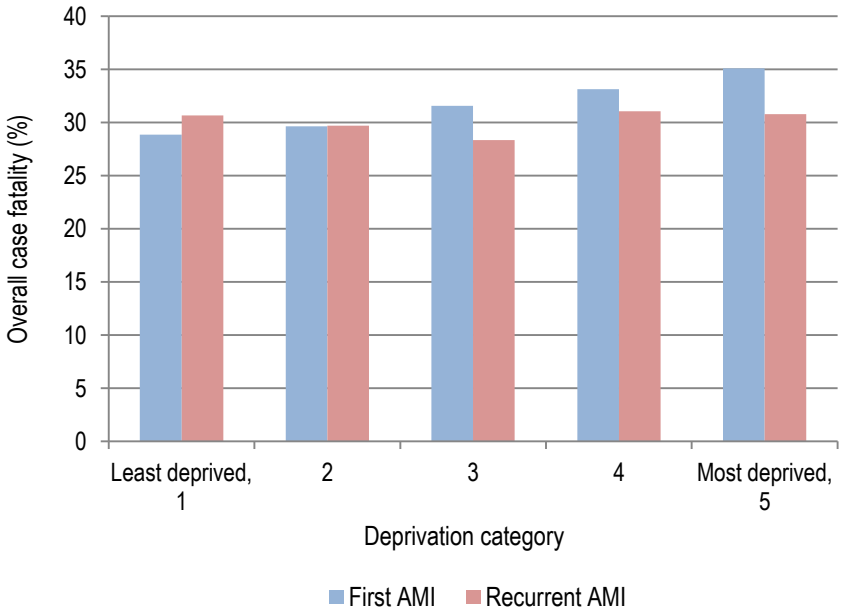
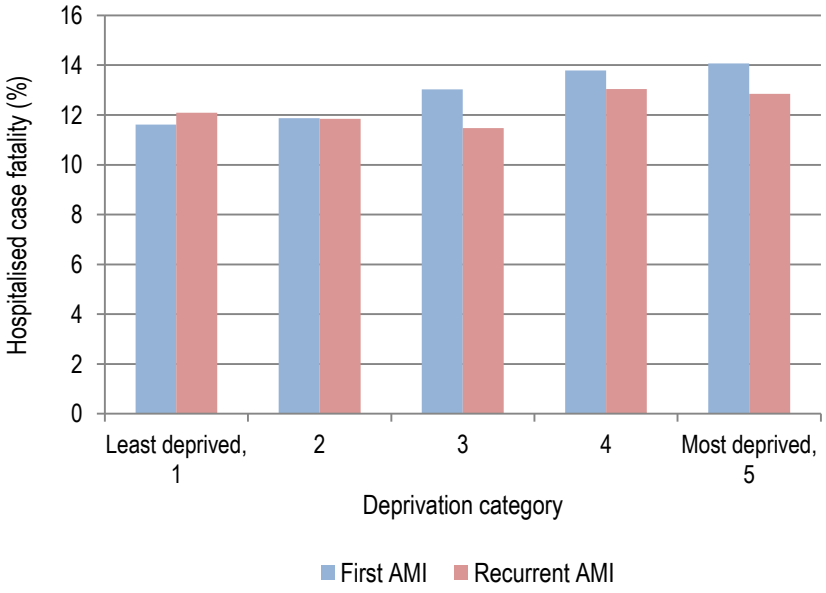


Figure 29. Age-standardised hospitalised case fatality rates by deprivation category and type of acute myocardial infarction, 2007, England.



A deprivation gradient in case fatality for first AMIs persisted within each age group for both overall and hospitalised case fatality and was more pronounced in younger than older individuals. Figure 30 and Figure 31 show age-specific overall and hospitalised case fatality rates, respectively, by deprivation category. The relative risk of death in individuals in the most deprived category compared with individuals in the least deprived category consistently decreased with increasingly older age from 1.66 (95% CI: 1.42-1.95) in the 30-54 years age group to 1.06 (95% CI: 1.01-1.11) in the age group of 85 years and older for all fatal cases and from 1.51 (95% CI: 0.97-2.33) in the 30-54 years age group to 1.01 (95% CI: 0.92-1.12) in the 85 years and over age group for hospitalised fatal cases (Table 33).

Figure 30. Age-specific overall case fatality rate for first acute myocardial infarction by deprivation category, 2007, England.

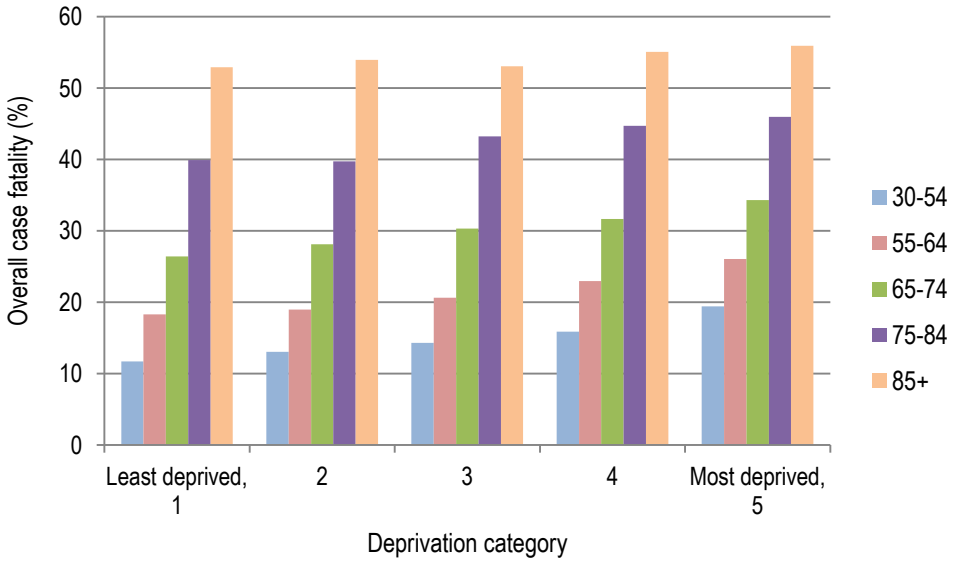


Figure 31. Age-specific hospitalised case fatality rate for first acute myocardial infarction by deprivation category, 2007, England.

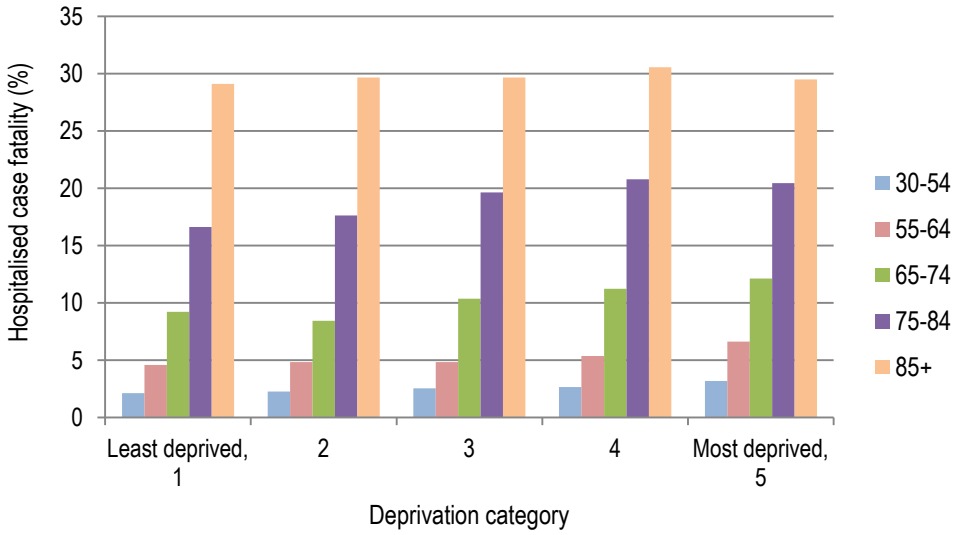


Table 33. Relative risk of death in individuals in the most deprived category compared with individuals in the least deprived category experiencing a first acute myocardial infarction by age, 2007, England.

Age group	Overall case fatality			Hospitalised case fatality		
(years)	Risk ratio	95% CI		Risk ratio	95% CI	
30-54	1.66	1.42	1.95	1.51	0.97	2.33
55-64	1.42	1.28	1.58	1.45	1.12	1.87
65-74	1.30	1.21	1.40	1.31	1.12	1.54
75-84	1.15	1.10	1.21	1.23	1.11	1.37
85+	1.06	1.01	1.11	1.01	0.92	1.12

Discussion

This study provides a comprehensive account of recent national population-based statistics on the rate of occurrence of first, recurrent, and all AMI events in England, with complete enumeration of 30-day case fatality. Three quarters of all AMIs occurred in individuals aged 65 years and older. Approximately one in seven AMIs were reinfarctions for both men and women, and this proportion increased with older age. One third of all AMIs were fatal, and of these, two thirds were sudden AMI deaths. Case fatality rates for hospitalised individuals were around half of the overall rates, which included sudden AMI deaths. A north-to-south gradient was found for incidence of AMI, but not case fatality. High area deprivation was associated with lower survival after first AMI, and this effect was stronger among younger individuals.

Occurrence of AMI

Approximately 90,000 AMI events occurred in England in 2007. The established patterns of a higher incidence for men than women, at all ages including the very elderly, and a steep age gradient in both sexes were confirmed.[16, 65] However, the difference between men and women in age-specific incidence rates decreased with increasingly older age.

The age-standardised incidence rates found in this study (151 and 63.9 per 100,000 population for men and women, respectively) are lower than previously reported estimates from the MONICA centres in Glasgow and Belfast[3] in the 1980s and the Oxford Myocardial Infarction Incidence Study (OXMIS)[26] in the 1990s. However, the results for incidence of first AMI per 100,000 population are still lower than the more recent Oxford Vascular Study (OXVASC) estimates of 162 in men and 92 in women in 2002-05[67] and The Health Information Network (THIN) estimates of 230 for men and

130 for women in 2005.[68] The generalisability and representativeness of results from both OXVASC and THIN can be questioned because both studies are based on relatively small study populations. Overall, direct comparisons between the results presented in this chapter and the studies mentioned above are difficult because of differences in methodology and case ascertainment. (OXVASC used both hot and cold pursuit methods and had complete clinical information for making the diagnosis. THIN relied on clinical classification codes recorded in participating general practice electronic information systems.) Furthermore, the findings from the above studies are based on data before 2007, and the apparent differences are no doubt attributable, at least in part, to the declining trends in CHD incidence in the UK.[5, 68, 73, 74]

The results of this study concur with findings by others that the incidence of sudden AMI deaths is more common among men.[31, 34-36] The finding that around a quarter of all events were sudden deaths falls within the internationally reported figures, such as 18% in New Zealand,[35] 22% in Finland,[12] 25% in Sweden,[66] and 35% in France.[321] Similarly to Scotland,[27] Netherlands,[65] and Sweden,[66] but unlike Finland[36] and the United States,[322] the proportion of AMI patients who survived to reach hospital decreased with older age.

The large proportion of all AMI cases that manifest as sudden deaths reinforces the importance of primary prevention. Furthermore, the results show that around a quarter of sudden deaths are recurrent events, meaning that they are not unexpected and there is a documented history of a previous AMI event. Other studies have reported that up to a half of all sudden cardiac deaths occur in people with pre-existing CHD.[33, 36] Therefore, these results highlight the importance of secondary prevention in patients with chronic CHD.

This study also provides insight into the differences and similarities between first and recurrent AMIs. It was found that recurrent events are equally prevalent among women

and men, and, inevitably, happen in an older cohort of patients compared with first events. The substantial proportion of AMIs that are recurrent events impacts on estimates of true (first-ever) incidence if the events are not correctly, if at all, classified as first-ever or recurrent. This can become an especially great problem when estimating incidence in the older age groups, where up to a third of all events may be recurrent.

The results show that the regional patterns in incidence follow closely those of mortality, with the north part of the country experiencing higher rates than the south.[61, 127] Geographical variation in disease occurrence is often seen to partially reflect differences in the prevalence of cardiovascular risk factors and socioeconomic deprivation. For instance, the British Regional Heart Study attributed more than half of the regional variation in AMI incidence to differences in well-established main risk factors prevalent in local populations.[85] The results of the MONICA study suggested that 38% of the variation in event rates between different populations could be explained by differences in the levels of smoking, high blood pressure, and high cholesterol levels.[79] Individual-level socioeconomic characteristics and area deprivation have also been shown to independently contribute to regional variability in AMI incidence.[83, 87, 128, 222, 233, 323, 324]

Case fatality

There were no large differences in the rates for overall and hospitalised 30-day case fatality from AMI reported in this study with the rates reported previously by others. The overall age-standardised case fatality rates for men and women in this study (34% for men, 33% for women) were lower than the earlier estimates from Oxfordshire, Glasgow, Belfast and MONICA centres at 41% and 44%, 48% and 46%, 41% and 42%, 49% and 51%, respectively.[26, 29,20] However, given that these earlier estimates are based on data from the 1980s and the 1990s, and in light of the declining trend in AMI case fatality rate

in the UK,[5, 49, 68, 73, 74] the results of this study are likely to be accurate and representative of the current situation. Hospitalised case fatality in this study (15% for men and women) was lower than the rates of 22% reported in Scotland,[49] 18% in Denmark,[94] and the median rates of 22% in men and 27% in women in MONICA centres.[20] The OXMIS study in Oxfordshire during the 1990s produced case fatality rates for hospitalised patients of 15.4% in men and 21.5% in women.[26]

In line with other epidemiological studies, it was found that two thirds of fatal AMIs occur as sudden deaths without a record of hospital care for AMI. These findings are comparable with the results of the UK Heart Attack Study and OXMIS, which reported that 74% and 69%, respectively, of all AMI fatalities occurred outside hospital.[26, 28] Other reports also concur that about seven out of every ten fatal cases of AMI occur suddenly out-of-hospital and this proportion increases with age.[3, 20, 24-29] This finding underscores the importance of primary and secondary prevention.

It has been shown previously that the effect of sex on short-term case fatality from AMI varies by whether or not sudden out-of-hospital deaths are included. In general, while 30-day case fatality rates that include sudden deaths are higher for men than women, case fatality rates in those who survive long enough to be admitted to hospital are higher for women than men.[39, 48, 66, 109, 111-113] This study's findings confirm that. The data showed that men have a slightly higher risk than women in overall 30-day case fatality that includes sudden AMI deaths, after adjusting for age, history of a previous event, and deprivation. However, women had a slightly higher 30-day hospitalised case fatality. This sex difference has been explained by the fact that, of those who are destined to die soon after AMI, a higher percentage of women than men survive long enough to reach hospital alive, but die shortly afterwards.[111]

It was found that deprivation was an important independent prognostic factor for 30-day case fatality after first AMI events. This is in agreement with previous reports of a higher case fatality in lower socioeconomic classes and more deprived neighbourhoods.[220-223, 229-231] The deprivation gradient was present for first, but not recurrent AMI events, and for younger, but not older, individuals. Other research on short-term AMI case fatality has also shown that the greatest socioeconomic variation in health occurs in younger age groups.[27, 212, 230, 233, 235] For example, data from Scotland showed that the most deprived members of society who are under 65 years have twice the risk of a sudden death out of hospital from an AMI compared with the least deprived members of society; for those aged above 75 years, there were no substantial differences between deprivation categories.[235]

In general, the modification of the effect of deprivation on case fatality by age is likely to be a reflection of the developmental pattern of CHD over the life course and the increasingly more influential effects of multiple comorbidities and poorer health that are associated with older age.[212] However, socioeconomic inequalities in case fatality stem from a variety of causes,[235] such as less frequently recognised AMIs in more deprived populations,[233] higher risk profiles in the lower social classes,[222, 227] and less access to hospital services or inequitable treatment experienced by the more deprived individuals.[131, 219, 232]

Even though case fatality rates differed between Government Office Regions, there was no clear geographic pattern, such as a north-to-south gradient. It follows that factors affecting case fatality would themselves show regional variation in England, but no consistent gradient. These factors may include patient demographic characteristics and risk profile, infarct severity, access to health services, ambulance response, effectiveness of medical treatment received, and decision-making practices of health care providers

across different local jurisdictions.[82, 127] Individual-level and area-based socioeconomic factors are also likely to play a role.[87, 107, 212, 325]

Conclusion

This study provides recent information about AMI incidence and short-term prognosis in England, distinguishing between first and recurrent events. In particular, it reports that reinfarctions are relatively common and most of AMI fatalities still occur as sudden deaths. Overall 30-day case fatality rates that include sudden AMI deaths are thus more than twice as high as hospitalised rates, indicating that the clinical prognosis for those who survive long enough to be admitted to hospital is much better than overall AMI prognosis. The findings reinforce the importance of primary and secondary prevention in reducing AMI morbidity and mortality.

CHAPTER 8: SURVIVAL AND OUTCOMES AFTER AMI, 2003-2007

This chapter provides estimates of long-term (five-year) survival following acute myocardial infarction (AMI), compares the risk of overall mortality between first and recurrent AMI as well as between AMI survivors and the English general population, and examines cause of death by time to death in the survivors who died during the study period. Prognostic effects of sex, age, history, deprivation, revascularisation procedures, and comorbidities on survival after AMI are investigated. The risk of a second AMI and prognostic factors for recurrence are also reported.

Introduction

Long-term survival following acute myocardial infarction (AMI) has improved over the last three decades in the UK[49, 141] and other developed countries.[110, 118, 134, 142-144] Studies from Israel and Denmark have reported an improving prognosis for both first and recurrent AMIs in patients admitted to hospital and surviving the initial event.[149, 162] These improvements in survival have been attributed to an increasingly widespread use of revascularisation procedures, effective medication and treatment during the acute phase, and secondary prevention.[49, 134, 141, 143, 145, 147, 326]

As survival from AMI is improving, the study of long-term outcomes, especially recurrence, is becoming increasingly more important. However, much of the existing data on outcomes after AMI are from clinical trials and only a few population-based studies have examined long-term survival and recurrence.[132-134, 159, 162, 202, 327] Of those that did,

most used a combined end point of reinfarction or death from any cause,[132, 202, 327] as opposed to analysing the risk of reinfarction and the risk of death separately.[159, 162]

In England as well, population-based representative national data on outcomes and prognosis for AMI survivors are sparse. In particular, long-term survival rates distinguishing between men and women and first and recurrent AMI are not available; it is unknown how mortality in AMI survivors compares with mortality in the general population; and there is no information on the risk of a second AMI in survivors of first events. Reliable recent epidemiological data on long-term prognosis in AMI survivors is important for patients, their doctors, health care managers, and funders of health care.

The objectives of this chapter are:

1. To examine five-year survival in 30-day survivors of first and recurrent AMI in England for 2003-2007 nationally and by Government Office Region (GOR);
2. To compare the risk of death among AMI survivors with the general population;
3. To report cause of death by time to death for 30-day AMI survivors;
4. To estimate the risk of a second AMI in the survivors of first AMI; and
5. To determine prognostic factors for risk of death and of a second AMI.

Methods

Study population

Residents of England who had an AMI event between 1 January 2003 and 31 December 2007 and were still alive 30 days after the event date were included in the study. In this chapter, the definitions of AMI event, hospital admission, sudden AMI death, fatal and

non-fatal AMI, comorbidities, deprivation, coronary revascularisation procedures, and Government Office Region are the same as those in Chapter 2 (Methods).

For each person, the first occurrence of a hospital admission for AMI during the study period was flagged as the index event. To classify each index AMI as first or recurrent, a five-year clinical history (defined as a previous hospital record with AMI as primary or secondary diagnosis) was used from the hospital admission linked file. If the index AMI event occurred in individuals with no clinical history of AMI during the previous five years, it was categorised as a first index AMI, as a proxy for true first AMI. Otherwise, the index event was classified as a recurrent index AMI, or reinfarction. Individuals were followed until 31 March 2008, with a minimum follow-up period of three months.

Statistical analyses

Survival time was calculated as the time from the date of admission for the index AMI to the date of death from any cause or the end of the study period (31 March 2008), whichever came first. Survival curves were estimated using Kaplan-Meier methods for individual age groups, for men and women, and following first and recurrent index AMI. Comparisons of survival between groups were performed using log-rank tests.

Cox proportional hazards models were used to examine the independent effect on survival of age, sex, history of AMI, deprivation category, coronary revascularisation procedures, and comorbidities. Results are reported separately for men and women and for different age groups because of an observed strong interaction between sex and age (likelihood ratio test $p<0.001$). The proportional hazards assumption was checked visually by plotting Nelson-Aalen curves of the cumulative hazard function.

Age-standardised mortality ratios (SMRs) were used to compare mortality rates for AMI survivors with those of the general English population (published by the Office for National Statistics).[328] SMRs were calculated by dividing the observed number of deaths over the expected number of deaths in the survivors, and multiplied by 100. The observed number of deaths was equal to the sum of all deaths in all age groups for each sex. The expected number of deaths was obtained by applying age group- and sex-specific reference mortality rates to the observed number of individuals in each age group for each sex in the survivors and then adding the results. Average values over five years (2003-2007) for the English mortality rates for each five-year age group and sex combination were used as the reference rates. SMRs were calculated for deaths at four months, eight months, one year, and then each subsequent year up to five years after the index AMI.

To investigate the causes of death following AMI, the following broad categories were constructed for the underlying cause of death in death records linked to a hospital record with an admission for AMI (ICD-10 codes): AMI (I21-I22), other CHD (I20, I23-I25), heart failure (I50), cerebrovascular disease (G45, I60-I69), other cardiovascular disease (CVD) (I00-I99 except I20-I25, I50, and I60-I69), and other causes (all other codes).

For the analysis of risk of a second AMI, or recurrence risk, only survivors whose index event was their first AMI were included. The recurrence risk was calculated using cumulative incidence methods for survival data, developed by Fine and Gray[329] for situations where individuals can experience a competing event instead of the event of interest during the follow-up period. In this study, the event of interest is a second AMI (fatal or non-fatal) and the competing event is death from causes other than AMI. In the presence of competing events, traditional survival analysis and Kaplan-Meier methods

are not appropriate, because they assume that censoring[h] is non-informative – in other words, individuals who leave the study (regardless of the reason) are treated as having approximately the same risk of experiencing the event of interest as those who still remain in the study. While this assumption holds true for survival analysis where the event of interest is death from any cause and there are no competing events, this is not the case for the analysis of a second event in the presence of competing risks. Individuals who die before experiencing a second AMI are no longer at risk for it – their risk drops to zero, leading to informative censoring of study subjects. A cumulative incidence model takes into account those patients who were censored because they died and provides adjusted estimates of the recurrence risk.

In the models of survival and recurrence risk, the following prognostic factors were included in addition to age and sex: deprivation, coronary revascularisation procedures (PTCA and CABG), and comorbidities.

Results

Survivor cohort

Between 1 January 2003 and 31 December 2007, 328,832 individuals were admitted to hospital for AMI. Of these, 277,755 (85%) survived for at least 30 days and were included in the study. Table 34 shows the characteristics of the survivors for first and recurrent index AMI. The mean age at admission was higher for survivors of reinfarction than for survivors of first AMI (74.2 versus 69.5 years, $p<0.001$). The prevalence of the examined comorbidities was significantly higher for women than men ($p<0.001$ for each

[h] In survival analysis, censored subjects are those individuals who leave the study and are no longer followed.

comorbidity) and higher in survivors of recurrent AMI than in survivors of first AMI ($p<0.001$ for each comorbidity). Almost a quarter of all patients with first AMI and half of all those with recurrent AMI died within five years of the index event. Median follow-up time was 2.1 years.

Long-term survival after AMI

Figure 32 and Figure 33 show five-year Kaplan-Meier survival curves by sex and type of index AMI, and by sex and age group for first and recurrent AMI, respectively. Overall, survivors of first AMI fared better than survivors of reinfarction ($p<0.001$); men fared better than women for both first and recurrent AMI ($p<0.001$ for both); and survival was worse with older age at the time of event ($p<0.001$, comparing the oldest age group with the youngest). For instance, among first AMI survivors, almost all were still alive five years after the event in those aged 30-54 years, compared with only about one fifth in those aged 85 years and older. For both first and recurrent AMI, similar survival patterns were observed between men and women within the same age group.

Table 35 shows survival rates by type of index AMI, sex, and age based on survival curves illustrated in Figure 32 and Figure 33. For all ages, survival estimates by sex and type of AMI indicated that five-year survival after a first AMI was almost twice as high than survival after a reinfarction. Amongst survivors of a first index AMI, 72% (95% CI: 72-73) of men and 58% (95% CI: 58-59) of women were still alive after five years. For those who survived a recurrent index AMI, five-year survival was 45% (95% CI: 43-47) in men and 31% (95% CI: 29-33) in women. With results for men and women combined, about one third of survivors died within five years of the index event among first AMI survivors and about 60% died among recurrent AMI survivors.

Table 34. Characteristics of acute myocardial infarction (AMI) 30-day survivors by type of AMI, England, 2003-2007.

Characteristic	Total AMI survivors	Survivors of first AMI			Survivors of recurrent AMI		
		All survivors	Deaths during study period		All survivors	Deaths during study period	
	n	n	n	%	n	n	%
Total	277,755	266,727	59,622	22	11,028	5,404	49
Sex							
Male	176,427	169,719	31,907	19	6,708	2,974	44
Female	101,328	97,008	27,715	29	4,320	2,430	56
Age (years)							
Mean	69.5	69.3	79.2	-	74.2	79.2	-
Median	71	71	81	-	77	81	-
0-29	464	460	14	3	4	0	0
30-54	42,187	41,270	1,292	3	917	108	12
55-64	53,691	52,339	3,705	7	1,352	273	20
65-74	68,564	66,076	11,019	17	2,488	1020	41
75-84	76,077	72,008	24,844	35	4,069	2424	60
85+	36,772	34,574	18,748	54	2,198	1579	72
Deprivation category							
Least deprived, 1	55,532	53,737	11,067	21	1,795	886	49
2	55,456	53,386	11,646	22	2,070	1,024	50
3	55,448	53,290	12,139	23	2,158	1,041	48
4	55,467	53,181	12,382	23	2,286	1,133	50
Most deprived, 5	55,467	52,762	12,280	23	2,705	1,312	49
Revascularisation procedure							
CABG	2,126	2,082	185	9	44	10	23
PTCA	35,243	34,640	2,110	6	603	113	19
Comorbidity							
Cancer	6,369	6,047	3,451	57	322	256	80
Cardiovascular disease	189,907	180,832	45,043	25	9,075	4,511	50
Diabetes	48,916	45,857	13,585	30	3,059	1,650	54
Respiratory disease	50,324	47,890	17,369	36	2,434	1,465	60
Renal disease	13,947	12,853	6,715	52	1,094	796	73

CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

Figure 32. Five-year survival in 30-day survivors of acute myocardial infarction (AMI) by type of AMI, sex, and time since index AMI, 2003-2007, England.

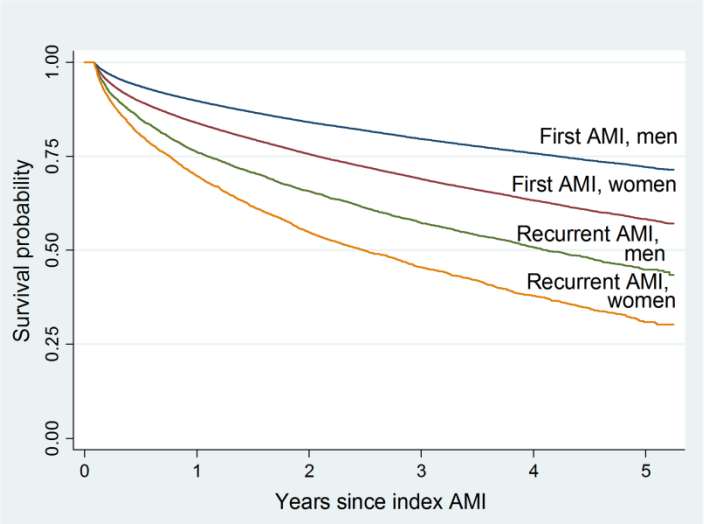


Figure 33. Five-year survival in 30-day survivors of acute myocardial infarction (AMI) by type of AMI, sex, age, and time since index AMI, 2003-2007, England.

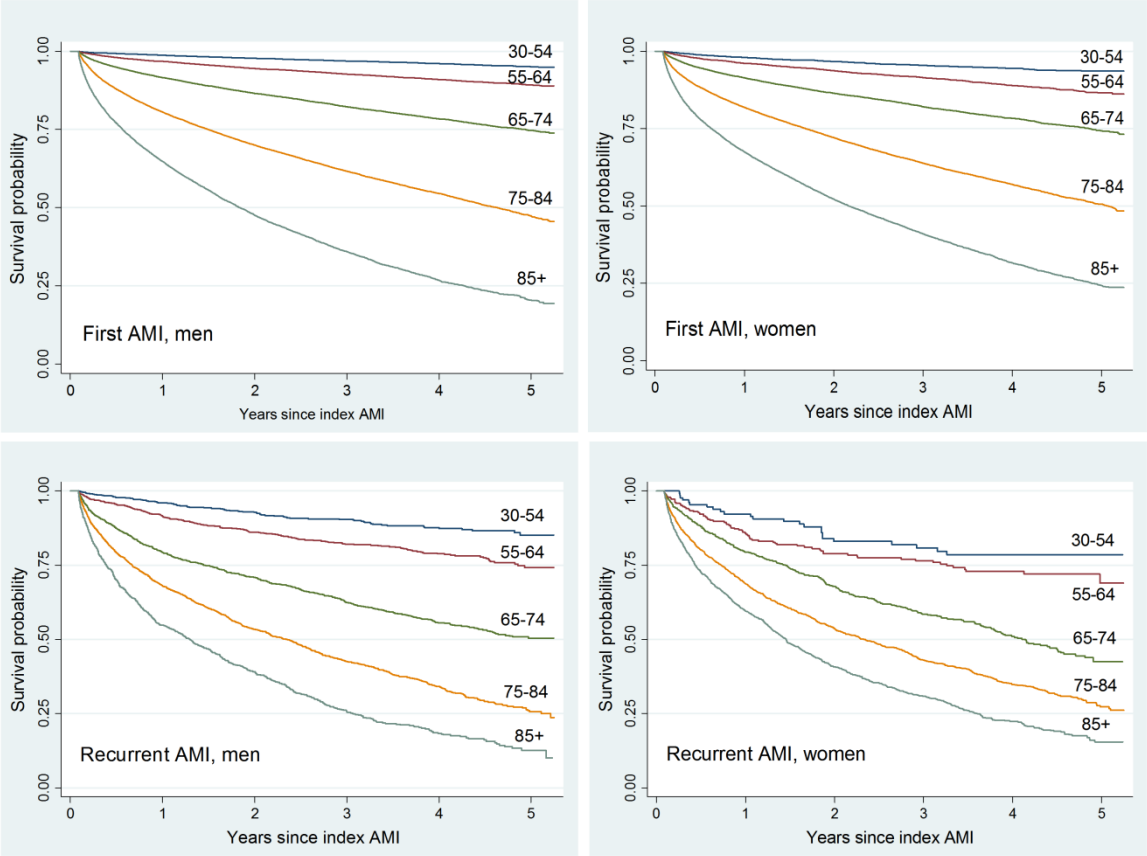


Table 35. Five-year survival in 30-day survivors of acute myocardial infarction (AMI) by type of AMI, sex, age, and time since index AMI, 2003-2007, England.

Age group (years)	Time since index AMI (years)	First AMIs						Recurrent AMIs					
		Men			Women			Men			Women		
		Survival (%)	95% CI		Survival (%)	95% CI		Survival (%)	95% CI		Survival (%)	95% CI	
30-54	1	99	99	99	98	98	98	96	94	97	92	86	96
	2	98	98	98	97	96	97	93	91	94	83	75	89
	3	97	97	97	95	95	96	90	88	92	81	72	87
	4	96	96	96	95	94	95	88	85	90	78	69	85
	5	95	95	95	94	93	94	85	81	88	78	69	85
55-64	1	97	97	97	96	96	96	91	90	93	86	81	89
	2	95	94	95	94	93	94	86	84	88	79	73	83
	3	93	92	93	91	91	92	82	80	84	76	71	81
	4	91	91	91	89	88	90	79	76	81	73	67	78
	5	89	89	90	87	85	88	74	70	78	69	60	76
65-74	1	92	91	92	91	91	92	79	77	81	79	76	82
	2	87	86	87	86	86	87	71	69	73	68	64	71
	3	82	82	83	82	82	83	62	60	65	58	55	62
	4	78	78	79	78	78	79	56	53	58	51	47	55
	5	75	74	75	74	73	75	50	47	54	42	37	47
75-84	1	81	80	81	82	81	82	68	66	70	69	67	71
	2	70	70	71	72	72	73	53	51	56	54	51	56
	3	62	61	62	64	63	64	43	40	45	43	41	46
	4	54	54	55	57	56	58	34	32	36	35	32	37
	5	47	46	48	51	50	52	26	23	28	27	24	30
85+	1	65	64	66	68	67	68	55	51	58	60	57	62
	2	48	47	49	52	51	53	39	36	42	41	38	44
	3	36	35	37	41	40	42	26	23	29	31	28	34
	4	27	26	28	32	31	32	18	15	22	22	20	25
	5	20	19	22	24	23	25	13	9	16	15	12	19
All ages	1	90	90	90	84	84	84	76	75	77	70	68	71
	2	84	84	84	76	75	76	66	65	67	55	53	56
	3	80	79	80	69	69	69	57	56	59	45	44	47
	4	76	76	76	63	63	64	51	49	52	38	36	40
	5	72	72	73	58	58	59	45	43	46	31	29	33

Figure 34 illustrates five-year Kaplan-Meier survival curves by sex and GOR for first and recurrent AMI. Table 36 shows the survival rates that are illustrated in Figure 34. Survival rates were almost twice as high after first AMI compared with recurrent AMI for both sexes and for all GORs. For both first and recurrent AMI, survival rates were higher in men than women in all GORs. Overall, both Figure 34 and Table 36 clearly show that in each subgroup, survival patterns were similar between all GORs, especially for first AMI. Low absolute numbers and wide confidence intervals for the survival rates after recurrent AMI resulted in some variation between the GORs.

Figure 34. Five-year survival in 30-day survivors of acute myocardial infarction (AMI) by type of AMI, sex, and Government Office Region, 2003-2007, England.

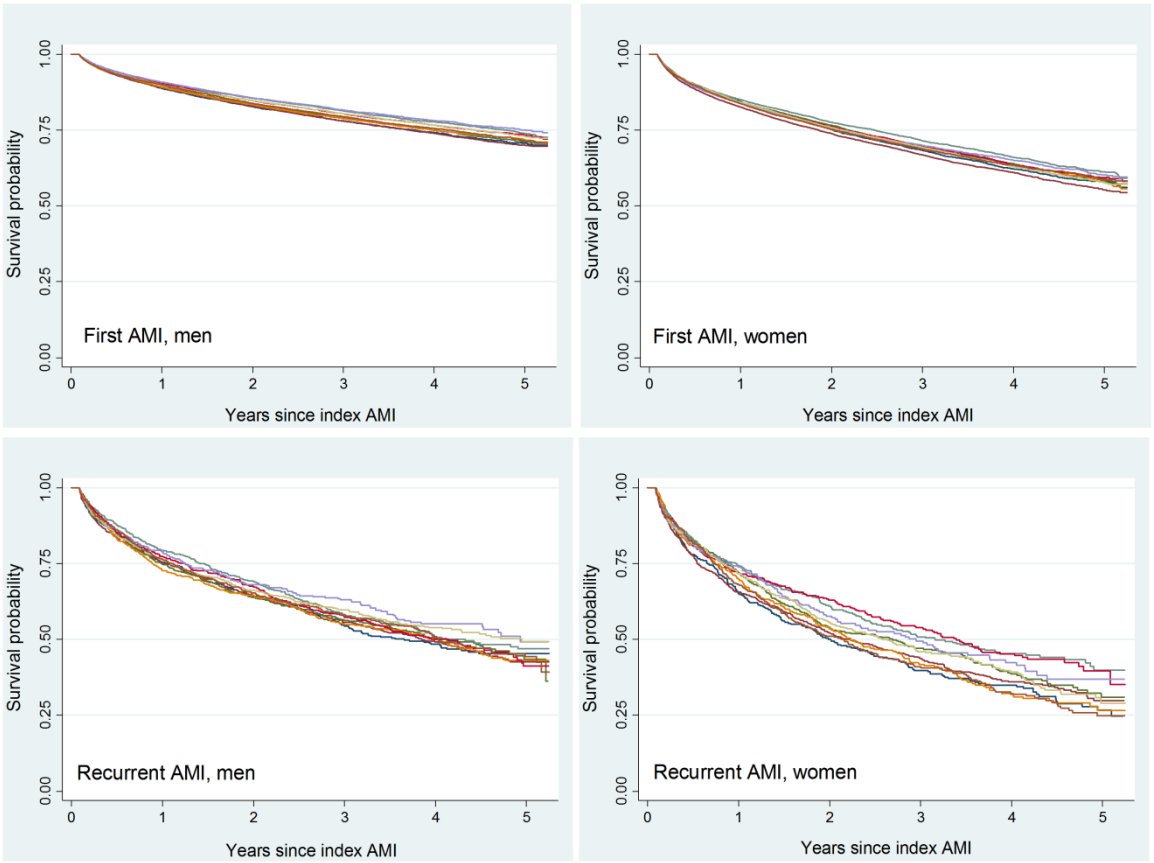


Table 36. Five-year survival in 30-day survivors of acute myocardial infarction (AMI) by type of AMI, sex, and Government Office Region, 2003-2007, England.

Government Office Region	First AMI						Recurrent AMI					
	Men			Women			Men			Women		
	Survival (%)	95% CI		Survival (%)	95% CI		Survival (%)	95% CI		Survival (%)	95% CI	
East England	73	72	74	59	58	61	41	35	47	40	33	46
East Midlands	72	71	73	58	56	60	43	38	48	27	21	33
London	75	74	76	60	58	62	49	42	56	37	29	44
North East	71	69	72	58	56	60	45	40	50	27	21	33
North West	70	69	71	55	54	57	43	39	46	30	26	34
South East	73	72	74	58	56	59	49	45	54	29	23	35
South West	71	70	73	59	57	60	44	39	49	25	20	30
West Midlands	74	73	75	61	60	63	47	42	52	40	33	46
Yorkshire	71	70	72	58	57	60	43	38	49	31	25	37

Prognostic factors for mortality in AMI survivors

A number of factors influenced survival after index AMI beyond 30 days. Table 37 shows both unadjusted and adjusted hazard ratios (HRs) for risk of all-cause death after 30 days in men and women, after adjustment for age, previous AMI, deprivation, revascularisation procedures, and comorbidities. Age was the strongest determinant of mortality, with a hazard ratio of 21.3 (95% CI: 19.9-22.7) in men and 15.8 (95% CI: 14.2-17.7) in women, when comparing those aged 85 years and over with those aged 30-54 years. Clinical history of a previous AMI was associated with an increased risk of dying for both men (HR=1.60, 95% CI: 1.54-1.66) and women (HR=1.54, 95% CI: 1.47-1.60). Deprivation also had a significant effect on mortality, with hazard ratios of 1.34 (95% CI: 1.30-1.39) in men and 1.17 (95% CI: 1.13-1.21) in women in the most deprived

compared with the least deprived group. The risk of dying in those who underwent CABG and PTCA procedures was less than half the risk of those who did not. Comorbidities were significant independent factors for the risk of dying in both men and women, with cancer and renal disease being the most influential.

Table 38 shows unadjusted and adjusted HRs for risk of death after 30 days among survivors of AMI by age. There were sex differences within each age group. After adjusting for previous AMI, deprivation, revascularisation procedures, and comorbidities, women faced a slightly higher risk of dying than men for those aged under 55 years, but men faced a higher risk of dying than women aged 75 years and older; there was no sex difference for individuals aged 55-74 years. Overall, the results show that younger men have a lower risk than younger women, but their risk increases more with older age.

The effects of other prognostic factors also varied by age (Table 38). The strength of the negative effects on survival of previous AMI, deprivation, and comorbidities decreased with older age, while the association between CABG and PTCA procedures and good prognosis increased with older age. For instance, the adjusted HRs for previous AMI changed from 2.43 (95% CI: 1.99-2.96) for those aged 30-54 years to 1.25 (95% CI: 1.18-1.31) for those aged 85 years and over. For deprivation (comparing the most deprived to the least deprived), the corresponding changes were from 1.62 (95% CI: 1.36-1.92) to 1.06 (95% CI: 1.01-1.11).

Table 37. Factors influencing all-cause mortality in 30-day survivors of acute myocardial infarction (AMI) by sex, 2003-2007, England.

Factor	Men						Women					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Age (years)												
30-54	Ref.			Ref.			Ref.			Ref.		
55-64	2.35	2.19	2.52	2.17	2.03	2.33	1.97	1.74	2.24	1.89	1.67	2.14
65-74	6.12	5.75	6.53	4.89	4.59	5.22	4.31	3.85	4.82	3.76	3.36	4.21
75-84	15.2	14.2	16.1	10.8	10.1	11.5	9.73	8.72	10.85	7.99	7.15	8.92
85+	31.1	29.1	33.1	20.5	19.2	21.9	19.0	17.0	21.2	15.4	13.8	17.2
History												
No history of AMI	Ref.			Ref.			Ref.			Ref.		
Previous AMI	2.44	2.35	2.54	1.58	1.52	1.64	2.10	2.02	2.19	1.53	1.46	1.59
Deprivation												
Least deprived, 1	Ref.			Ref.			Ref.			Ref.		
2	1.07	1.04	1.11	1.06	1.03	1.10	1.04	1.00	1.08	1.03	1.00	1.07
3	1.10	1.06	1.13	1.11	1.07	1.15	1.08	1.04	1.12	1.09	1.05	1.13
4	1.15	1.11	1.19	1.21	1.17	1.26	1.08	1.04	1.12	1.12	1.08	1.16
Most deprived, 5	1.19	1.15	1.23	1.34	1.29	1.38	1.03	0.99	1.06	1.17	1.13	1.21
Procedure												
CABG	0.49	0.42	0.57	0.46	0.39	0.54	0.34	0.26	0.46	0.48	0.36	0.64
PTCA	0.27	0.26	0.28	0.44	0.42	0.46	0.24	0.23	0.26	0.41	0.38	0.44
Comorbidity												
Cancer	4.60	4.42	4.79	2.57	2.47	2.68	3.33	3.13	3.54	2.91	2.74	3.09
Cardiovascular disease	1.85	1.80	1.89	1.33	1.29	1.36	1.58	1.53	1.62	1.27	1.23	1.30
Diabetes	1.68	1.64	1.72	1.40	1.36	1.43	1.38	1.35	1.42	1.39	1.35	1.43
Respiratory disease	2.68	2.62	2.74	1.71	1.67	1.75	1.69	1.64	1.73	1.50	1.46	1.54
Renal disease	4.11	3.98	4.24	1.87	1.81	1.93	2.84	2.74	2.95	1.88	1.81	1.95

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors*

***Multivariate model, adjusted for all other factors shown*

Table 38. Factors influencing mortality in 30-day survivors of acute myocardial infarction by age, 2003-2007, England.

Factor	30-54 years						55-64 years						65-74 years					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Sex																		
Women	Ref.			Ref.			Ref.			Ref.			Ref.			Ref.		
Men	0.69	0.61	0.78	0.87	0.76	0.98	0.82	0.77	0.88	0.95	0.88	1.02	0.98	0.95	1.02	1.01	0.97	1.05
History																		
No history of AMI	Ref.			Ref.			Ref.			Ref.			Ref.			Ref.		
Previous AMI	3.36	2.76	4.09	2.43	1.99	2.96	2.63	2.33	2.97	1.98	1.75	2.24	2.50	2.35	2.67	1.91	1.79	2.04
Deprivation																		
Least deprived, 1	Ref.			Ref.			Ref.			Ref.			Ref.			Ref.		
2	0.99	0.80	1.22	1.01	0.81	1.24	1.10	0.98	1.23	1.07	0.96	1.20	1.21	1.14	1.29	1.14	1.07	1.22
3	1.44	1.19	1.74	1.41	1.16	1.71	1.27	1.14	1.41	1.22	1.10	1.36	1.28	1.20	1.36	1.18	1.11	1.26
4	1.32	1.09	1.59	1.25	1.03	1.50	1.53	1.38	1.70	1.39	1.25	1.54	1.52	1.43	1.61	1.35	1.27	1.43
Most deprived, 5	1.81	1.52	2.15	1.62	1.36	1.92	1.98	1.79	2.19	1.64	1.49	1.82	1.79	1.69	1.90	1.47	1.39	1.56
Procedure																		
CABG	1.34	0.74	2.43	0.75	0.42	1.37	0.47	0.28	0.78	0.33	0.20	0.54	0.62	0.49	0.77	0.48	0.38	0.60
PTCA	0.56	0.48	0.66	0.52	0.44	0.61	0.49	0.44	0.55	0.48	0.43	0.53	0.43	0.40	0.46	0.45	0.42	0.48
Comorbidity																		
Cancer	18.4	14.6	23.3	17.01	13.5	21.5	10.3	9.14	11.6	9.20	8.16	10.4	4.86	4.54	5.20	4.56	4.26	4.88
Cardiovascular disease	1.71	1.53	1.91	1.55	1.38	1.74	1.61	1.50	1.72	1.44	1.34	1.54	1.53	1.46	1.59	1.36	1.31	1.42
Diabetes	2.92	2.60	3.28	2.08	1.84	2.36	2.50	2.34	2.67	1.96	1.83	2.11	1.93	1.86	2.01	1.58	1.52	1.64
Respiratory disease	2.51	2.19	2.88	1.89	1.65	2.18	2.81	2.62	3.02	2.21	2.05	2.37	2.22	2.14	2.31	1.91	1.83	1.98
Renal disease	11.3	9.45	13.6	6.51	5.38	7.88	5.82	5.19	6.54	3.56	3.16	4.01	3.51	3.31	3.72	2.48	2.34	2.64

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors; **Multivariate model, adjusted for all other factors shown*

Table 38 (cont'd). Factors influencing mortality in 30-day survivors of acute myocardial infarction by age, 2003-2007, England.

Factor	75-84 years						85+ years					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Sex												
Women	Ref.			Ref.			Ref.			Ref.		
Men	1.08	1.05	1.10	1.05	1.03	1.08	1.13	1.10	1.16	1.08	1.05	1.11
History												
No history of AMI	Ref.			Ref.	0.00	0.00	Ref.			Ref.	0.00	0.00
Previous AMI	1.81	1.74	1.89	1.62	1.55	1.69	1.32	1.26	1.39	1.25	1.18	1.31
Deprivation												
Least deprived, 1	Ref.			Ref.			Ref.			Ref.		
2	1.09	1.05	1.13	1.07	1.03	1.11	1.00	0.96	1.04	0.99	0.95	1.03
3	1.17	1.13	1.22	1.13	1.09	1.18	1.02	0.98	1.07	1.01	0.97	1.06
4	1.24	1.19	1.29	1.18	1.13	1.22	1.08	1.03	1.12	1.05	1.01	1.10
Most deprived, 5	1.34	1.29	1.39	1.23	1.18	1.28	1.10	1.05	1.15	1.06	1.01	1.11
Procedure												
CABG	0.50	0.40	0.62	0.44	0.36	0.55	0.42	0.19	0.92	0.40	0.18	0.89
PTCA	0.39	0.37	0.42	0.40	0.38	0.43	0.38	0.32	0.44	0.37	0.32	0.43
Comorbidity												
Cancer	2.45	2.33	2.58	2.32	2.21	2.45	1.88	1.75	2.01	1.77	1.65	1.90
Cardiovascular disease	1.35	1.31	1.39	1.27	1.23	1.30	1.25	1.21	1.29	1.21	1.17	1.25
Diabetes	1.44	1.40	1.48	1.30	1.26	1.33	1.21	1.16	1.26	1.16	1.11	1.20
Respiratory disease	1.72	1.68	1.76	1.58	1.54	1.62	1.44	1.40	1.48	1.37	1.33	1.42
Renal disease	2.25	2.17	2.34	1.93	1.86	2.01	1.62	1.55	1.68	1.49	1.43	1.56

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

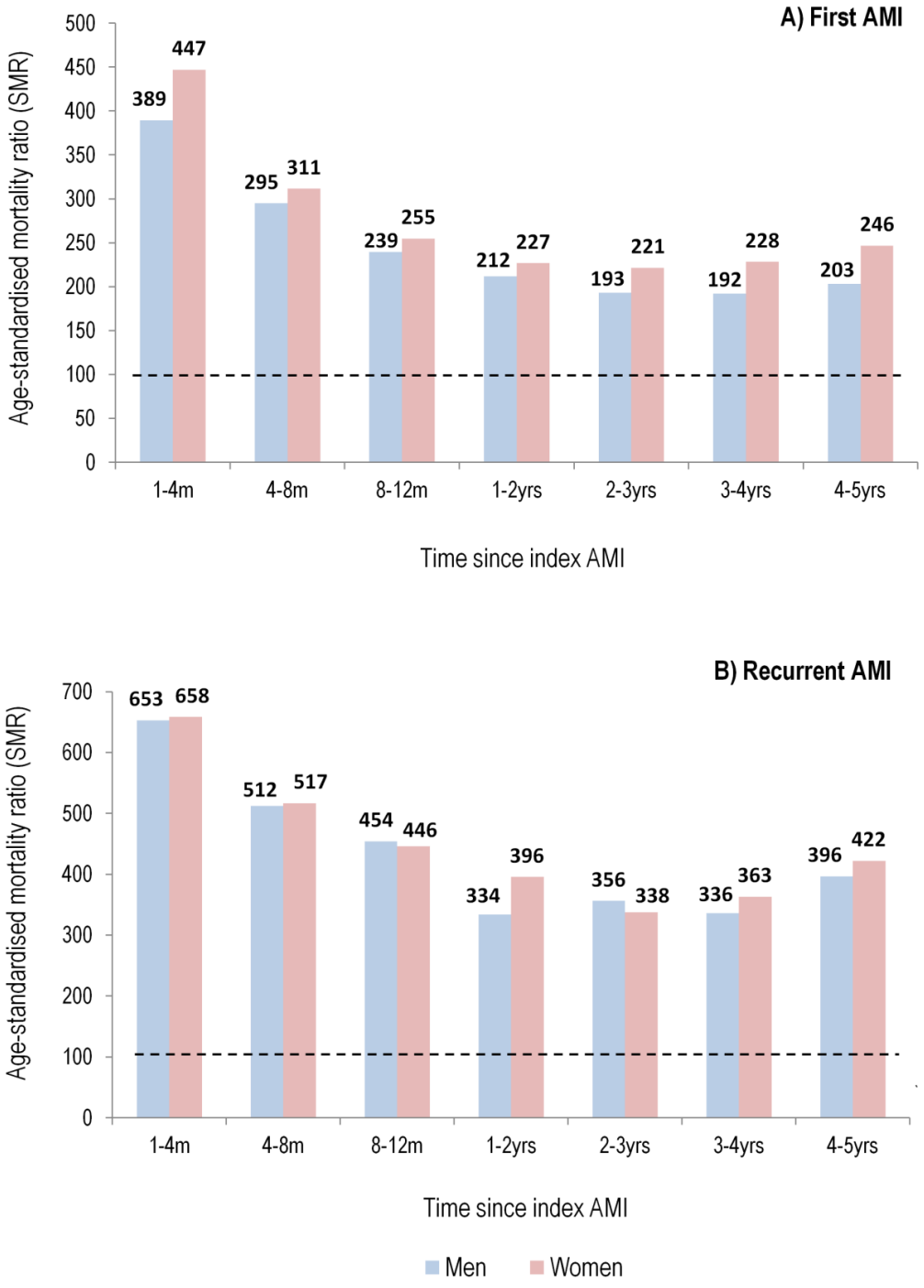
**Univariate model, unadjusted for any other factors; **Multivariate model, adjusted for all other factors shown*

Standardised mortality ratios

Risk of death for 30-day AMI survivors was compared with the risk of death for the general population by calculating age-standardised mortality ratios (SMRs) for different time periods since the date of AMI. The SMR at four months after a first index AMI was 389 (95% CI: 381-398) for men and 447 (95% CI: 437-457) for women (Figure 35A). SMRs declined with time and stabilised at three years at about 200 for both sexes, without any noteworthy changes in the following two years. The SMR was higher for women compared with men at all time points. At five years, the risk of all-cause mortality in male and female survivors of first AMI was about twice the risk of all-cause mortality in the English general population.

For survivors of a recurrent index AMI, the SMR at four months was 653 (95% CI: 607-702) in men and 658 (95% CI: 608-713) in women (Figure 35B). The SMR for both sexes had halved by two years, with no clear pattern in the following three years. There were also no clear patterns in the differences between men and women. By five years, the risk of all-cause mortality for both male and female survivors of recurrent AMI was about four times higher than the risk of dying in the English general population.

Figure 35. Age-standardised mortality ratios in 30-day survivors of A) first and B) recurrent acute myocardial infarction (AMI) by sex, 2003-2007, England.



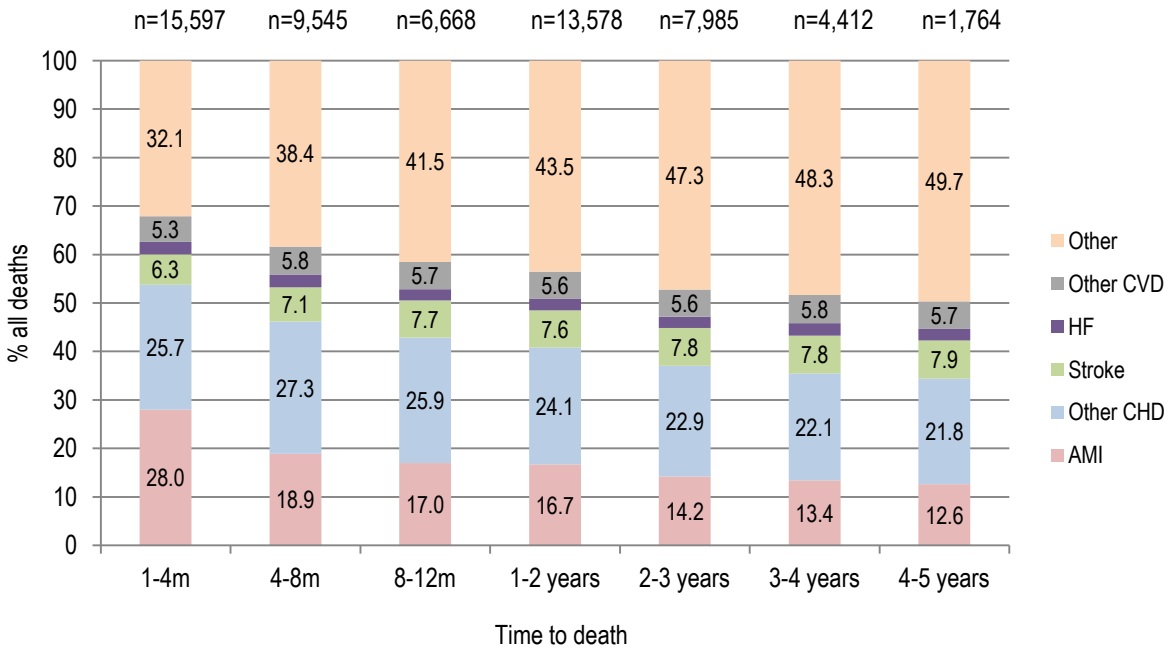
Cause of death

For 30-day AMI survivors who had died within five years, the underlying cause of death coded on the death certificate varied with time since the date of admission for index AMI (Figure 36). AMI featured as the underlying cause of death in 28% and 30% of patients who died within the first four months for first and recurrent index AMI, respectively. The corresponding figures for five years declined to 13% and 17%, respectively.

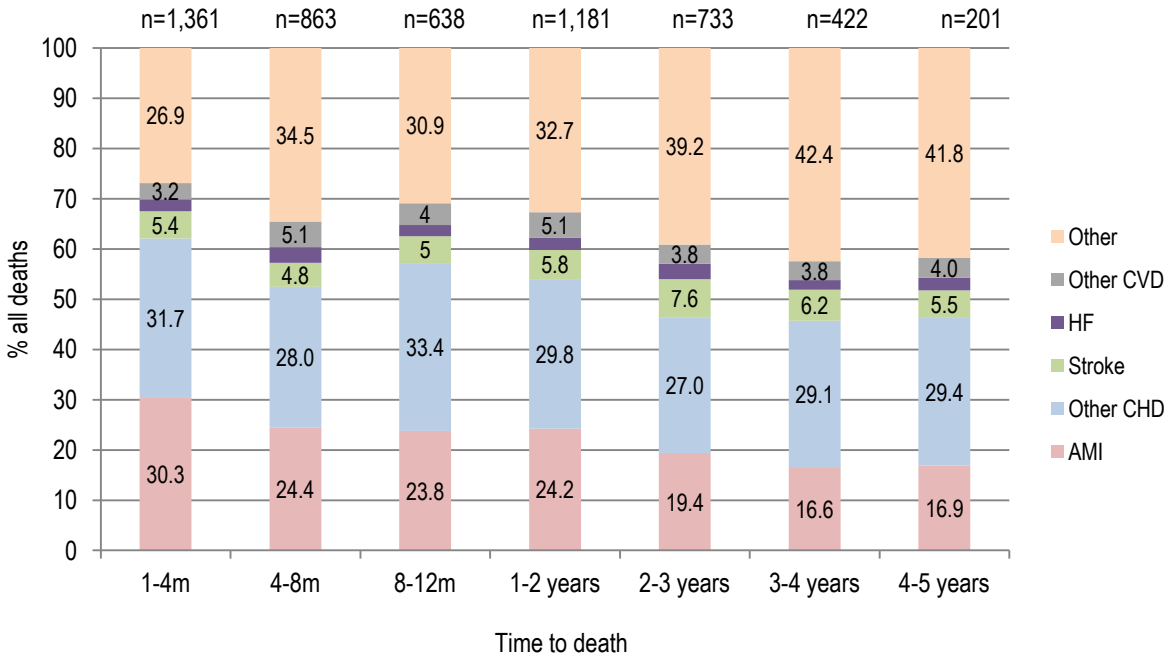
Figure 36 shows clear trends in the cause of death distribution over time among AMI survivors who subsequently died within five years by type of AMI. The proportion of deaths certified with AMI or other CHD as the underlying cause of death decreased with increasing survival time since the initial event. Deaths certified as due to stroke slightly increased with time. No notable changes in the frequency of deaths certified with heart failure or other CVD as the underlying cause of death were noted with increasing time since the index AMI. The proportion of deaths following an index AMI that were certified as being due to all other causes increased with increasing time since the event: from 32% within four months to 50% within five years for first AMI, and from 27% within four months to 42% within five years for recurrent AMI.

Figure 36. Cause of death as % of all deaths in survivors of A) first and B) recurrent acute myocardial infarction (AMI) by time to death, 2003-2007, England.

A) First AMI



B) Recurrent AMI



CHD=coronary heart disease; CVD=cardiovascular disease; HF=heart failure; Stroke = cerebrovascular disease

Risk of a second AMI

Of all 30-day AMI survivors, 266,727 (96%) had experienced a first AMI as the index event. Among these individuals, 26,983 (10%) experienced a second AMI event (fatal or non-fatal) and 43,522 (16%) died from a cause other than AMI within five years of the index event. Of all second AMIs that occurred within five years, 9,945 (37%) were fatal.

Figure 37 and Figure 38 show cumulative incidence plots for risk of a second AMI over five years by sex and age group, for any second AMIs (fatal and non-fatal) and non-fatal AMIs, respectively. For both instances, the recurrence risk was greatest in the first year following the index event, accounting for about half the cumulative five-year risk. The risk continued to increase in subsequent years, but the increase was more gradual.

Table 39 and Table 40 list the recurrence risks by age group, sex, and time since the index admission for a first AMI, as estimated from the cumulative incidence plots in Figure 37 and Figure 38. For men, the risk of any (fatal or non-fatal) second AMI at one year and five years was 6% (95% CI: 6-6) and 12% (95% CI: 12-12), respectively. The risk of non-fatal second AMI was 5% (95% CI: 5-5) at one year and 9% (95% CI: 9-10) at five years. For women, the corresponding figures for any second AMI were 8% (95% CI: 8-8) at one year and 15% (95% CI: 15-16) at five years, and for non-fatal second AMI, the risk was 6% (95% CI: 6-6) at one year and 12% (95% CI: 11-12) at five years.

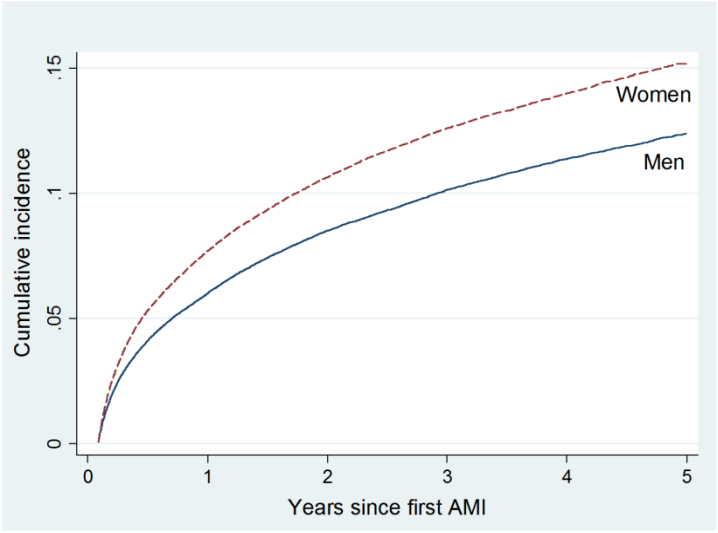
The risk of a second AMI increased with older age for both sexes. Five-year risk of any second AMI was about four times as high for those aged 85 years and older compared with those aged 30-54 years in men (24% versus 7%, respectively) and about three times as high in women (20% versus 6%, respectively) (Table 39). Age differences for one-year risk of recurrence were even greater: it was about seven times as high in men aged 85 years and older compared with men aged 30-54 years: 14% versus 2%, respectively; in

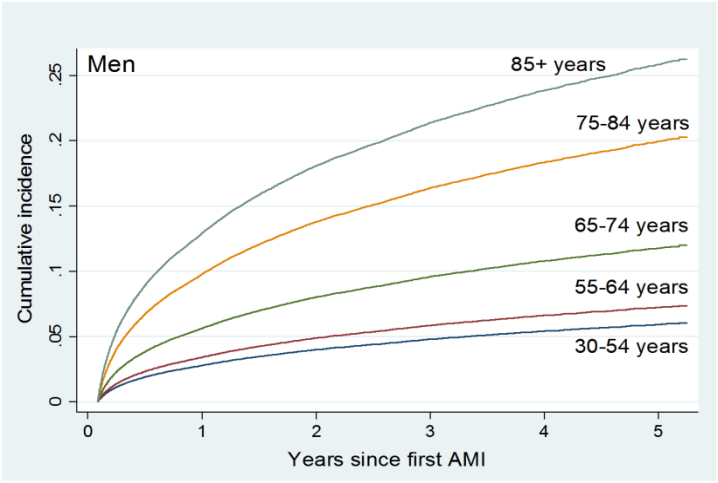
women, the difference was about four times: 11% versus 3%, respectively. Similar patterns were observed for non-fatal AMIs (Table 40).

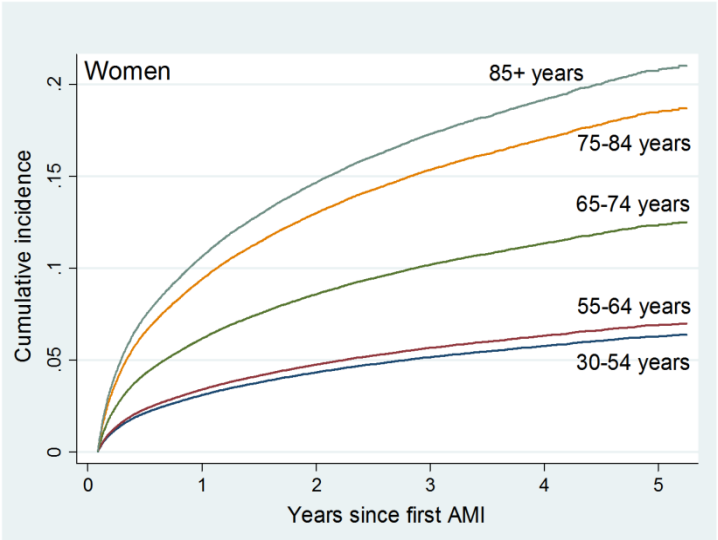
Within each age group, the risk of a second AMI was similar for men and women at each time period of follow up, with one exception: for those aged 85 years and older, the risk was slightly, but significantly, higher in men compared with women, as can be seen from non-overlapping confidence intervals in Table 39.[i] In particular, for any second AMI in the oldest age group, the recurrence risk in men was 24% (94% CI: 23-25) and in women, it was 20% (95% CI: 19-21). For non-fatal second AMI, the corresponding figures were 17% (95% CI: 16-17) and 14% (95% CI: 14-15).

[i] There are no official tests available in STATA to compare cumulative incidence curves and thus it was not possible to produce p-values for the differences.

Figure 37. Risk[j] of a second acute myocardial infarction (AMI) among 30-day survivors of first AMI by sex, age, and time since first AMI, 2003-2007, England.





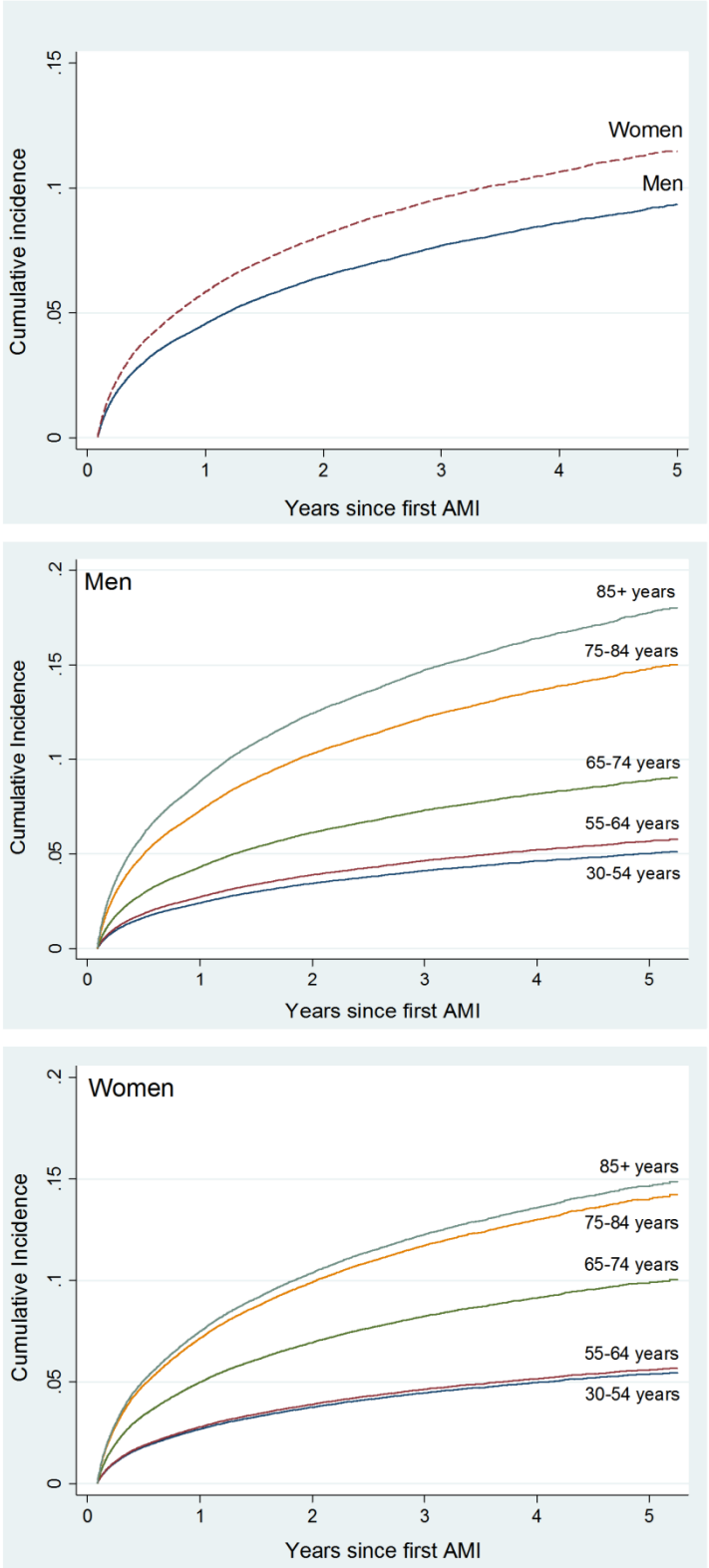


[j] Risk of a second AMI in % = cumulative incidence x 100

Table 39. Risk of a second acute myocardial infarction (AMI) among 30-day survivors of first AMI by sex, age, and time since first AMI, 2003-2007, England.

Age group (years)	Time from admission (years)	Men			Women		
		Recurrence risk (%)	95% CI		Recurrence risk (%)	95% CI	
30-54	1	2.3	2.2	2.5	2.8	2.5	3.2
	2	3.7	3.4	3.9	4.2	3.7	4.7
	3	4.8	4.5	5.0	5.2	4.6	5.8
	4	5.7	5.4	6.0	6.0	5.3	6.7
	5	6.7	6.2	7.1	6.4	5.7	7.2
55-64	1	3.1	3.0	3.3	3.0	2.7	3.3
	2	4.7	4.5	5.0	4.4	4.1	4.8
	3	5.9	5.6	6.2	5.7	5.3	6.2
	4	6.8	6.5	7.1	6.8	6.2	7.3
	5	7.5	7.1	7.9	7.3	6.7	8.0
65-74	1	5.7	5.5	5.9	6.1	5.8	6.4
	2	8.0	7.7	8.3	8.4	8.0	8.8
	3	9.5	9.2	9.8	10.1	9.7	10.6
	4	10.8	10.4	11.1	11.4	10.9	11.9
	5	11.7	11.3	12.2	12.5	11.9	13.1
75-84	1	10.1	9.8	10.4	9.3	9.0	9.6
	2	13.9	13.6	14.3	12.9	12.5	13.3
	3	16.3	15.9	16.8	15.3	14.9	15.8
	4	18.1	17.6	18.5	17.1	16.6	17.6
	5	19.5	19.0	20.1	18.8	18.2	19.4
85+	1	13.8	13.2	14.4	11.3	10.8	11.7
	2	18.9	18.2	19.6	15.1	14.6	15.7
	3	21.5	20.7	22.3	17.3	16.8	17.9
	4	23.2	22.3	24.0	18.7	18.1	19.3
	5	24.4	23.4	25.4	19.8	19.1	20.6
All ages	1	6.0	5.9	6.1	7.7	7.5	7.9
	2	8.5	8.4	8.6	10.6	10.4	10.8
	3	10.1	10.0	10.3	12.6	12.4	12.8
	4	11.4	11.2	11.5	14.0	13.7	14.2
	5	12.4	12.2	12.6	15.2	14.9	15.5

Figure 38. Risk[k] of a non-fatal second acute myocardial infarction (AMI) among 30-day first AMI survivors by sex, age, and time since first AMI, 2003-2007, England.



[k] Risk of a second non-fatal AMI in % = cumulative incidence x 100

Table 40. Risk of a non-fatal second acute myocardial infarction (AMI) among 30-day first AMI survivors by sex, age and time since first AMI, 2003-2007, England.

Age group (years)	Time from admission (years)	Men			Women		
		Recurrence risk (%)	95% CI		Recurrence risk (%)	95% CI	
30-54	1	2.0	1.9	2.2	2.5	2.1	2.9
	2	3.1	2.9	3.3	3.6	3.2	4.1
	3	4.1	3.9	4.3	4.5	4.0	5.0
	4	4.9	4.6	5.2	5.2	4.6	5.8
	5	5.7	5.4	6.1	5.6	4.9	6.3
55-64	1	2.5	2.3	2.7	2.5	2.2	2.8
	2	3.8	3.6	3.9	3.7	3.3	4.0
	3	4.7	4.5	4.9	4.7	4.3	5.2
	4	5.4	5.1	5.6	5.5	5.0	6.0
	5	6.0	5.6	6.3	6.0	5.4	6.6
65-74	1	4.4	4.2	4.6	4.9	4.6	5.2
	2	6.1	5.9	6.4	6.9	6.6	7.3
	3	7.3	7.0	7.5	8.2	7.8	8.6
	4	8.2	7.9	8.5	9.2	8.8	9.6
	5	8.8	8.4	9.1	9.9	9.4	10.5
75-84	1	7.5	7.3	7.8	7.1	6.8	7.4
	2	10.5	10.1	10.8	9.8	9.5	10.1
	3	12.2	11.9	12.6	11.7	11.3	12.1
	4	13.4	13.0	13.8	13.0	12.6	13.4
	5	14.4	14.0	14.9	14.2	13.7	14.7
85+	1	9.6	9.1	10.1	8.0	7.6	8.3
	2	13.2	12.6	13.8	10.8	10.3	11.2
	3	14.9	14.3	15.6	12.3	11.8	12.8
	4	15.7	15.0	16.5	13.3	12.8	13.9
	5	16.5	15.7	17.3	14.0	13.5	14.6
All ages	1	4.6	4.5	4.7	5.8	5.7	6.0
	2	6.5	6.3	6.6	8.1	7.9	8.3
	3	7.7	7.6	7.8	9.6	9.4	9.8
	4	8.6	8.4	8.8	10.6	10.4	10.9
	5	9.3	9.1	9.5	11.5	11.2	11.7

Prognostic factors for a second AMI

Table 41 and Table 42 show both unadjusted and adjusted HRs for the risk of a second AMI by sex, for any second AMI (fatal or non-fatal) and non-fatal second AMI only, respectively. Adjusting for other factors, the risk of any second AMI increased with older age and deprivation: the hazard ratios were 3.93 (95% CI: 3.67-4.20) in men and 3.16 (95% CI: 2.83-3.53) in women, when comparing the age group of 85 years and older with the age group of 30-54 years; and 1.37 (95% CI: 1.31-1.44) in men and 1.17 (95% CI: 1.10-1.24) in women, when comparing the most deprived group with the least deprived group (Table 41). Exposure to PTCA and CABG procedures was associated with lower risk of recurrent AMI, while presence of the examined comorbid conditions significantly increased the risk of a second AMI. In particular, the risk of a second AMI was about 60% higher among patients with diabetes, after adjusting for other factors. Similar patterns were observed for the risk of a non-fatal second AMI (Table 42).

Table 43 and Table 44 show unadjusted and adjusted HRs by age group, for any second AMI and non-fatal second AMI, respectively. Generally, there were no large sex differences, with men having only slightly higher recurrence risk than women after adjusting for other factors. However, in those aged 85 years and older, men faced about a 30% higher risk than women even after adjustment (Table 43). The effect of deprivation on recurrence risk decreased with older age. The effects of comorbidities varied by age group, but generally also attenuated with increasing age. Diabetes continued to be a risk factor for a second AMI for all age groups. The strength of association between PTCA and CABG and longer survival increased with older age; however, very few patients aged 85 years and over had undergone CABG and its effect could not be determined in this age group. Similar patterns were observed for the risk of a non-fatal second AMI (Table 44).

Table 41. Factors influencing the risk of a second acute myocardial infarction (AMI) among 30-day survivors of first AMI by sex, 2003-2007, England.

Factor	Men						Women					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Age (years)												
30-54	Ref.			Ref.			Ref.			Ref.		
55-64	1.23	1.15	1.31	1.16	1.09	1.24	1.10	0.97	1.25	1.06	0.93	1.21
65-74	2.05	1.93	2.18	1.77	1.67	1.88	2.03	1.81	2.27	1.82	1.63	2.04
75-84	3.65	3.45	3.86	2.98	2.81	3.16	3.15	2.83	3.51	2.73	2.45	3.05
85+	4.91	4.60	5.23	3.93	3.67	4.20	3.59	3.22	4.01	3.16	2.83	3.53
Deprivation												
Least deprived, 1	Ref.			Ref.	0.00	0.00	Ref.			Ref.	0.00	0.00
2	1.10	1.04	1.15	1.09	1.03	1.14	1.01	0.96	1.08	1.01	0.95	1.07
3	1.19	1.13	1.25	1.20	1.14	1.26	1.04	0.98	1.10	1.04	0.98	1.10
4	1.21	1.15	1.27	1.24	1.18	1.30	1.08	1.02	1.15	1.10	1.03	1.16
Most deprived, 5	1.30	1.23	1.36	1.37	1.31	1.44	1.11	1.05	1.18	1.17	1.10	1.24
Procedure**												
CABG	0.29	0.21	0.39	0.26	0.19	0.35	0.27	0.16	0.46	0.29	0.17	0.48
PTCA	0.43	0.41	0.46	0.54	0.51	0.58	0.43	0.39	0.47	0.53	0.48	0.58
Comorbidity												
Cancer	1.39	1.28	1.52	0.96	0.88	1.05	0.89	0.76	1.03	0.82	0.70	0.95
Cardiovascular disease	1.65	1.59	1.70	1.38	1.33	1.43	1.64	1.57	1.72	1.44	1.37	1.50
Diabetes	1.84	1.78	1.91	1.61	1.55	1.66	1.71	1.64	1.79	1.65	1.58	1.72
Respiratory disease	1.66	1.60	1.72	1.22	1.17	1.27	1.16	1.11	1.21	1.04	1.00	1.09
Renal disease	2.03	1.92	2.15	1.20	1.14	1.28	1.42	1.31	1.53	1.08	1.00	1.16

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors*

***Multivariate model, adjusted for all other factors shown*

Table 42. Factors influencing the risk of a non-fatal second acute myocardial infarction (AMI) among 30-day survivors of first AMI by sex, 2003-2007, England.

Factor	Men						Women					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Age												
30-54	Ref.			Ref.			Ref.			Ref.		
55-64	1.13	1.05	1.22	1.08	1.00	1.16	1.04	0.90	1.20	1.00	0.87	1.15
65-74	1.80	1.69	1.93	1.58	1.48	1.69	1.88	1.66	2.13	1.69	1.50	1.91
75-84	3.10	2.91	3.30	2.62	2.45	2.79	2.73	2.43	3.07	2.38	2.12	2.69
85+	3.79	3.52	4.07	3.18	2.95	3.43	2.86	2.54	3.23	2.56	2.27	2.89
Deprivation												
Least deprived, 1	Ref.			Ref.			Ref.			Ref.		
2	1.06	1.00	1.12	1.04	0.99	1.11	1.04	0.97	1.11	1.03	0.96	1.11
3	1.18	1.12	1.25	1.19	1.12	1.26	1.08	1.01	1.16	1.08	1.01	1.16
4	1.22	1.15	1.29	1.24	1.17	1.31	1.11	1.04	1.19	1.12	1.05	1.20
Most deprived, 5	1.28	1.21	1.36	1.34	1.27	1.42	1.13	1.05	1.21	1.17	1.10	1.26
Procedure**												
CABG	0.29	0.20	0.41	0.26	0.18	0.37	0.31	0.18	0.55	0.32	0.18	0.56
PTCA	0.48	0.45	0.52	0.59	0.55	0.63	0.47	0.42	0.52	0.55	0.49	0.61
Comorbidity												
Cancer	1.32	1.20	1.46	0.95	0.86	1.06	0.90	0.75	1.07	0.84	0.71	1.00
Cardiovascular disease	1.54	1.48	1.61	1.31	1.26	1.37	1.64	1.55	1.72	1.45	1.38	1.53
Diabetes	1.88	1.80	1.96	1.67	1.60	1.74	1.75	1.67	1.84	1.68	1.60	1.77
Respiratory disease	1.53	1.47	1.60	1.17	1.12	1.22	1.10	1.04	1.15	1.00	0.95	1.05
Renal disease	1.71	1.60	1.83	1.06	0.99	1.14	1.20	1.09	1.31	0.93	0.85	1.02

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors*

***Multivariate model, adjusted for all other factors shown*

Table 43. Factors influencing the risk of a second acute myocardial infarction (AMI) among 30-day survivors of first AMI by age group, 2003-2007, England.

Factor	30-54 years						55-64 years						65-74 years					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Sex																		
Women	Ref.			Ref.			Ref.			Ref.			Ref.			Ref.		
Men	0.92	0.82	1.04	1.03	0.92	1.16	1.03	0.95	1.13	1.14	1.04	1.25	0.94	0.89	0.99	0.99	0.94	1.04
Deprivation																		
Least deprived, 1	Ref.			Ref.			Ref.			Ref.			Ref.			Ref.		
2	1.07	0.90	1.28	1.07	0.90	1.27	1.14	1.00	1.30	1.12	0.98	1.28	1.13	1.04	1.23	1.09	1.00	1.19
3	1.28	1.08	1.50	1.24	1.05	1.46	1.42	1.25	1.61	1.36	1.20	1.55	1.24	1.14	1.35	1.17	1.07	1.27
4	1.38	1.18	1.62	1.32	1.13	1.54	1.53	1.35	1.73	1.43	1.27	1.63	1.40	1.29	1.53	1.27	1.17	1.39
Most deprived, 5	1.59	1.37	1.85	1.51	1.30	1.75	1.93	1.71	2.17	1.72	1.53	1.95	1.63	1.50	1.77	1.42	1.31	1.54
Procedure																		
CABG	0.52	0.23	1.15	0.39	0.17	0.86	0.47	0.26	0.84	0.36	0.20	0.65	0.34	0.22	0.50	0.26	0.17	0.40
PTCA	0.86	0.76	0.97	0.80	0.71	0.90	0.65	0.58	0.73	0.62	0.55	0.69	0.51	0.46	0.56	0.50	0.45	0.56
Comorbidity																		
Cancer	1.41	0.77	2.57	1.34	0.73	2.47	1.48	1.10	1.98	1.39	1.03	1.88	1.21	1.04	1.41	1.16	1.00	1.35
Cardiovascular disease	1.34	1.22	1.47	1.27	1.15	1.40	1.44	1.33	1.56	1.36	1.25	1.47	1.54	1.45	1.64	1.44	1.35	1.53
Diabetes	2.12	1.90	2.37	1.86	1.66	2.08	2.40	2.21	2.60	2.11	1.94	2.29	2.17	2.05	2.28	1.90	1.80	2.01
Respiratory disease	1.60	1.40	1.84	1.41	1.23	1.63	1.60	1.46	1.77	1.39	1.26	1.54	1.52	1.43	1.61	1.36	1.28	1.44
Renal disease	4.02	3.16	5.11	2.85	2.22	3.65	2.52	2.09	3.05	1.77	1.45	2.15	1.95	1.77	2.16	1.48	1.34	1.64

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors*

***Multivariate model, adjusted for all other factors shown*

Table 43 (cont'd). Factors influencing the risk of a second acute myocardial infarction (AMI) among 30-day survivors of first AMI by age group, 2003-2007, England.

Factor	75-84 years						85+ years					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Sex												
Women	Ref.			Ref.			Ref.			Ref.		
Men	1.07	1.03	1.11	1.10	1.06	1.15	1.26	1.20	1.33	1.29	1.22	1.35
Deprivation												
Least deprived, 1	Ref.			Ref.			Ref.			Ref.		
2	1.12	1.06	1.19	1.11	1.04	1.18	0.93	0.86	1.00	0.93	0.86	1.01
3	1.18	1.11	1.25	1.15	1.08	1.22	0.97	0.89	1.04	0.98	0.90	1.05
4	1.24	1.17	1.32	1.20	1.13	1.27	0.95	0.88	1.03	0.96	0.88	1.04
Most deprived, 5	1.27	1.19	1.35	1.21	1.13	1.29	1.02	0.94	1.11	1.04	0.95	1.13
Procedure**												
CABG	0.22	0.13	0.36	0.20	0.12	0.33	-	-	-	-	-	-
PTCA	0.46	0.41	0.51	0.44	0.40	0.49	0.51	0.40	0.65	0.47	0.37	0.61
Comorbidity												
Cancer	0.89	0.80	1.00	0.86	0.77	0.96	0.81	0.69	0.95	0.76	0.65	0.90
Cardiovascular disease	1.43	1.36	1.50	1.41	1.34	1.48	1.33	1.25	1.42	1.34	1.26	1.43
Diabetes	1.58	1.52	1.65	1.49	1.43	1.56	1.23	1.15	1.32	1.19	1.11	1.27
Respiratory disease	1.15	1.10	1.21	1.10	1.05	1.15	0.94	0.88	1.00	0.91	0.85	0.97
Renal disease	1.20	1.12	1.29	1.08	1.01	1.16	1.02	0.93	1.11	0.97	0.89	1.06

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors*

***Multivariate model, adjusted for all other factors shown*

Table 44. Factors influencing the risk of a non-fatal second acute myocardial infarction (AMI) among 30-day survivors of first AMI by age group, 2003-2007, England.

Factor	30-54 years						55-64 years						65-74 years					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Sex																		
Women	Ref.			Ref.			Ref.			Ref.			Ref.			Ref.		
Men	0.92	0.81	1.04	1.01	0.89	1.15	1.00	0.91	1.11	1.10	0.99	1.21	0.88	0.83	0.94	0.93	0.88	0.99
Deprivation																		
Least deprived, 1	Ref.			Ref.			Ref.			Ref.			Ref.			Ref.		
2	1.09	0.91	1.32	1.09	0.91	1.32	1.10	0.95	1.28	1.09	0.94	1.26	1.09	0.99	1.20	1.05	0.95	1.16
3	1.28	1.07	1.53	1.25	1.04	1.49	1.38	1.20	1.58	1.33	1.16	1.53	1.23	1.12	1.35	1.16	1.05	1.27
4	1.43	1.20	1.69	1.37	1.15	1.62	1.51	1.32	1.74	1.43	1.24	1.64	1.39	1.26	1.52	1.25	1.14	1.38
Most deprived, 5	1.57	1.33	1.84	1.49	1.26	1.75	1.85	1.62	2.11	1.67	1.46	1.91	1.58	1.44	1.73	1.37	1.25	1.51
Procedure																		
CABG	0.50	0.21	1.20	0.39	0.17	0.94	0.59	0.33	1.06	0.47	0.26	0.85	0.28	0.17	0.47	0.23	0.14	0.38
PTCA	0.88	0.78	1.00	0.84	0.73	0.96	0.71	0.63	0.80	0.68	0.60	0.77	0.56	0.50	0.62	0.56	0.50	0.62
Comorbidity																		
Cancer	1.18	0.59	2.38	1.14	0.56	2.29	1.19	0.83	1.71	1.13	0.78	1.62	1.13	0.94	1.35	1.10	0.92	1.31
Cardiovascular disease	1.25	1.13	1.38	1.18	1.06	1.31	1.36	1.24	1.48	1.28	1.17	1.40	1.47	1.37	1.57	1.35	1.26	1.44
Diabetes	2.02	1.79	2.27	1.81	1.60	2.05	2.26	2.06	2.47	2.02	1.84	2.22	2.24	2.11	2.38	2.01	1.89	2.14
Respiratory disease	1.52	1.30	1.77	1.36	1.17	1.59	1.52	1.36	1.69	1.34	1.19	1.50	1.46	1.37	1.56	1.32	1.23	1.41
Renal disease	3.36	2.55	4.44	2.47	1.86	3.28	2.12	1.69	2.66	1.53	1.21	1.93	1.69	1.50	1.91	1.29	1.14	1.46

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors*

***Multivariate model, adjusted for all other factors shown*

Table 44 (cont'd). Factors influencing the risk of a non-fatal second acute myocardial infarction (AMI) among 30-day survivors of first AMI by age group, 2003-2007, England (cont'd).

Factor	75-84 years						85+ years					
	HR*	95% CI		HR**	95% CI		HR*	95% CI		HR**	95% CI	
Sex												
Women	Ref.			Ref.			Ref.			Ref.		
Men	1.04	1.00	1.09	1.08	1.03	1.13	1.21	1.14	1.29	1.25	1.18	1.33
Deprivation												
Least deprived, 1	Ref.			Ref.			Ref.			Ref.		
2	1.09	1.02	1.17	1.08	1.01	1.16	0.95	0.86	1.04	0.95	0.86	1.04
3	1.18	1.10	1.27	1.15	1.08	1.24	1.01	0.92	1.11	1.02	0.93	1.12
4	1.23	1.15	1.32	1.20	1.11	1.28	0.97	0.88	1.06	0.98	0.89	1.08
Most deprived, 5	1.23	1.14	1.32	1.18	1.10	1.27	1.03	0.93	1.14	1.04	0.94	1.15
Procedure**												
CABG	0.24	0.13	0.42	0.22	0.12	0.38	-	-	-	-	-	-
PTCA	0.47	0.41	0.53	0.45	0.40	0.51	0.54	0.40	0.72	0.50	0.37	0.67
Comorbidity												
Cancer	0.95	0.84	1.08	0.93	0.82	1.05	0.75	0.62	0.92	0.72	0.59	0.88
Cardiovascular disease	1.40	1.33	1.48	1.39	1.32	1.47	1.39	1.29	1.50	1.40	1.30	1.52
Diabetes	1.61	1.53	1.69	1.53	1.45	1.61	1.29	1.19	1.40	1.25	1.15	1.35
Respiratory disease	1.08	1.03	1.14	1.04	0.99	1.10	0.86	0.80	0.93	0.84	0.78	0.91
Renal disease	1.03	0.94	1.12	0.93	0.85	1.01	0.89	0.80	0.99	0.85	0.77	0.95

HR=hazard ratio; CABG=Coronary Artery Bypass Graft; PTCA=Percutaneous Transluminal Coronary Angioplasty

**Univariate model, unadjusted for any other factors*

***Multivariate model, adjusted for all other factors shown*

Discussion

This study provides a comprehensive account of five-year prognosis in 30-day AMI survivors in England between 2003 and 2007. The results show that long-term survival declined markedly with older age at index AMI for both men and women, and for both first and recurrent AMI. Overall, around seven out of ten men and six out of ten women were still alive five years after their first index event; for survivors of a recurrent AMI, only half as many were still alive. By five years, all-cause mortality in survivors of first and recurrent AMI remained about two and four times higher than that of the English general population, respectively. Amongst those with a first AMI as the index event, around one in eight men and one in six women experienced a second AMI within the following five years, with the risk increasing with older age.

Long-term survival

Overall, this study confirms that survivors of AMI are a high-risk group of patients, with around one third of survivors of first index AMI and six out of ten survivors of recurrent index AMI dying within five years of the event. These results are comparable to the figures for five-year mortality among one-month survivors of AMI reported from Sweden (28% for men, 32% for women)[131] and Canada (27% for men, 39% for women)[140] in the 1990s, but lower than figures from Scotland (41%)[132] and New Zealand (45%)[35] for the same time period. The findings also show that there is little geographic variation within England in long-term survival after an AMI event.

In this study, survivors of both first and recurrent AMI had a continuing worse prognosis than the English general population, with the risk of all-cause mortality at five years being about two and four times higher than that of the sex- and age-matched general

population. Studies from Canada and Sweden also found a similarly higher mortality risk in AMI survivors compared with the general population (about three times as high at one year after the event).[134, 135]

The results of this chapter confirm that long-term prognosis for AMI survivors is worse for younger and better for older women than men, a finding similar to earlier reports from US,[139] Canada,[140] Norway,[110] and Sweden.[66] Others have found no sex differences in age-adjusted long-term mortality following AMI,[109, 133, 178, 185] but age-specific rates for men and women were not reported in these studies. Some of the higher mortality in younger women can be attributed to a higher prevalence of diabetes and other comorbidities and more in-hospital complications than men.[39, 66, 136, 137, 139, 158, 178, 183, 203] Other possible explanations include premature coronary heart disease, different pathophysiological mechanisms, anatomical differences, and atypical symptom presentation.[139, 180-183]

Similarly to previous research, the results indicate that age, deprivation, history of AMI, and presence of comorbidities all contribute to a worse long-term prognosis following an AMI event.[128, 131, 132, 140, 144, 231, 250, 330] Age was confirmed as the most powerful predictor for death;[49, 132, 133, 330] in this study, only about 20% of individuals aged 85 years and older who survived a first index AMI were still alive after five years, in comparison with over 90% for those aged 30-54 years. Survivors of reinfarction were about 50% more likely to die within five years than survivors of first AMI, highlighting the significant influence of prior history. This finding supports earlier observations that recurrent AMI is a strong and independent predictor for death.[149, 152, 153, 162]

Of the examined comorbidities, cancer and renal disease had the strongest predictive effects on all-cause mortality after an index AMI. In addition, it was demonstrated that the effects of prior AMI, deprivation, and comorbidities as prognostic factors for death

decrease with older age, while the association with revascularisation procedures became stronger with older age. The strong association between coronary revascularisation procedures and longer survival could be influenced by a patient selection effect: patients who are selected to undergo these procedures may be healthier and fitter, perhaps particularly so in the older age groups, and a better survival rate among them is thus not surprising. While it was important to control for the use of procedures in the statistical models, the actual effect sizes of the procedures as reported in this study should be interpreted with caution. This is because observational studies cannot provide definitive evidence about the effect of treatment on survival, since it is not possible to fully control for the distribution of important covariates among treatment groups in such studies.[330]

Risk of a second AMI

Around one in eight men (12%) and around one in six women (15%) who survived their first index AMI experienced a second AMI, fatal or non-fatal, within five years; about half occurred in the first year. These results indicate that patients who survived their first AMI are most prone to recurrence in the first year following the infarct, suggesting that the influence of predisposing factors for a second AMI lessens with time. A Swedish study of recurrence among survivors of AMI between 1972 and 2001 found that the risk of a recurrent AMI decreased sharply within the first two years, reached its minimum at five years, and then started to slowly increase again.[159] The higher recurrence risk during the first few years immediately following the initial event could be due to ongoing disease processes. These findings indicate that patients experiencing an AMI will benefit from prompt prescription of evidence-based secondary prevention treatments.

The risk of any second AMI or non-fatal second AMI was slightly higher in men than women for most age groups, after adjusting for other factors (there were no sex

differences for those aged 65-74 years). The slightly higher recurrence risk in men continued for the older age groups. Others also found that men face a higher recurrence risk of AMI than women. For example, a Finnish MONICA study reported that men are more likely than women to have a fatal recurrent CHD event within six years of AMI (HR=1.74).[158] A MONICA study from Iceland reported a 1.17 male-to-female ratio for recurrence rate of second AMI.[331] Another MONICA study from Denmark reported that the relative risk for recurrent AMI was 31% higher in men than women.[69] However, MONICA studies only examined individuals aged under 65 years. In Scotland, linked hospital and mortality statistics between 1990 and 2000 for an unselected cohort of patients, inclusive of all ages, showed that around 50% more men than women experienced a non-fatal AMI within five years of the initial event (9.9% versus 6.3%).[132]

Prognostic factors for a second AMI were similar to those for death: older age, higher deprivation, and presence of comorbidities. The effect of deprivation and comorbidities decreased with age. Diabetes was confirmed to be a strong independent risk factor for recurrence for both men and women and for all age groups.[200, 202, 327] Because of the limited demographic and clinical information available in the dataset used for this study, the effect of the main cardiovascular risk factors (smoking status, high blood cholesterol levels, and high blood pressure), which have been shown to affect not only the occurrence, but also the recurrence of AMI,[327] could not be assessed. Other factors that could have influenced recurrence, but could not be investigated in this study, include infarct severity, pharmaceutical treatment, patient compliance with drug therapy, and psychological and social environment.

While trends in recurrence risk could not be examined in this study due to the limited time span of the dataset, prescribing practices of effective medications such as aspirin, statins, beta-blockers, and ACE-inhibitors upon discharge have been improving over the

last decade in England.[61, 141, 148, 332, 333] The effective use of evidence-based treatments during the initial admission to hospital as well as after discharge has been shown to reduce the occurrence of recurrent fatal and non-fatal AMI events.[334] Furthermore, the risk factor profile has been improving in the English population.[61] Therefore, it is very plausible that the risk of a second AMI among the survivors of first AMI has been declining in the UK.

Conclusion

This study extends and updates current information for England on prognosis following an AMI, specifically survival differences between first and recurrent events. Older age, history of AMI, higher deprivation, and comorbidities are associated with decreased long-term survival. For all survivors, the risk of death is highest during the first year, but it remains above the level of the general population for at least five years following an AMI event. A substantial proportion of survivors of first AMI experience a second AMI within five years, and the recurrence risk increases with older age. The results reinforce the importance of acute clinical care and secondary prevention in patients hospitalised for AMI, and highlight AMI survivors as a high-risk group for mortality and recurrence.

CHAPTER 9: DISCUSSION

This chapter summarises the main research findings from the studies presented in this thesis. It discusses the strengths and limitations of the data sources and study design. The implications of the findings for research, clinical practice, and public policy are outlined and suggestions are made for future research. The overall conclusion of the thesis is stated at the end of the chapter.

Introduction

The aim of this thesis was to provide a comprehensive analysis of the epidemiology of acute myocardial infarction (AMI) in England over the last decade. The main outcome measures included: trends in AMI event rates and case fatality, and their contribution to the trends in AMI mortality from 1999 to 2007; trends in characteristics of, and hospital care for, AMI patients admitted to hospital between 1999 and 2007; incidence and case fatality rates for first and recurrent AMI in 2007; and five-year survival and risk of a second AMI from 2003 to 2007. The research undertaken was a population-based study using person-based linked routine hospital records from Hospital Episode Statistics (HES) and mortality records from the Office for National Statistics (ONS) for England. The objectives of this chapter are: to summarise the main findings from the presented studies, to discuss the strengths and limitations of the thesis and the implications of its findings, and to suggest directions for future research.

Summary of main findings

Trends in AMI event rate

The event rates for AMI have declined for both sexes, almost all age groups, and all Government Office Regions in England between 1999 and 2007. The age-standardised overall AMI event rate fell by around one third, while the hospitalised AMI event rate declined by around one fifth and sudden AMI death rate fell by half. Trends differed by age group: the greatest annual declines in overall event rates occurred in middle-aged individuals and the smallest declines occurred in the youngest and oldest individuals. However, the rate of occurrence of hospitalised AMI actually increased among men and women aged 85 years and older. These findings indicate that there were fewer new AMI events in England each year, but relatively more occurred among older individuals.

Trends in AMI case fatality

Case fatality rates for AMI have declined for both sexes, all age groups, and all Government Office Regions in England between 1999 and 2007. Hospitalised case fatality, overall case fatality, and sudden AMI death rates all declined by around one third over this time period. Similar to trends in event rates, case fatality trends differed by age group: for overall and hospitalised case fatality, the greatest declines occurred in middle-aged individuals, while the proportion of all AMIs that were sudden deaths without hospitalisation for AMI increased with older age and was greatest for those aged 85 years and older. The findings suggest that overall short-term prognosis after AMI has improved, particularly for middle-aged individuals, and that more people are surviving to reach hospital after the onset of an AMI event, particularly older individuals.

Explaining trends in AMI mortality

Total age-standardised AMI mortality rates fell by approximately half for both sexes between 1999 and 2007 in England. However, the declines were more marked among middle-aged individuals and less so among younger and older individuals. Approximately half of the overall decline in total AMI mortality could be attributed to a reduction in event rate and the remaining half to a reduction in case fatality. The relative contributions of event rate and case fatality reductions to the decline in AMI mortality differed by sex, age, and Government Office Region, with changes in case fatality playing a greater role for women, older individuals, and in the south-east region of the country. Throughout the study period, the majority of AMI fatalities continued to be sudden deaths.

Trends in characteristics of, and hospital care for, the AMI patient population

Comparison of individuals hospitalised for AMI in England between 1999 and 2007 showed that the AMI patient population became increasingly elderly, presenting with more comorbidities, and undergoing more coronary revascularisation procedures. Of all AMI hospitalisations in 2007, over one third of those in men and around two thirds of those in women were in those aged 75 years and older, emphasising the importance of including the elderly in epidemiological studies of AMI. On average, AMI patients spent about one week in hospital during the last decade. Generally, the length of stay was longer for women and older patients. The results also suggest that shorter lengths of stay may not be associated with a higher mortality within 30 days or one year after discharge from the index hospital admission for AMI.

Incidence and case fatality of AMI in 2007

Approximately 90,000 AMI events occurred in England in 2007. The results confirmed the established patterns of a higher incidence in men compared with women, for all ages including the very elderly. However, the difference between men and women in age-specific incidence rates decreased with increasingly older age. Recurrent events were equally prevalent among women and men, with approximately one in seven AMIs being reinfarctions for both sexes, and this proportion increased with older age. One third of all AMIs were fatal, and of these, two thirds were sudden AMI deaths. Hospitalised case fatality rates were around half of the overall rates (which included sudden AMI deaths), indicating that the clinical prognosis for those who survive long enough to be admitted to hospital is much better than overall AMI prognosis.

Survival and outcomes following AMI

Overall, amongst those experiencing an AMI between 2003 and 2007, around seven out of ten men and six out of ten women were still alive at five years after their first index event; for survivors of a reinfarction, only half as many were still alive. For all AMI survivors, the risk of death was highest during the first year, but it remained above that of the general population for the first five years following an AMI event. Older age, history of AMI, greater deprivation, no revascularisation procedure, and presence of comorbidities were associated with lower long-term survival, i.e. greater risk of death. Amongst those with a first AMI as the index event, around one in eight men and one in six women experienced a second AMI within five years. The risk of a second AMI increased with older age and was highest in the year immediately after the initial event.

Strengths and limitations

The strengths of the studies presented in this thesis include the large size of the cohort, population-level representation, complete national coverage, and recent statistics. In fact, the dataset used for this thesis, comprising more than one million AMIs, is one of the largest linked AMI datasets in the world and is six times the size of the WHO MONICA study population.[3] It is based on the entire English population: approximately 50 million residents. The large size of the study cohort allowed for stratification by sex, five-year age groups, deprivation categories, and Government Office Regions. Because the study cohort was unselected, it included individuals who might otherwise not have been included in other research – all ages, all locations, and no exclusions related to medical, cultural, ethnic or other factors. The vast majority of hospitals in England are publicly funded by the National Health Service (NHS); therefore the hospital dataset included almost all patients who experienced an AMI in England during the study period. Accordingly, the external validity of the presented studies is very high.

This thesis fills gaps in knowledge about recent changes in the epidemiology of AMI in the English population in a comprehensive manner. It is rare to find reports of all major epidemiological measures (incidence, case fatality, mortality, and survival) for a specific condition that are based on the same population over the same period of time. The timeliness of this research is particularly relevant in the context of the recent debate on the NHS reforms, where AMI mortality has attracted recent political attention, driven by the government's view that the NHS has not been performing well.[18, 19, 335] This thesis provides evidence of the success of the English NHS in recent years. Such data are needed for health services to become more sensitive and responsive to health outcomes and for comparison of NHS performance with the health care systems in other countries.

From a practical perspective, using routine administrative data to conduct this research was very cost effective. Routine databases are readily available and continuously updated, allowing for retrospective long-term follow-up of populations at a much lower cost than that of designing and implementing large-scale cohort studies or clinical registries. For instance, maintenance costs of HES have been estimated at £1 per record, compared with a range of £10 to £60 per record for disease registries.[336] Finally, this thesis used standard definitions that are commonly employed in epidemiological studies of AMI, including those using linked hospital and mortality statistics, making the findings internationally comparable.

The main limitation of this thesis is the reliance upon the accuracy and validity of routine hospital data. Although HES data have been subject to a number of criticisms, two systematic reviews of studies comparing routine hospital discharge statistics with medical records in England, Wales and Scotland reported, on average, high overall coding accuracy rates in the United Kingdom.[272, 275] In addition, the quality of hospital data varies by condition, and common diagnoses like AMI are less likely to be subject to miscoding than rare ones.[274, 337] Linked Scottish Morbidity Record Database and Patient Episode Database for Wales, which are the Scottish and Welsh counterparts to the English HES, have been reported to have high accuracy rates for the diagnosis of AMI.[202, 338] Finally, a recent comparison study of AMI diagnoses in HES and general practice clinical records showed an agreement of over 90%.[276]

Further limitations include the absence of clinical information, making it impossible to take into account coronary risk factors and infarct severity, or to report on the diagnostic criteria used in making the clinical diagnosis of AMI. Some AMI hospital admissions with a length of stay of two days or less and live discharge, or with only a secondary diagnosis of AMI – excluded from this analysis – could have been true instances of AMI.

Some deaths coded with non-AMI CHD as the underlying cause of death could have been true cases of AMI, but, as this is not knowable, they could not be included. It is possible that some AMIs that were identified as recurrent (based on the 30-day cut off to distinguish separate events) might not have been new events and were still related to the previous AMI event. Information on previous episodes of AMI was limited to nine years of prior history and, inevitably, some events that were classified as "first" or "incident" were, in fact, recurrent. However, a nine-year history period is the longest that could be used within the limits of the English national record linkage dataset that was produced for this thesis.

A limitation of the trends in rates analyses was the inability to distinguish AMI events as first or recurrent. This was not possible because the length of time covered by the dataset did not allow for a clearance period to identify AMI events at the same time as studying trends over time. However, it has been shown that even though the event rate overestimates the true incidence of disease, for the purposes of tracking changes over time, any systematic bias in the data does not affect estimates of trends.[17] Therefore, the reported findings for overall rates are likely to be a good reflection of reality.

The introduction of new diagnostic criteria for AMI in 2000[89] is likely to have influenced the presented trends for event rates and the scale of their decline may have been slightly underestimated. Other studies have demonstrated that changing the criteria to include troponin measurement (a highly sensitive biomarker for detecting myocardial damage) tends to increase the number of hospitalised admissions with manifestations of CHD that are diagnosed and recorded as AMI, thus obscuring some of the downward trend in hospitalisation rates.[72, 93, 94, 97] Unfortunately, it was not possible to directly quantify the effect of the change in diagnostic criteria for AMI on trends in hospital admissions reported in this thesis because of the unavailability of clinical information used in making

the diagnosis of AMI. The change in diagnostic criteria for AMI has been shown not to affect trends in hospitalised case fatality.[94, 102, 104]

Another limitation is the likely incomplete data on patient comorbidities. Conditions recorded as secondary diagnoses, defined as comorbidities in this study, probably did not include all relevant conditions of a patient because comorbidities tend to be underreported in routine hospital statistics.[191, 281, 339-342] Underreporting may arise for a number of reasons, including the limited capability of administrative data to capture clinical detail; inability to distinguish between comorbidities and in-hospital complications; differences between institutional practices of coding active or controlled comorbidities; and selection bias for certain diagnostic codes related to hospital funding incentives. However, the issue of underreporting does not apply to all diagnoses (for example, diabetes and previous AMI are well reported as secondary diagnoses)[281, 341, 342] nor does it significantly alter predictive risk value in mathematical models of patient mortality.[281, 341] When using hospital discharge data, listed secondary diagnoses can be useful sources of comorbidities and provide data for the calculation of a comorbidity index.[191, 340]

The assessment of the association between the length of stay and postdischarge mortality was limited by the available variables for which the logistic regression model could be adjusted. The effect of length of stay on postdischarge mortality could not be adequately addressed because of limited clinical information that was available. More clinical information on AMI severity, disease history, comorbidities, complications, and medications would have greatly improved the models.

The dataset used for this thesis accounts for most, but not all, AMI events that occurred in England during the study period. It is impossible to estimate the number of AMIs that were not included, but, given the acute nature of the condition, it is unlikely to be a large

number because hospital and mortality statistics would capture such a serious, acute event. Any AMIs that occurred while under private hospital care would not be captured by HES and could not be included in this study; however, these events are likely to represent a very small proportion of all AMIs in England. The vast majority of English private hospitals do not have 24 hours/7 days a week emergency departments nor do they answer the 911 calls or offer ambulance services.

Any migration into or out of England was not accounted for, and may have affected some results, particularly long-term survival rates following AMI. However, comprehensive data on English residents experiencing an AMI overseas simply do not exist – it is a general limitation of population-based research in today's highly migrant world. Individuals from other countries who came to England, had a heart attack, and were treated under the NHS care, were not included because only residents of England, as identified in the HES and ONS records, were counted in this thesis.

Silent AMIs that did not lead to a hospital admission or a death record could not be captured by the available data and thus would not have been included in the study. It is very difficult to estimate how many such silent infarcts occur in England. By definition, silent AMIs could not be identified in the dataset used for this thesis. While some data may exist in general practice records and/or clinical studies, it is unlikely that these data would be representative of the whole population because silent infarcts are usually identified incidentally. An accurate estimate of prevalence of silent infarcts would require a large population-based screening exercise of ECG readings.

Implications of findings

The results of studies presented in this thesis carry a number of research, clinical, and public policy implications. These are now discussed.

Research implications

The most important research implication of this thesis is that linked administrative records can make valuable contributions to epidemiological and health services research. Specifically, record linkage of hospital and death certificate data can be used to estimate mortality, incidence, case fatality, and survival patterns of acute conditions in a population by sex, age group, time, socioeconomic deprivation, and geographic region. This thesis has provided evidence of this using AMI as an example. It has also highlighted that researchers need to undertake thorough cleaning and validation of data fields, have realistic and relevant research objectives, clear case definitions, and apply appropriate methods when using administrative datasets.

Exploratory analyses of the thesis dataset confirmed that the use of a retrospective clearance period to identify first events is a valid and useful approach to studying incidence rates in the absence of information about prior clinical history. This thesis also provides a template for future research for the following methodological approaches, not yet reported in the literature, to perform epidemiological analyses of AMI through routine data: recurrence risk analysis using a competing risk model, as developed by Fine and Gray,[329] to study the risk of a second event, and the MONICA Study statistical approach[3] to explain changes in mortality using changes in event rate and case fatality.

Clinical implications

One of the most important findings for clinicians is that the characteristics of the AMI patient population are changing: in recent years, a higher percentage are women, older patients, and patients presenting with a greater number of comorbidities. This demographic shift implies that AMI patients in the future will likely experience a later onset and require more complex care afterwards, most of which rests with general practice. Because of the older age, and thus more fragile health and a higher risk of adverse outcomes, the careful use of appropriate evidence-based therapies is especially important in this patient population.

Declining event rates suggest that primary prevention is working and should be continued, perhaps even increased. This is an important message for general practice and public health physicians and nurses who deliver most of primary coronary prevention interventions to the population. Declining case fatality rates and shorter hospital stays imply a possible need for more outpatient follow-up and postdischarge care, thus increasing the workload for primary care teams. While this thesis has shown that shorter lengths of stay do not lead to a higher risk of death or recurrence within one year, it is possible that they may lead to other adverse outcomes in the short term and/or a higher risk of death or recurrence in the long term.

The presented studies also provide population-based information on clinical prognosis following AMI. In turn, this can be used to give clinical insights into the likely prognosis at the level of the individual patient. For example, one in three patients will die within 30 days of an AMI. However, of those who survive long enough to be admitted to hospital, only one in six will die within 30 days. Amongst those who survive the first 30 days, around one in three men and one in four women will die within five years after a first

AMI, and around one in eight men and one in six women will experience a second AMI during that time. The risk of death or a second AMI is highest in the year immediately following the initial event. Finally, this thesis confirms that diabetic patients are at a higher risk of adverse outcomes after AMI compared with non-diabetics.

Public policy implications

Estimates of the event rates, case fatality, and mortality rates presented in this thesis can be used to quantify the population-level burden of AMI in England. The estimates of the average annual changes can be integrated into various policy and economic models that focus on predicting the future trends in the occurrence of, and fatality from, AMI and/or CHD. The presented estimates for trends can also be used in health policy planning to monitor population health by sub-groups, geographic regions, and time; to track the performance of any national strategies to improve health care delivery; and to compare progress in England with other countries.

AMI is becoming a disease of older people. As the English population ages, there will be greater numbers of older individuals and thus more total cases of AMI, even if age-specific rates continue to fall. The shift in the occurrence of AMI toward older ages and the ageing underlying population, combined with increasingly better survival, will likely lead to increased prevalence of CHD in England and the need for further preventive efforts, acute treatment, and long term care for individuals with CHD.

Finally, the fact that the majority of fatal AMIs and a substantial proportion of all AMIs are sudden deaths underscores the importance of both primary and secondary prevention. Thus, if decreasing the burden of disease from CHD in terms of new events, mortality, and case fatality is a government priority, control of cardiovascular risk factors in

England is essential to sound public health policy. As Geoffrey Rose famously said, "*It is better to be healthy than ill or dead. That is the beginning and the end of the only real argument for preventive medicine. It is sufficient.*"[343]

Population-level preventive approaches that have been shown to be effective, cost-effective, and politically and financially feasible include: promotion of healthy diets (particularly lowering sodium intake), increasing physical activity, quitting/prevention of smoking, decreasing alcohol consumption, and increasing the use of evidence-based therapies.[344, 345] Government interventions that can be implemented or expanded are: mass-media campaigns and public education; reformulation of food products by industry to reduce the levels of saturated and trans fats, salt, and sugar; taxes on unhealthy foods; food labeling; restrictions on marketing of unhealthy food products to children and adolescents; control of price, promotion, and availability of alcohol and tobacco; and up-to-date and evidence-based clinical guidelines on effective preventive medications.[344, 345]

Future research

To further expand the knowledge base on the epidemiology of AMI in England, more research is required to better understand the drivers behind the declining event, case fatality, and mortality rates, i.e. to elucidate the roles of changes in population risk factor profiles, primary and secondary prevention, and acute medical treatment. Estimates of trends in incidence of first AMI and recurrence of AMI over the last decade still need to be produced. This information would be helpful in further understanding the declining mortality from AMI and formulating public policies to further reduce the burden of this condition in the English population.

Future research also needs to focus on trends over time in long-term survival after AMI. Currently, the NHS Information Centre's Clinical and Health Outcomes Knowledge base, generated by the National Centre for Health Outcomes Development (NCHOD), only provides indicator information on 30-day case fatality after operation or admission for AMI,[12] yet with current technological advances, survival over a longer period of time might be a better indicator for quality of care.

To improve patient care, more research is needed to investigate the factors that determine the length of hospital stay for AMI patients in England and the association between length of stay and health outcomes other than postdischarge mortality. Exploration of health outcomes in AMI survivors beyond risk of death and reinfarction would provide further insight into the prognosis and quality of life of patients after AMI.

Research projects in England that use record linkage would greatly benefit from additional clinical and pharmaceutical information that can be obtained by linking HES and ONS records to other datasets, such as general practice clinical records and prescription databases. This would greatly enhance the explanatory potential of the data by providing more relevant variables.

More generally, to underpin the recent focus on health service performance that emphasises clinical outcomes in the UK,[335] it is increasingly important that health outcomes for many diseases are routinely and reliably measured on a national level. Statistics such as the ones presented in this thesis, based on record linkage, can be produced on a routine basis for a wide range of diseases. Nowadays, the data exist, record linkage is possible, the data processing technologies are cheap, and reliable information on population health and health care can become readily available.

[12] Online datasets for a variety of indicators, including those for AMI, can be accessed at www.nchod.nhs.uk

Conclusion

This thesis provides recent national-level population-based data on the changing AMI epidemiology in England from 1999 to 2007. The findings indicate substantial reductions in mortality and event rate and improvements in short-term survival over the last decade. Approximately half of the observed decline in AMI mortality in England can be attributed to a reduction in event rate and half to improved 30-day survival. These declines were driven by improvements in primary and secondary prevention and acute medical treatment, and the findings presented in this thesis reinforce the importance of both prevention and treatment in reducing AMI morbidity and mortality.

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APPENDIX 1: DATA SOURCES

Hospital Episode Statistics (HES)

The HES system was established in 1987 and data are available for each financial year from 1989-90 onwards. The HES data warehouse is managed by the NHS Information Centre for Health and Social Care on behalf of the Secretary of State for Health. The processing of HES data is carried out by the HES staff at Northgate Information Solutions. In brief, patient clinical and administrative data are collected directly by healthcare providers commissioned by the NHS and submitted to a central collection point called the Secondary Uses Service, which sends the data to the HES team for validation and cleaning at the HES Data Warehouse. Once the data are processed and cleaned, it becomes available to users (academics, government employees, or anyone else who has applied for and received permission to access the data). All complete HES records are compiled into annual datasets based on English financial years, meaning each starts on April 1st and ends on March 31st.

HES comprises three datasets: admitted patient data, including all hospital in-patient and day case admissions; outpatient data; and accident and emergency department data (the latter available for 2007-08 only; still in the experimental stage). Currently, over 12 million in-patient records are collected each year, which include all hospital in-patient and day case admissions. The admissions encompass all public and private patients treated in NHS trusts in England and those funded by the NHS but carried out at non-NHS external providers of care.

HES information is stored as a large collection of records for each period of care. The main unit of recording is the Finished Consultant Episode (FCE), which is defined as a continuous period of time spent by a patient under the care of a particular consultant or allied healthcare professional at a single healthcare provider.[m] Each FCE record contains over 50 distinct items of data, including the patient's clinical information about diagnoses and procedures as well as consultant and specialty; demographic information such as age, sex, ethnic category, and deprivation score; administrative information on dates, method and source of admission and discharge as well as waiting time and length of stay; and geographical information on the area of residence and area of treatment.

A transfer between consultants or providers generates a new record, i.e. another FCE. As such, a continuous period of hospital care may include more than one FCE record. Using NHS numbers and other identifying fields, FCEs can be combined into continuous in-patient admissions to generate the total continuous period of time that a patient spends under NHS-commissioned hospital care. The more advanced databases have the capacity to link HES records over multiple years, enabling long term follow up of patients.

Diagnoses in HES are coded according to the International Classification of Diseases, 10th revision (ICD-10), which is substantially different from the previous ICD-9. For AMI, the ICD-9 code of 410 has been split into I21 for an implied first-ever AMI and I22 for subsequent AMI (by ICD definition an AMI occurring at least four weeks after any previous AMI. The HES system implemented ICD-10 coding of diagnoses in 1995.

Clinical diagnoses, as recorded in medical notes, are translated into ICD-10 codes by trained clinical coders. The main discharge diagnosis, found in the first diagnostic

[m] HES Data Dictionaries gives several types of healthcare providers: NHS foundation trust; independent sector provider; primary care trust, NHS trust or a treatment centre at independent sector provider site or at NHS trust site.

position and assigned at the end of each FCE, is defined by HES as the main reason why the patient was admitted to hospital.[n] The main diagnostic code is assigned at the end of each FCE. Secondary diagnoses describe other conditions relevant to the admission, and may include conditions that patients may have at the time of admission (co-morbidities) or that arose during their stay (in-hospital complications).[o]

HES records include information about deaths but only for those patients who died during their hospital stay not for those who died after hospital discharge. This field has been shown to be a reliable source of in-hospital deaths, which is recorded as "dead" in the discharge method.[p] However, one limitation is that HES does not capture the cause of death, which might be different from patient's main diagnosis. Another limitation is that deaths that occur prior to a formal hospital admission (for example, in the ambulance or in the emergency department very soon after arrival) or after discharge from hospital are not recorded in HES. Using identification numbers, HES can be linked to the mortality data available from the Office for National Statistics (ONS), which does contain information available from death certificates, including the underlying cause and contributing causes of death.

Office for National Statistics

The ONS was established in 1996 as the custodian of all mortality data for England and Wales (prior to this it was the Office of Population Censuses and Surveys). Legal

[n] Health and Social Care Information Centre. Hospital Episode Statistics: User Guide. 2009.

[o] NHS Information Centre. HES Data Dictionary. Available from: http://www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=571

[p] Murray G, Lawrence A, Boyd J. Linkage of hospital episode statistics (HES) data to Office for National Statistics (ONS) mortality records. Bristol Royal Infirmary Inquiry. 2000.

registration of deaths has been a requirement in England and Wales since 1837, and doctors have been required to certify the cause of death for their patients since 1841. ONS mortality data are collected when a death is registered. Information on the causes of death is obtained from the death certificate completed by either the attending doctor or coroner. Like HES, the ONS system uses ICD-10 codes for all causes of death mentioned on the death certificate.[q] Much of the ONS coding has been performed using automated coding software that was introduced in 1993. The current software is called Medical Mortality Data Software and was developed in the United States (US).[r] The software is rigorously tested on a regular basis and any identified errors are reported back to the US. These errors are bypassed in the ONS system and the correct code is allocated manually by more experienced coders who have passed an international exam on cause of death coding techniques.[s]

Using ICD rules or WHO rules, conditions mentioned on the death certificate are coded by ONS as the underlying cause and as contributory causes. English mortality statistics are based on the underlying cause of death, defined by WHO as "a) the disease or injury which initiated the train of morbid events leading directly to death, or b) the circumstances of the accident or violence which produced the fatal injury."[t] In most cases, the condition considered the underlying cause of death has been entered in the appropriate line on the death certificate and can be used as recorded for the ONS dataset.[u]

[q] 10th version of the ICD was used since 2001; prior to that, 9th version of the ICD was used.

[r] ICD-10 specific software is provided by the National Center for Health Statistics in the USA.

[s] Office for National Statistics. Personal communication. 2011.

[t] World Health Organisation. International Statistical Classification of Diseases and Related Health Problems, Tenth Revision. Volumes 2: Instruction Manual. WHO. 1992.

[u] Rooney C, Smith S. Implementation of ICD-10 for mortality data in England and Wales from January 2001. Health Statistics Quarterly. 2000; 8: 41-51.

In circumstances when the death certificate was not completed correctly, selection rules for the underlying cause must be applied, as set out by the ICD rules.

Following selection rules, modification rules, which are also defined in ICD, are then applied to particular conditions, combinations or circumstances in order to improve the quality of data in a systematic way. For example, several conditions can be combined to form a composite underlying cause; a specific condition may be chosen over that which is mentioned first but is also broader or more vague (e.g. myocardial infarction over coronary heart disease); and certain poorly recorded or trivial conditions may be ignored. For myocardial infarction, the vast majority of deaths are assigned to ICD-10 code I21.9 (acute myocardial infarction, unspecified), because often not enough information is written on the death certificate to code a more specific type.

APPENDIX 2: RECORD LINKAGE METHODOLOGY

A brief overview

In simple terms, record linkage means the bringing together of multiple records from different data sources that relate to the same individual and/or event. The idea behind record linkage is that several items of data collected for the same individual at different times and/or in different places have a larger informative value than the same items considered separately. Record linkage is particularly important for routine administrative data, which is often structured and stored as a series of distinct records without any groupings of records that relate to the same individual or event. Without linkage, routine data are limited and can only be used to answer a narrow range of questions. Record linkage, on the other hand, enhances the data and facilitates its use for research purposes on a range of topics, including epidemiologic and health services research.

In England, the first medical record linkage system was established by Sir Donald Acheson in 1962 and became known as the Oxford Record Linkage Study (ORLS). ORLS is currently managed by the Unit of Health-Care Epidemiology (UHCE) at the Department of Public Health, University of Oxford. A number of other countries have similar systems, such as the Scottish Record Linkage System, the Western Australia Data Linkage System, the Swedish Demographic Database, the British Columbia Linked Health Database in Canada, and the Rochester Epidemiology Project in the United States.

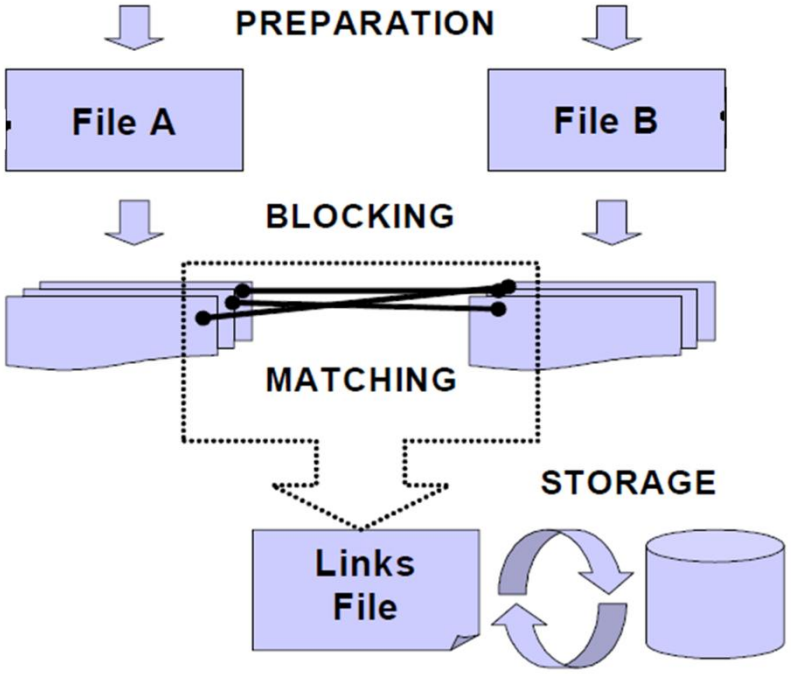
In 2003, the UHCE was commissioned by the Department of Health to build a national linked file of hospital and mortality records nationwide for England, using the matching

and linkage approaches that are based on principles and methods used in the ORLS.[v] The initiative was a success and UHCE continues to perform linkage of administrative hospital and mortality data from Hospital Episode Statistics (HES) and Office for National Statistics (ONS) on HES and ONS datasets to present day. The process of data linkage by the UHCE staff involves the following key steps (see Figure 1):

1. **Data preparation**: Data cleaning, such as correcting invalid or missing values; removing duplicates; putting the data into the right format; compressing long fields; defining and grouping certain variables; and general file exploration.
2. **Record blocking**: Sorting the files into blocks that share the same identifiers, such as NHS number, date of birth, sex, and postal code. Blocks can be simple, i.e. based on one identifier (e.g. NHS number) or compound, i.e. based on a combination of identifiers (e.g. sex and date of birth and postal code). This step is done in order to increase the efficiency of the matching process.
3. **Matching**: Identifying records within the same block that belong to the same individual. Each record is systematically compared with all other "candidate" records within the block and probability matching techniques are used to determine whether the two records belong to the same person.
4. **Linking**: Bringing together matched records that were identified as relating to the same individual during the matching step. The records are grouped together, usually in a chronological order, as a composite record that relates to one particular individual. Validation and correction of the linkage is a very important component of this step, such as checking for internal consistency of records belonging to the same individual.

[v] Gill L, Goldacre M. English national record linkage of Hospital Episode Statistics and death registration records. National Centre for Health Outcomes Development, Unit of Health-Care Epidemiology, University of Oxford 2003.

Figure 1. Steps involved in record linkage



Adapted from: Holman, D'Arcy. Introductory Analysis of Linked Health Data: a short course workbook. 2009.

Data matching is the most important step and will now be described in more detail. Unique identifiers that are used to bring records together may differ between records that genuinely belong to the same individual because of human errors in data recording. For this reason, probabilistic matching technique was used by UHCE staff in linking the data used in this thesis – to allow for some variation of key identifying variables between records. Using this approach, it is not necessary for all unique identifiers to match perfectly; records are brought together if the probability of them belonging to the same individual is above a certain threshold level. This threshold level is derived from a complex combination of decision rules that are built into the algorithm in the software package that performs the linkage.

APPENDIX 3: THESIS-RELATED WORK

Presentations and papers arising from this thesis

Smolina K, Wright L, Rayner M, Goldacre M. The determinants of the decline in mortality from acute myocardial infarction in England between 2002 and 2010: a linked national database study. *[BMJ 2012;344:d8059]*

Smolina K, Wright L, Rayner M, Goldacre M. Incidence and 30-day case fatality for acute myocardial infarction in England in 2010: national linked database study. *[Published in the European Journal of Public Health, PMID: 22241758]*

Smolina K, Wright L, Rayner M, Goldacre M. Five-year survival and outcomes following first and recurrent acute myocardial infarction in England, 2003-2007. *[Manuscript submitted]*

Smolina K, Wright L, Rayner M, Goldacre M. Acute myocardial infarction: incidence and 30-day case fatality in England for first and recurrent events. *Journal of Epidemiology and Community Health.* 2011; 65(S1):A314. Presented at the World Congress of Epidemiology. August 7-11th, 2011, Edinburgh, UK. *[Poster]*

Smolina K. The value of linked hospital and mortality statistics for population health and health services research. *Revistae Salud,* 2011; 7(26). Presented at the International Forum on Health Care and Information Communication Technology. March 8-10th, 2011, Barcelona, Spain. *[Oral presentation]*

Scarborough P, Bhatnagar P, Wickramasinghe K, **Smolina K**, Mitchell C and Rayner M. Coronary Heart Disease Statistics. 2010. London: British Heart Foundation.

Scarborough P, Bhatnagar P, Kaur A, **Smolina K**, Wickramasinghe K, and Rayner M. Ethnic Differences in Coronary Heart Disease. 2010. London: British Heart Foundation.

BMJ

BMJ 2012;344:d8059 doi: 10.1136/bmj.d8059 (Published 25 January 2012)

RESEARCH

Determinants of the decline in mortality from acute myocardial infarction in England between 2002 and 2010: linked national database study

OPEN ACCESS

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Abstract

Objective To report trends in event and case fatality rates for acute myocardial infarction and examine the relative contributions of changes in these rates to changes in total mortality from acute myocardial infarction by sex, age, and geographical region between 2002 and 2010.

Design Population based study using person linked routine hospital and mortality data.

Setting England.

Participants 840 175 people of all ages who were admitted to hospital for acute myocardial infarction or died suddenly from acute myocardial infarction.

Main outcome measures Acute myocardial infarction event, 30 day case fatality, and total mortality rates.

Results From 2002 to 2010 in England, the age standardised total mortality rate fell by about half, whereas the age standardised event and case fatality rates both declined by about one third. In men, the acute myocardial infarction event, case fatality, and total mortality rates declined at an average annual rate of, respectively, 4.8% (95% confidence interval 3.0% to 6.5%), 3.6% (3.4% to 3.7%), and 8.6% (5.4% to 11.8%). In women, the corresponding figures were 4.5% (1.7% to 7.1%), 4.2% (4.0% to 4.3%), and 9.1% (4.5% to 13.8%). Overall, the relative contributions of the reductions in event and case fatality rates to the decline in acute myocardial infarction mortality rate were, respectively, 57% and 43% in men and 52% and 48% in women; however, the relative contributions differed by age, sex, and geographical region.

Conclusions Just over half of the decline in deaths from acute myocardial infarction during the 2000s in England can be attributed to a decline in event rate and just less than half to improved survival at 30 days. Both prevention of acute myocardial infarction and acute medical treatment have contributed to the decline in deaths from acute myocardial infarction over the past decade.

Introduction

Declines have been observed in population based mortality rates from coronary heart disease and acute myocardial infarction in many developed countries, including England, since the 1970s.[1 2] For any given condition, the mortality rate in a population is a function of the event rate and case fatality rate. Several studies have investigated the drivers of the decline in mortality from coronary heart disease. The most notable is the World Health Organization's Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) project, which examined trends in mortality rates, event rate, and one month case fatality in men and women aged 35-64 from 38 populations in 21 countries over 10 years, from 1985-7 to 1995-7. The MONICA study found that, between the mid-80s and mid-90s, two thirds of the decline in mortality from coronary heart disease in people aged less than 65 years could be attributed to the decline in coronary event rate and one third to the decline in case fatality.

Studies from the MONICA centres showed that the relative contributions of event rate and case fatality to the decline in mortality from coronary heart disease vary by region and country. The MONICA populations in the United Kingdom were Glasgow and Belfast—there was no English population. The relative contributions of event rate and case fatality for acute myocardial infarction to the observed decline in mortality from acute myocardial infarction have not been studied for England. Routinely collected national hospital and mortality data can be informative. However, data linkage is necessary to undertake a systematic analysis of the occurrence of person based disease from routine national statistics. Since 1998 it has been possible to link routinely collected hospital and mortality data for the entire population of England. Using such a linked dataset, we report trends in event rate and case fatality for acute myocardial infarction and examine the relative contributions of

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Incidence and 30-day case fatality for acute myocardial infarction in England in 2010: national-linked database study

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Background: There are limited national population-based epidemiological data on acute myocardial infarction (AMI) in England, making the current burden of disease, and clinical prognosis, difficult to quantify. The aim of this study was to provide national estimates of incidence and 30-day case fatality rate (CFR) for first and recurrent AMI in England. **Methods:** Population-based study using person-linked routine hospital and mortality data on 79 896 individuals of any age, who were admitted to hospital for AMI or who died suddenly from AMI in 2010. **Results:** Of 82 252 AMI events in 2010, 83% were first. Age-standardized incidence of first AMI per 100 000 population was 130 (95% CI 129–131) in men and 55.9 (95% CI 55.3–56.6) in women. Age-standardized 30-day overall CFRs including sudden AMI deaths for men and women, respectively, were 32.4% (95% CI 32.0–32.9) and 30.3% (95% CI 29.8–30.9) for first AMI and 29.7% (95% CI 28.7–30.7) and 26.7% (95% CI 25.5–27.9) for recurrent AMI. Age-standardized hospitalized 30-day CFR was 12.0% (95% CI 11.6–12.3) for men and 12.3% (95% CI 11.9–12.7) for women. **Conclusions:** While the majority of AMIs are not fatal, of those that are, two-thirds occur as sudden AMI deaths. About one in six of all AMIs are recurrent events. These findings reinforce the importance of primary and secondary prevention in reducing AMI morbidity and mortality.

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Poster session 2

Chronic disease

P2-333 Acute myocardial infarction: incidence and 30-day case fatality in England for first and recurrent events

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Author Affiliations

Abstract

Introduction There are several population-based English studies of AMI, but they are local rather than national, do not necessarily distinguish first events and re-infarctions, and are out of date. Our objective was to study AMI incidence and 30-day case fatality rates (CFRs) for first and recurrent events in England in 2007 (population 51.8 million).

Methods Analysis of linked routine national hospital and mortality data, with an 8-year washout period to identify people who already had a prior event, in order to distinguish whether each AMI in 2007 was first or recurrent.

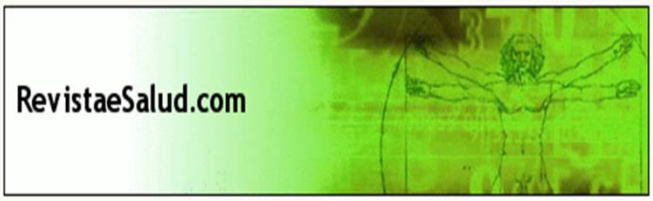
Results Of 88 311 AMI events in 2007, 86% were first events. Age-standardised incidence of first AMI (per 100 000 person years) was 151 (150–152) in men and 64 (63–65) in women. Age-standardised 30-day overall CFRs including sudden deaths without hospitalisation for first AMI were 35.5% (35.1–36.0) and 34.4% (33.3–35.4) in men and 34.4% (33.9–35.0) and 31.0% (29.8–32.3) in women, for first AMIs and re-infarctions, respectively. Age-standardised 30-day hospitalised CFRs were much lower at 14.5% (14.1–14.9) and 14.1% (13.2–15.0) in men and 15.2% (14.7–15.7) and 13.9% (12.8–15.0) in women for first AMIs and re-infarctions, respectively.

Conclusions This study provides, for the first time, total national-level population-based estimates of first and recurrent AMI as well as overall AMI incidence and case fatality in England. It holds informative value in better understanding AMI epidemiology and prognosis that should prove useful to practitioners and policy makers.

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THE VALUE OF LINKED HOSPITAL AND MORTALITY STATISTICS FOR POPULATION HEALTH AND HEALTH SERVICES RESEARCH. UNIT OF HEALTH-CARE EPIDEMIOLOGY

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Introduction:

With the ageing population and the spiralling healthcare costs in many countries around the world, it is becoming increasingly essential to have access to up-to-date and representative public health data in order to evaluate the health of the population and to plan and monitor healthcare spending effectively.

Aims:

This workshop will discuss the advantages and limitations of using linked electronic hospital and mortality records for epidemiological and health service research purposes. It aims to increase understanding of the opportunities provided by information technology, such as large linked administrative databases, to study disease pathways, social determinants of health, geographical distribution, ethnic differences, and patient health outcomes on population level.

Methods:

Population-based retrospective cohort study of the disease burden and health outcomes in individuals who experienced a heart attack in England between 1998 and 2008 using a large linked dataset of millions of hospital and mortality records.

Results:

Several examples of insights into population health derived from linked data are covered, including the latest and the only national-level data on incidence, case fatality, hospital utilization, geographical distribution and ethnic inequalities of first and recurrent heart attacks in England. The obtained results stand up to previous cohort studies done in the UK and other countries, thus supporting national hospital and mortality statistics as a valuable research resource for public health data.

Conclusions:

Thorough data cleaning and validation, accompanied by realistic and relevant research objectives, clear case definitions, and appropriate methodology may offer great potential for the research findings using linked electronic records and modern computational technology to make valuable contributions to health evaluation, health services management, and health policy.