Sex differences in survival in patients with a hospital admission for acute myocardial infarction in Scotland 1990-2000

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ABBREVIATIONS

AMI	Acute myocardial infarction
CHD	Coronary heart disease
PVD	Peripheral vascular disease
CVD	Cardiovascular disease
CVA	Cerebrovascular accident
COPD	Chronic obstructive pulmonary disease
TIA	Transient ischaemic attack
WHO	World Health Organisation
ECG	Electrocardiograph
CK-MB	Creatine kinase (MB isoenzyme)
MONICA	Multinational Monitoring of Trends and Determinants of Cardiovascular Disease
ISIS	International Study of Infarct Survival
GISSI	Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico
GUSTO	The Global Use of Strategies to Open Occluded Coronary Arteries
OPTIMAAL	Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan
NHANES	National Health and Nutrition Examination Survey
REGICOR	Registre Gironi del Cor, Gerona Heart Registry
TRACE	The Trandolapril Cardiac Evaluation Study
SPRINT	Secondary Prevention Reinfarction Israeli Nifedipine Trial
EPESE	Established Populations for Epidemiologic Studies of the Elderly
OXMIS	Oxford Myocardial Infarction Incidence Study
OMID	Ontario Myocardial Infarction Database
MITRA	Maximum Individual Therapy in Acute Myocardial Infarction
MIR	Myocardial Infarction Registry
ARIC	Atherosclerosis Risk in Communities Study
TIMI	Thrombolysis in Myocardial Infarction
CIBIS	The Cardiac Insufficiency Bisoprolol Study
SAVE	Survival and Ventricular Enlargement Trial.
AIRE	Acute Infarction Ramipril Efficacy Study

SUMMARY

Background

Acute myocardial infarction (AMI) is an important cause of morbidity and mortality in men and women. Much of the existing literature has either focussed on men or has examined men and women together. There is a growing evidence to suggest that men and women represent distinct entities in terms of the epidemiology of AMI. This study therefore aims to examine and compare the baseline characteristics, burden of disease and survival of men and women hospitalised between 1990 and 2000 following a first and second AMI and also to determine factors that influence survival in men and women.

Methods

The Scottish Linked Morbidity Record Database was used to identify all patients hospitalised with a first and a second AMI between 1990 and 2000. Baseline characteristics including demographics, comorbid diagnoses and the burden of disease (including incidence, length of stay and revascularisation rates) were examined in men and women. Sex specific case fatality was calculated at a number of time points from 30 days to five years. Multivariate modelling was then used to examine factors affecting prognosis in different age groups and determine trends over time in men and women separately.

Results

Between 1990 and 2000, a total of 110,226 individuals were hospitalised with a first AMI (41% women) and 9,664 individuals (40%) were hospitalised with a second AMI. Comorbid diagnoses were coded in almost half of all men and women with a first AMI and two thirds of those with a second AMI.

Between 1990 and 2000, first AMI incidence declined by about one half in men and by one third in women whilst hospitalisation rates for second AMI halved. Thus, burden of disease (incidence and length of stay) fell whilst revascularisation rates increased.

Unadjusted short and longer term survival was greater in men than in women. After adjusting for age and other factors women with a first AMI fared worse than men in the short term but better than men in the longer term. Short term sex differences were restricted to younger age groups. In the multivariate analyses men and women had similar short and longer term outcomes following a second AMI.

Between 1990 and 2000, short term case fatality declined by approximately half in men and by one third in women over the study period. These improvements were more evident following a first AMI and in younger age groups.

Conclusions

Younger women hospitalised with a first AMI have high levels of comorbid disease and a worse short term prognosis than men. However women fare better than men in the longer term. Sex differences are not apparent in survival following a second AMI. This may reflect differences in treatment and in secondary prevention, and merits further research.

1 INTRODUCTION

This thesis will examine sex differences in the baseline characteristics, survival and National Health Service burden of individuals hospitalised with a first and second acute myocardial infarction (AMI) in Scotland. It will define a research question, review the relevant literature and report the results of a study examining sex differences in baseline characteristics and survival in patients with a first and second acute myocardial infarction in Scotland between 1990 and 2000.

1.1 Acute Myocardial Infarction

Acute myocardial infarction (AMI) is a major public health problem, especially in developed countries with ageing populations. Acute myocardial infarction is an important cause of mortality and morbidity. Mortality rates attributable to AMI depend on both incidence and case-fatality.[1] Although case-fatality has declined over the past two decades, it remains high and approximately 50% of individuals die within an hour of onset.[2] Consequently, a large proportion of people do not even reach hospital so that the potential impact of treatment on population mortality rates is limited. Mortality rates from coronary heart disease have also declined significantly in most developed countries.[1] The relative contributions of changing incidence and case-fatality to this decline have been examined but are not clearly understood.

Coronary heart disease has traditionally been considered to be more common in men than in women. However, whilst onset of disease is often later in women, coronary heart disease still accounts for approximately one fifth of all deaths in Scottish women.[3] In 2002, coronary heart disease accounted for 22.3% and 18.1% of all deaths in men and women respectively. In individuals aged less than 65 years, these figures were 18.5% and 10.3%.[3]

1.2 Definition of acute myocardial infarction

Acute coronary syndrome

Acute coronary syndrome refers to a range of acute myocardial ischaemic conditions that share a common underlying pathophysiological mechanism.[4] This includes ST segment elevation AMI, non-ST segment elevation AMI and unstable angina.

Changing terminology

An acute myocardial infarction results in prolonged ischaemia and subsequent death of cardiac myocytes[5] Almost all acute myocardial infarctions result from coronary atherosclerosis. Defining acute myocardial infarction is not simple and the definition can arise from a number of different perspectives, according to clinical, biochemical, pathological and electrocardiographic (ECG) characteristics. In the past, there was a general consensus for the meaning of the term 'acute myocardial infarction.' This consensus was based on the World Health Organisation (WHO) definition which required the presence of two of the following three features: symptoms of myocardial ischaemia for more than 20 minutes, significant cardiac enzyme rise and typical ECG changes[5] This basic system was widely used but variably interpreted, resulting in a lack of comparability within and between studies.

Development of new, more sensitive tests, such as cardiac troponins and creatine kinase (CK) - MB mass, have meant that it is now possible to identify patients who have had very small infarcts, that would not previously been considered an AMI. This means that people who were formally given a diagnosis of angina pectoris might today be diagnosed as having had an AMI.

The availability of new more sensitive technologies shed doubt on the validity of the WHO definition. A consensus conference was therefore convened by the European Cardiac Society and the American College of Cardiology in order to examine the definition of AMI. The report published by this committee in 2000 was intended to give guidance to clinicians faced with new diagnostic methods and scientific literature.[5]

The new definition requires documentation of a rise and fall in troponin or CK-MB as well as ischaemic symptoms or coronary intervention (Table 1). The previous definition allowed a diagnosis to be made on the basis of serial ECG changes alone, or a combination of symptoms and 'probable' ECG changes and /or abnormal plasma enzymes.

Table 1 Definition of acute myocardial infarction

	OLD: DEFINITE ACUTE MYOCARDIAL INFARCTION
1	Definite ECG or
2	Symptoms typical or atypical or inadequately described, together with probable ECG or abnormal enzyme, or
3	Symptoms typical with abnormal enzymes with ischaemic or non-codable ECG or ECG not available, or
4	Fatal case, whether sudden or not, with naked eye appearance of fresh myocardial infarction and /or recent coronary occlusion found at necropsy
	New: either one of the following criteria satisfies the diagnosis for an acute, evolving or recent MI
1	Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:
a	Ischaemic symptoms;
b	Development of pathological Q waves on the ECG;
c	ECG changes indicative of ischaemia (ST segment elevation or depression); or
d	Coronary artery intervention (coronary angioplasty)
2	Pathological findings of an acute MI

Implications of the new definition of myocardial infarction

The redefinition of myocardial infarction has implications for individuals, for clinical practice and for the study of the epidemiology of AMI. It is estimated that the new definition for AMI will increase the number of non-ST elevation acute coronary syndromes by about 40%.[6] This lower diagnostic threshold will impact upon patients and their families and has implications for issues such as employment and health insurance. The new definition of AMI has not yet been adopted by all clinicians,[6] and it is likely to take some time before the new diagnostic criteria are universally incorporated into clinical practice. In theory, widespread use of a standardised definition should allow more valid epidemiological comparisons between different populations and within populations over time.

The new definition has been criticised and there are concerns that it is 'not applicable to more than a proportion of coronary events in the real world'.[7] One of the main concerns is that it requires documentation of a rise and fall of troponin or CK-MB, which is not always available. The criteria therefore do not cover early and other fatal cases or non-fatal cases where tests are incomplete, delayed or missing.

The impact of the redefinition of AMI on the recorded incidence of AMI is not clear. It has been suggested that it may lead to an underestimation of disease incidence, because of the likelihood of missing biochemical data and relatively high proportion of fatal cases[8] Alternatively, lowering the diagnostic threshold could increase the reported incidence of AMI.[6]

1.3 Pathophysiology of acute myocardial infarction

Almost all AMIs occur as a result of coronary atherosclerosis, usually with superimposed coronary thrombosis. Atherosclerosis is thought to begin in childhood as deposits of cholesterol and fatty streaks in the intima of arteries.[9;10] Aortic fatty streaks are believed to develop first, though there appears to be little or no relationship between aortic fatty streaks and clinically important atherosclerotic lesions.[9] Fatty streaks begin to appear in the coronary arteries approximately five to ten years later than in the aorta.[9] Over time, more lipid may accumulate and become covered in a fibromuscular cap to form a fibrous plaque. It would seem therefore that in some individuals, juvenile fatty streaks in the coronary arteries progress to advanced atherosclerotic lesions within a few decades. Rupture or fissuring of the fibrous plaques results in platelet aggregation and thrombus formation and can lead to an acute coronary event. Exposure of constituents of the plaque such as lipid, smooth muscle and foam cells, leads to the production of thrombin and fibrin which promotes platelet aggregation and formation of thrombus.[11] In AMI, occlusion of the coronary artery is usually more complete than in unstable angina. ST segment elevation AMI is usually associated with red, fibrin-rich and occlusive thrombus. Unstable angina and non-ST elevation AMI are closely related conditions which may be undistinguishable in their clinical presentation. The difference between them depends upon whether the ischaemia is severe enough to cause myocardial necrosis as demonstrated by release of cardiac markers, especially cardiac troponin I and T.[12]

1.4 Clinical presentation

Ischaemic symptoms include chest, epigastric, arm, or jaw discomfort associated with exertion or occurring at rest. The pain associated with AMI usually lasts at least 20 minutes but may be shorter in duration. The pain may develop in the arm, epigastrium, shoulder, wrist or jaw but not in the chest, though this is unusual. The pain is not made worse by movement or inspiration. Other symptoms include nausea and vomiting, shortness of breath, weakness, dizziness or syncope. The pain may not be severe, especially in the elderly, in whom other symptoms may predominate. AMI may also occur without symptoms, an unrecognised AMI. Evidence of unrecognised AMI can be demonstrated on serial ECG or autopsy. Unrecognised AMIs are thought to account for between 20% and 40% of all AMIs and as such represent a significant public health problem.[13-15] In terms of examination, there are no specific physical signs that are diagnostic of AMI. Patients may have evidence of autonomic nervous system activation such as sweating and pallor and hypotension. Other features may include pulse irregularities and a third heart sound or evidence of heart failure.

1.5 Management of Acute Myocardial Infarction

Management of acute myocardial infarction has changed considerably over the last decade. Accurate, rapid diagnosis and early risk stratification of patients presenting with chest pain are essential in order to identify those patients in whom early interventions can improve outcome.[12] Initial management of patients therefore involves an assessment of risk and triage into different risk categories. Risk assessment is a continuous process and its primary aim is to identify or exclude life-threatening conditions such as myocardial infarction and unstable angina.[16] Initial management of AMI with ST-segment elevation differs from that of AMI without ST-segment elevation because of the presence of occlusive thrombus.

1.5.1 Diagnosis and early risk stratification

Early diagnosis and risk stratification of individuals presenting with acute chest pain is important to identify those individuals who are likely to benefit from early intervention.[12] Assessment of patients with suspected acute coronary syndrome is based on three criteria: clinical symptoms, electrocardiographic findings and measurements of biochemical markers.[16] Clinical symptoms include a history of severe, ischaemic chest pain lasting 20

minutes or more and not responding to nitroglyerine. An electrocardiogram (ECG) should be obtained as soon as possible and is rarely normal, even in the early stages of AMI.[16] ST segment elevation or new left bundle branch block would be an indication for immediate reperfusion therapy.[12] The majority of patients with ST segment elevation ultimately develop a Q-wave AMI whilst only a minority develop a non-Q wave AMI. The ECG often takes time to evolve and may be equivocal in the early hours. ECG monitoring should be initiated early to detect arrhythmias. Blood sampling for biochemical markers is routinely done in the acute phase. Cardiac troponin I and T are the preferred markers as they are more specific and reliable than creatine kinase or its isoenzyme creatine kinase MB. Cardiac troponin has nearly absolute myocardial tissue specificity as well as high specificity. Two dimensional echocardiography and perfusion scintigraphy may be helpful to exclude myocardial infarction.

1.5.2 Pre-hospital or early in-hospital care

General treatment measures

Analgesia is important in the management of AMI, for pain relief and also to reduce sympathetic activation. A wide variety of analgesic agents have been used to treat the pain associated with AMI, but morphine remains the drug of choice. Oxygen should also be administered, especially if the patient is breathless or in shock.

Aspirin

Aspirin is effective and is therefore indicated across the entire spectrum of acute coronary syndromes. Aspirin forms part of the initial management strategy of patients with suspected AMI. The aim of aspirin treatment is to prevent formation of thromboxane A_2 in platelets by cyclooxygenase inhibition, and therefore inhibit platelet aggregation[17] Convincing evidence of the effectiveness of aspirin was demonstrated by the ISIS-2 trial, in which it was shown that the benefits of aspirin and streptokinase were additive.[18] Aspirin should be given to all patients with an AMI as soon as possible after the diagnosis is thought probable.[12]

Nitrates

Nitrates increase coronary blood flow by coronary vasodilation and decrease ventricular preload by increasing venous capacitance. A meta-analysis of ten trials of early intravenous nitrate therapy showed an apparent mortality reduction.[19] However each of the

trials was small and subsequent studies including GISSI-3 and ISIS-4 failed to show any significant reduction in mortality.[20;21] The routine use of nitrates in the initial phase of myocardial infarction is not therefore recommended unless there is ongoing chest pain or evidence of coronary vasospasm[12]

Beta adrenoceptor blockers

Beta adrenoceptor blockers relieve pain, reducing the need for analgesics, and reduce infarct size and the incidence of fatal arrhythmias. Many trials of intravenous beta-blockade have been done in the acute phase of AMI because of these potential effects. Pooling of 28 trials of intravenous beta-blockade showed a significant reduction in mortality at seven days.[22] However, these studies were carried out before the use of fibrinolysis and studies carried out since the widespread use of fibrinolysis do not support the routine early intravenous use of beta blockers.[23;24] The American College of Cardiology recommends that it is reasonable to administer intravenous beta blockers in the acute phase of infarction but their use in the immediate treatment of AMI is very low in most countries[25] Oral beta blockers are commonly prescribed after the first 24 hours to patients without contraindications as part of secondary prevention.

Reperfusion therapy

It is recommended that all ST elevation AMI patients should undergo rapid evaluation for reperfusion therapy and have a reperfusion strategy implemented quickly.[12;25] AMI is a dynamic process that does not occur instantly but evolves over a period of hours. Persistent thrombotic occlusion is present in the majority of patients with ST elevation AMI whilst the myocardium is undergoing necrosis.[17] There is evidence to suggest that rapid restoration of flow in the obstructed infarct artery is an important determinant of short and longer term outcome following AMI, and most benefit is seen in those treated soonest after the onset of symptoms.[26;27] An occluded artery can be opened by two main methods; administering of a thrombolytic or fibrinolytic agent or by primary percutaneous transluminal coronary angioplasty.

Thrombolysis

Thrombolysis is the commonest reperfusion method used in ST segment elevation AMI, and there is a substantial body of evidence regarding the benefits of its use. For patients within 12 hours of the onset of symptoms, the overall evidence for the benefit of fibrinolytic treatment is overwhelming.[12] The Fibrinolytic Therapy Trialist' analysis

showed that approximately 20 deaths are prevented per 1000 patients treated who present with ST segment elevation AMI within six hours of symptom onset.[28] The ISIS-2 study demonstrated the important additional benefit of aspirin, with a combined reduction of approximately 50 lives per 1000 patients treated.[18] Overall the largest absolute benefit is seen in patients with the highest risk. Streptokinase is the most commonly used thrombolytic agent, though the choice of fibrinolytic agent will depend on an individual assessment of risk and benefit as well as availability and cost.

Primary angioplasty

Results of some randomised clinical trials have shown better clinical outcomes in patients receiving mechanical reperfusion than in those receiving pharmacological reperfusion.[29;30] Primary angioplasty mechanically disrupts the occlusive thrombus and compresses the underlying stenosis, thereby restoring blood flow.[11] A metaanalysis of 23 randomised trials showed a 27% reduction in short term mortality when primary angioplasty was compared to fibrinolytic therapy.[30] Primary angioplasty was also associated with a lower incidence of myocardial infarction, stroke and intracranial haemorrhage when compared to fibrinolysis.

The selection of reperfusion strategy should take into account a number of different factors including the time from onset of symptoms, the mortality risk, risk of bleeding and transport time. In practice, in the UK, the availability of primary angioplasty is an important determining factor in the choice of reperfusion strategy.

Treatment of AMI also involves the management of complications as they occur. This might include heart failure, shock, mechanical complications including cardiac rupture and mitral regurgitation as well as arrhythmias.

1.5.3Subsequent care

Management later in the hospital phase will be determined by the size of the infarct and by the presence of other comorbid diagnoses. Patients who are asymptomatic and with minimum myocardial damage may go home after a few days, whilst those with more extensive necrosis or complications may require a longer hospital stay.

1.5.4Prevention and long term treatment

After myocardial infarction it is important to stratify patients according to their risk of subsequent coronary events, and to intervene in order to reduce the risk of subsequent events occurring. In high risk patients, coronary interventions should be considered.[31] Clinical indicators of high risk in the early stage include persistent heart failure, malignant arrhythmias, and persistent chest pain or angina. Prevention of subsequent events involves lifestyle change as well as long term medical management.

Aspirin

There is good evidence to recommend long term antiplatelet treatment in patients who have had an AMI. This evidence comes mainly from a metaanalysis of 25 trials of antiplatelet therapy prescribed in the secondary prevention of cardiovascular disease.[32] This Antiplatelet Trialists' Collaboration demonstrated a 25% reduction in re-infarction and death in post-infarct patients.

Beta Adrenoceptor Blockers

A number of trials and metanalyses have shown that beta blockers reduce mortality and reinfarction by 20-25% in people post myocardial infarction.[33-35] A metanalysis of 82 randomised trials produced strong evidence for the long term use of beta blockers to reduce morbidity and mortality following a myocardial infarction.[23] Data suggests that beta blockers should be continued indefinitely in these patients.

Angiotensin converting enzyme (ACE) inhibitors

Evidence supports the use of ACE inhibitors post-myocardial infarction.[36;37] A number of clinical studies have shown that ACE inhibitors reduce the rates of reinfarction and decrease the risk of developing heart failure with a consequential reduction in mortality. The effect of ACE inhibitors is thought to be greatest in people who have experienced heart failure in the acute event or who have reduced left ventricular function.[38]

Statins

It is recommended that lipid lowering agents should be prescribed in accordance with guidelines derived from a number of clinical trials.[39-42] The European Society of Cardiology recommends that patients are prescribed statins if, in spite of dietary measures,

total cholesterol levels are greater than 4.9 mmol.l^{-1}and or LDL cholesterol levels of 2.97 mmol.l^{-1} still persist.[12]

Lifestyle changes

Stopping smoking is potentially the most effective of all secondary prevention measures. Evidence from observational studies suggests that following an AMI, people who stop smoking have more than a 50% reduction in mortality compared to those who continue to smoke.[43] Diet is also important and a Mediterranean type diet which is low in saturated fat and high in polyunsaturated fat and in fruit and vegetables, has been shown to reduce the rates of recurrent events in patients following their first AMI.[44] Fish oils are also associated with a reduction in mortality post AMI.[45] Physical activity is also important and is thought to reduce mortality and to improve well-being and cardiorespiratory fitness.[46;47]

2 LITERATURE REVIEW

2.1 Scope

A MEDLINE (1966-2004) search on appropriate subject headings yielded over 200,000 items. The subject headings used were: acute myocardial infarction, population, epidemiology, diagnosis, prognosis, survival, incidence, prevalence, mortality, revascularisation, trends, length of stay, socioeconomic deprivation, heart failure, atrial fibrillation, renal failure, hypertension, diabetes, cancer, peripheral vascular disease, angina, coronary heart disease, sex factors, sex characteristics, and women's health. Searches were combined and restricted to narrow the search. The search strategy was then repeated in EMBASE (1980-2004), using the synonymous EMBASE subject headings, and was extended by using lateral references.

The scope of the literature review aimed to encompass the following areas:

1. The epidemiology of first and second AMI including the incidence of the diagnosis with an emphasis on sex differences.
2. Temporal trends in the incidence of first and second AMI.
3. Baseline characteristics of men and women who are hospitalised with first and second AMI.
4. Temporal trends in the baseline characteristics of men and women hospitalised with first and second AMI.
5. The aetiology and pathophysiology of acute myocardial infarction in men and women.
6. Short and longer term survival of men and women with a diagnosis of first and second acute myocardial infarction.
7. Factors affecting survival following hospitalisation with first and second AMI in men and women.
8. Temporal trends in survival following hospitalisation with first and second AMI.
9. The potential mechanisms behind sex differences in survival from acute myocardial infarction.

2.2 Epidemiology of Acute Myocardial Infarction

The literature describing the epidemiology of acute myocardial infarction is extensive and varied. As in many areas of clinical epidemiology, there is a lack of uniformity and consistency between studies. Consequently, it is often difficult to make valid comparisons between data. Sex-specific data are not always reported in the literature, especially in older studies.

2.2.1 Study types and sources of data

Different studies have been designed to address particular questions. Data are principally available from four types of studies:

1. Population-based studies using hospital discharge data that are principally used to examine trends in hospitalisation.
2. Clinical trials and registries.
3. WHO MONICA Project studies carried out in 21 countries and within defined populations and set up to measure trends in CHD event rates, case-fatality, risk factors and acute coronary care over a 10 year period.
4. Cohort Studies such as the Framingham Study.

Not all studies have involved men and women, and women are undoubtedly underrepresented in clinical trials as they tend to focus on younger, male patients. The results of such studies are not always generalisable therefore to the general population of myocardial infarction patients.

2.2.2 Incidence of Acute Myocardial Infarction in men and women

A considerable number of studies have described incidence of myocardial infarction. Many of these studies were designed to examine trends over time and therefore report incidence data from more than one time period. A significant proportion do not report sex-specific data.[48] The majority of studies report on incidence of hospitalised AMI, though a growing number including many of the MONICA studies, include out of hospital events.[49-52] The definition of incident event varies according to the methodology employed. Many studies do not differentiate between first and subsequent events and report attack rates.[53]

Some studies using routine data are able to link records belonging to the same individual and therefore identify the first record belonging to that individual during a specified time period. Others involve examination of case notes or of electrocardiograms for evidence of previous events.

The Rochester Epidemiology Project used routine data to identify all individuals hospitalised with AMI between 1979 and 1994 (Table 2)[54] The case notes of these individuals were then examined in order to validate the diagnosis and to identify incident events. Researchers identified 1820 incident AMIs between 1979 and 1994, 44% of incident infarctions occurred in women. Age adjusted incidence rates were reported. In 1994, the age adjusted annual incidence was 260 per 100,000 in men and 180 per 100,000 in women. Sex-specific median age was not reported. The Minnesota Heart Survey randomly selected a 50% sample of all case notes of individuals aged 30-74 years discharged from hospital with a diagnosis of acute CHD in the Twin Cities of Minneapolis and St Paul in 1985 and 1990.[55] Standardised criteria were use to validate a diagnosis of AMI and first and recurrent events were distinguished by examining medical records. Over the course of 1985 and 1990, 4500 incident AMIs were identified. Of these, approximately 30% were in women. In 1990, the age adjusted annual incidence of first AMI was 298 per 100,000 in men and 107 per 100,000 in women. Neither the Rochester Epidemiology Project nor the Minnesota Heart Survey reported age specific incidence rates in men or in women. The Worcester Heart Attack Study examined temporal trends in the incidence of first AMI between 1975 and 1988.[56] The study sample comprised all 3,148 individuals hospitalised with validated first AMI in Worcester, Massachusetts. 39% were women. In 1988, the age-adjusted incidence rate of first AMI was 240 per 100,000 in men and 137 per 100,000 in women. The mean age of women was 71.7 years, 7.8 years older than men. The Atherosclerosis Risk in Communities Study (ARIC) examined incidence of CHD in four communities in the United States in individuals aged 35 to 74 years.[57] First events were identified and the diagnosis validated. In 1994, the age adjusted incidence of first AMI was 180 per 100,000 in women and 410 per 100,000 in women. The Toulouse MONICA Study reported incidence rates for first AMI in individuals aged 35 to 64 years living in the French department of Haute-Garonne.[58] In 1993, the age adjusted incidence rate for first AMI was 162 per 100,000 in men and 29 per 100,000 in women. These rates are lower than those reported by other studies and this is likely to reflect a lower prevalence of coronary heart disease in this population as well as a younger population. These studies have been consistent in their findings that incidence of

hospitalised AMI is greater in men than in women and that women are on average older at the time of their first presentation with AMI.

Table 2 Incidence of acute myocardial infarction in men and women

Study	Location	Type of study	Years of study	No of subjects (proportion of men)	Mean age men	Mean age women)	Overall incidence	Incidence in men	Incidence in women
Rochester (Minnesota) Epidemiology Project[54]	Olmsted County, Minnesota, USA	Retrospective longitudinal. Population-based. First AMIs from 1979-1994 All ages	1994	1820 (56%)	-	-	218 per 100,00*	260 per 100,000*	180 per 100,000*
Oxford Myocardial Incidence Study[59]	Oxford, UK	12 month prospective study. All AMIs. <80 years	1994-5	476 (72%)	Mean age NA	Mean age NA	-	171 per 100,000* Age 30-49, 47 per 100,000 Age 50-69, 358 per 100,000	50 per 100,000* Age 30-49, 7 per 100,000 Age 50-69, 115 per 100,000
Worcester Heart Attack Study[56]	Massachusetts, USA	Prospective study. Population-based. First and all AMIs. All ages	1988	3148 (61%) First AMIs over whole study period from 1975-1988	Mean age, 63.9 years	Mean age, 71.7 years	-	240 per 100,000*	137 per 100,000*
Minnesota Heart Survey[55]	Minneapolis-St-Paul, Minnesota, USA	Retrospective case note study. First events and all events. Age 30-74 years.	1990	4500 (70%) First AMIs	Mean age NA	Mean age NA		298 per 100,000*	107 per 100,000*
ARIC Study[57]	USA	Retrospective observational study. First AMIs. Age 35-74 years	1994	11,869 (34%) All events, not first. Numbers NA for first.	Mean age NA	Mean age NA		410 per 100,000*	180 per 100,000*
Toulouse MONICA Study[58]	France	Coronary event register. All AMIs including first and recurrent and out of hospital deaths. Age 35-64 years	1993	3,174 (85%) All AMIs	Mean age NA	Mean age NA		162 per 100,000*	29 per 100,000*

***age standardised**

2.2.3 Trends in incidence of AMI in men and women

The majority of studies describing incidence of hospitalised AMI have attempted to determine whether incidence and often survival have changed over time. All of the studies described above have examined temporal trends in AMI incidence in men and in women. Most of the studies examining trends in incidence of AMI are from the United States and there are few large British studies that have described temporal trends in men and women. Comparing the magnitude of changes between different studies is not straightforward as change is frequently measured using different parameters and in different population groups. The majority of studies have reported declining incidence in first AMI, though the overall and the age and sex-specific estimated magnitude of change are not consistent. The Minnesota Heart Survey reported non-significant declines in incident AMI of 5% in men and 4% in women between 1985 and 1990 (**Table** 3).[55] Age-specific changes were not reported. Actual figures were not reported. In the Toulouse MONICA Study, there was a 2% decline in the incidence of AMI in men and a 2.5% decline in women between 1985 and 1993.[58] This decline did not reach significance in women and age specific changes were not reported, presumably because of relatively small numbers. A number of studies have reported differences between men and women in the temporal trends of first AMI incidence.[54;57;60] In the Worcester Heart Attack Study, the age-adjusted incidence rates of initial AMI showed an overall decline of 26% in men and 22% in women between 1975 and 1988.[56] Temporal trends varied according to age and sex, tending to increase in magnitude with increasing age. The Rochester Epidemiology Project reported different trends in AMI incidence from 1979 to 1994 according to age and sex.[54] The age adjusted incidence of AMI increased in women by 2.1% per year between 1979 and 1994 (significant increase of 36% over the study period). In men age adjusted incidence decreased by 0.5% per year (non-significant decrease of 8% over the study period). The direction and magnitude of change varied according to age and sex. The greatest declines in incidence were seen in young men and the largest increases in elderly women. In the ARIC Study, the age adjusted incidence of hospitalisation for first AMI in men and women changed little between 1987 and 1994.[57] Analysis of age and sex-specific incidence rates revealed a significant increase of 4.6% per year in men aged 55-74 years, but not in any other age groups. The National Hospital Discharge Survey examined AMI hospitalisation rates in the United States between 1988 and 1997. The study reported stable age adjusted rates in men and women during this period although actual figures were not provided. In a recent report of the National Health and Nutrition Examination Survey Epidemiological Follow-up Study, the age standardised incidence of first AMI was non-significantly lower

among white and black men during 1982-1992 as compared with 1971-1982 but increased significantly by 21% among white women. Many of the MONICA Studies have described temporal trends in incidence of AMI. However the majority of studies have included out of hospital AMI deaths as well as hospitalised AMI and have excluded individuals aged greater than 64 years old.[52;58;61] Although inclusion of out of hospital deaths is a more accurate reflection of the real incidence of AMI, it is not comparable with many other studies that have included only hospitalised AMI.

Table 3 Trends in incidence of acute myocardial infarction in men and women

Study	Location	Type	Years of study	No of AMIs (% men)	Incidence in men at start of study period	Incidence in men at end of study period	Change in men	Incidence in women at start of study period	Incidence in women at end of study period	Change in women
Rochester (Minnesota) Epidemiology Project[54]	Olmsted County, Minnesota, USA	Retrospective longitudinal Population-based Incident AMI All ages	1979-1994	1820 (56%) First AMIs from 1979-1994	260 per 100,000*	260 per 100,000*	0.5% decline per year (non-sig) Age dependent Relative risk (relative to 1979): 40 yrs – 0.69 60 yrs – 0.83 80 yrs – 1.00	150 per 100,000*	180 per 100,000*	2.1% increase per year (Regression, significant) Age dependent Relative risk (relative to 1979): 40 yrs – 0.92 60 yrs – 1.24 80 yrs – 1.49
ARIC [62]Study	USA	Retrospective observational First AMIs. Age 35-74 years	1987-1996	14,842 events All events, not first (66%)	410 per 100,000*	410 per 100,000*	1.1% increase per year (non-sig). 0.6% decrease (non-sig). (definite AMI)	190 per 100,000*	180 per 100,000*	1.7% increase per year. Non-sig. (Regression). (definite /probable AMI) 0.3% increase., Non-sig. (definite AMI)
Oxford Myocardial Incidence Study[59]	Oxford, UK	12 month prospective and retrospective study. All AMIs Age< 80 years	1966-7 1994-5	476 (72%) in 1994-5 No data for 1966-7.	188 per 100,000* Age 30-49 years, 70 per 100,000 Age 50-69 years, 366 per 100,000	171 per 100,000* Age 30-49, 47 per 100,000 Age 50-69, 358 per 100,000	9% decline* (-28-10) Age 30-49,-34 (-72-54) Age 50-69, -2 (-24-20)	34 per 100,000* Age 30-49, 9 per 100,000 Age 50-69, 72 per 100,000	50 per 100,000* Age 30-49, 7 per 100,000 Age 50-69, 115 per 100,000	50% increase* (0-98). Crude Age 30-49, -15 (-130-104) Age 50-69, 61 (7-114)
Worcester Heart Attack Study[56]	Massachusetts, USA	Prospective study. Population-based. First AMIs All ages	1975-1988 (6- one year periods)	3148 (61%)	323 per 100,000*	240 per 100,000*	26%* decline Age 25-54, -26% Age 55-64, -15% Age 65-74, -25% Age 75-84, -33% Age >84, -54%	176 per 100,000*	137 per 100,000*	22% * decline Age 25-54, -1% Age 55-64, -29% *Age 65-74, +15%* Age 75-84, -24% Age >84, -55%

*** age standardised**

Continued over…

Table 3 *continued*

Study	Location	Type of study	Years of study	No of Events (% men)	Incidence in men at start of study period	Incidence in men at end of study period	Change in men	Incidence in women at start of study period	Incidence in women at end of study period	Change in women
Stockholm Study[63]	Stockholm County, Sweden	Retrospective hospital discharge register. First AMIs. Age 30-89 years	1984-1996	50,850 (61%)	NA	NA	18%* decline in age adjusted relative risk (0.83-0.90)	NA	NA	13%* decline in age adjusted relative risk (0.79-0.85)
Minnesota Heart Survey[55]	Minneapolis-St-Paul, Minnesota, USA	Retrospective case note study. First AMIs. Age 30-74 years	1985-1990	7,032 (70%) All AMIs First events, data not reported	315 per 100,000*	298 per 100,000*	-5% decline (crude)	111 per 100,000*	107 per 100,000*	-4% decline (crude)
Toulouse MONICA Study[58]	France	Coronary event register. All AMIs including first and recurrent and out of hospital deaths. Age 35-64 years	1985-1993	3,174 (85%) All events, not first	211 per 100,000*	162 per 100,000*	-2% decline (crude) Significant	27 per 100,000*	29 per 100,000*	-2.5% decline (crude) Non-significant
NHANES I Epidemiological Follow up Study[60]	United States	Two cohort Study	One cohort, 1971-1982 Second cohort, 1982-1992	20,643 individuals in cohort. 941 first AMI (60%) Age NA	NA	NA	-7.8%* decline in white men. Non-significant	NA	NA	+21% increase in white women. (Crude) Significant

*** age standardised**

2.3 Factors affecting incidence of AMI in men and women

2.3.1 Socioeconomic deprivation

There are many studies that have examined the relationship between socioeconomic deprivation and coronary heart disease. There are few studies that have examined the relationship between socioeconomic deprivation and incidence of coronary heart disease or AMI. The measurements used to determine socioeconomic deprivation vary and it is difficult to make valid comparisons between studies. A number of studies and reviews of the literature have focussed on psychosocial factors and coronary heart disease and the relationship between these factors and socioeconomic deprivation is complex.[64-66] Some studies have only included men.[67-71] In addition many studies have looked at the relationship between socioeconomic deprivation and coronary heart disease mortality, rather than incidence and survival.[67;68;72;73] It is therefore difficult to disentangle the different effects and to determine how socioeconomic deprivation might interact with these different indices. Different indicators of socioeconomic status including education, income and occupation as well as composite measures have been associated with coronary heart disease risk factors, morbidity and mortality.[64;67;68] A number of studies have looked at the association between socioeconomic status and coronary heart disease. The Minnesota Heart Survey described the distribution of coronary heart disease risk factors in different socioeconomic groups defined by education and income levels.[74] It found that education was significantly and inversely related to blood pressure, cigarette smoking and body mass index. Education was positively associated with physical activity and health knowledge. Women had healthier risk profiles overall. Associations with household income were less consistent in magnitude and direction. The Glasgow MONICA Study investigated the relationship between socioeconomic group and incidence of AMI in men and women between 1985 and 1991.[75] Socioeconomic status was derived from the postcode of residence using the Carstairs and Morris deprivation score.[76] They found that coronary event rates increased 1.7 fold in men and 2.4 fold in women from the least to the most deprived socioeconomic quarter. The socioeconomic gradient was steeper in women. The INTERHEART Study used a case control design to examine the relationship between psychosocial factors and the risk of AMI in 24,767 men and women in 52 countries.[65] The study found that the presence of psychosocial stressors including financial stress was associated with an increased risk of AMI. The effects were similar in men and women. The FINMONICA Study examined the relationship between socioeconomic status and

incidence of AMI in men and women aged 35 to 64 years.[77] Age adjusted incidence of first AMI was higher in men and women with low incomes compared to those with higher incomes. The age adjusted incidence rate ratios were 1.67 (1.57-1.78) in men and 1.52 (1.38-1.68) in women in the low income category compared with the high income category.

2.3.2Age

The vast majority of studies that have examined incidence or survival following AMI have included a description of the age distribution of the patients involved. Not all studies have included sex specific figures. In addition a number of studies have used inclusion or exclusion criteria, often based around age or coronary care admission, which introduce a selection bias into the age distribution of individuals included. The only studies that can be used to examine distribution of age in individuals hospitalised with AMI are therefore population based studies. All studies have shown that women are on average older than men at the time of admission to hospital with an AMI. The National Registry of Myocardial Infarction 2 included all consecutive hospitalisations with AMI between 1994 and 1998. The study excluded individuals aged less than 30 years or greater than 90 years.[78] Within these confines, the mean age of men was 65.6 years compared to 72.4 years in women. The Yorkshire AMI Study included all consecutive hospitalisations with AMI during a three month period in 1995. Women were on average seven years older than men with a mean age of 74.9 years (SD 10.9) compared to 68.0 years (SD 11.9) in men. In the Göteborg Study, which included consecutive hospitalisations with AMI between 1986 and 1987, the median age of men was 69 years compared to 76 years in women.[79] The Alberta Health and Wellness database contains information on 15,809 men and 7158 women hospitalised with an AMI between 1993 and 2000.[80] It is a population based study that includes all individuals admitted to hospital over the age of 18 years. The median age of women during this time was 73 years compared to 64 years in men. The Worcester Heart Attack Study is a population based study that involved the analysis of survival in all men and women hospitalised with a first AMI between 1975 and 1988.[56] The mean age of men was 71.7 years compared to 63.9 years in women who were therefore on average 7.8 years older than men at the time of their first AMI. In the Framingham Study the incidence of cardiovascular disease increased more steeply with age in women than in men, so that the rates almost converged at 85-94 years.[81] The rate of development of coronary heart disease in women increased three-fold from age 35-64 years to 65-94 years, whereas in

men it increased 2.25 fold. Women lagged behind men in the incidence of cardiovascular disease by ten years.

Comorbidity

There is a substantial amount of data relating to the prevalence of comorbid conditions in individuals hospitalised with AMI. However there is a lack of consistency regarding these data. Different comorbid conditions have been included by different studies and the definition of these conditions is not standardised. For example, hypertension is frequently included as a comorbid condition but the parameters of this diagnosis are rarely included in the methods. It is not always clear whether the comorbid diagnosis preceded the AMI or developed subsequently to the index event, for example heart failure. Also few studies include only first events so that comparison is difficult. In addition a number of studies have looked at survivors, the definition of which vary and may introduce significant selection bias.

2.3.3 Diabetes

Many studies that have explored survival following AMI have looked at the prevalence of diabetes (Table 4). There is wide variation in reported prevalence of diabetes in individuals hospitalised with AMI. In the Northern Sweden MONICA Project, 14.9% of men and 19.7% of women hospitalised with AMI had a diagnosis of diabetes.[82] This sex difference was statistically significant. These admissions were not necessarily first AMIs. In the ISIS-3 Study, women hospitalised with AMI were more likely to have diabetes than men.[83] The prevalence of diabetes increased with age in both sexes. 14% of women aged less than 60 years had a diagnosis of diabetes compared to 7% of men. This figure rose to 18% in women and 12% in men aged greater than 69 years. The National Registry of Myocardial Infarction 2 is a prospective study that enrolled consecutive patients hospitalised with AMI.[78] Between 1994 and 1998, 229,313 men and 155,565 women were included in this study. The mean age of men was 65.6 years compared to 72.4 years in women. Of these 25% of men and 33% of women had a history of diabetes ascertained on case note review. Younger women were more likely than younger men to have a history of diabetes. This sex based difference was not apparent in older age groups. The Gerona Heart Registry (The REGICOR Study) recorded information on all individuals aged less than 75 years hospitalised with a first Q wave infarction between 1978 and 1997.[84] Of these, 18% of men and 46% of women had a history of diabetes. The prevalence of diabetes varied with age in men and women so that 16% of men and 43% of women aged

less than 65 years had a diagnosis of diabetes rising to 23% in men and 48% in women aged 65 to 74 years. A prospective study examined risk factors and survival in 2196 consecutive patients hospitalised with AMI in Yorkshire in 1995.[85] The cohort included 2153 people of whom 60% were men. Of these, 11% of men and 16% of women had a diagnosis of diabetes, as determined by case note review. The mean age of men was 68 years compared to 75 years in women. This sex difference was statistically significant. The Göteborg Study examined baseline characteristics and survival in 300 women and 621 men who were hospitalised in Göteborg, Sweden with an AMI between 1986 and 1987.[79] The median age of the patients was 69 years in men and 76 years in women. 11% of men and 15% of women had a history of diabetes. This sex difference was not statistically significant. In the Alberta Health and Wellness Database, 16% of men and 22% of women hospitalised with an AMI had a diagnosis of diabetes on their discharge record.[80] The median age of men was 64 years compared to 73 years in women. The TRACE Study examined baseline characteristics and survival in 2170 women and 4501 men admitted to coronary care units ion Denmark between 1990 and 1992.[86] Women were on average five years older than men with a median age of 72 years in women compared to 67 years in men. Overall 14% of women and 9% of men had a diagnosis of diabetes based on their medical history derived through interview and case note analysis. The prevalence of diabetes increased with age in both sexes but remained higher in women than in men at all ages. The Worcester Heart Attack Study examined trends in incidence and survival of first AMI between 1975 and 1988.[56] Comorbid diagnoses were determined through examination of case notes. 16% of men and 27% of women hospitalised with a first AMI had a history of diabetes. This sex difference was statistically significant.

2.3.4 Heart failure

There is a lack of data examining the risk of AMI in men and women with heart failure. There are however numerous studies that have examined the prevalence of heart failure in individuals hospitalised with AMI (Table 5). In the Northern Sweden MONICA Project, 6.5% of men and 7.6% of women hospitalised with an AMI, had a clinical diagnosis of heart failure at the time of discharge.[82] These proportions were not significantly different between men and women and heart failure was not defined using uniform diagnostic criteria. In the National Registry of Myocardial Infarction 2, 13% of men and 21% of women had a history of congestive cardiac failure.[78] Again, younger women were more likely than younger men to have a diagnosis of heart failure though this difference was not apparent in older age groups. In the REGICOR Study which examined baseline

characteristics in individuals hospitalised with a first AMI, 8% of men and 19% of women had a history of cardiac failure.[84] The prevalence increased substantially with age in both sexes so that 6% of men and 14% of women aged less than 65 years had a history of cardiac failure, rising to 11% in men and 23% in women aged 65 to 74 years. In the Yorkshire AMI Study, 9% of men and 11% of women hospitalised with AMI had a previous history of heart failure (p=0.08).[85] In the Göteborg Study, 18% of men and 29% of women had a history of congestive cardiac failure.[79] The diagnosis of heart failure was made on clinical history. In the Alberta Health and Wellness database, 26% of women and 17% of men had a diagnosis of previous congestive heart failure on their discharge record.[80] This sex difference was statistically significant. In the TRACE Study 50% of men and 60% of women had a diagnosis of congestive heart failure.[86] The prevalence of this diagnosis increased with age so that only 24% of men and 27% of women aged <55 years had a diagnosis of congestive heart failure rising to 73% of men and 74% of women aged greater than 75 years. This diagnosis included those individuals with a prior history of heart failure as well as those who developed heart failure during the index admission.

2.3.5Hypertension

Blood pressure measurements have often been included in baseline measurements of individuals hospitalised following AMI. However the definition of hypertension is not consistent. The ISIS-3 Study included measurement of systolic blood pressure which was categorised into three groups, <100, 100-174 and ≥175 mm Hg.[83] Only 6% of men and women aged less than 60 years hospitalised with AMI had a systolic blood pressure greater or equal to 174 mm Hg. This figure increased with age rising to 10% of women and 9% of men aged greater than 69 years. The distribution of systolic blood pressure was similar in men and women (Table 6). In the Framingham Study the incidence of cardiovascular disease was noted to rise in men and women in relation to their blood pressure without any evidence of a critical value.[81] In the Rochester Epidemiology Project, 89% of women and 56% of men who survived 30 days following hospitalisation for their first AMI between 1960 and 1979, had a diagnosis of hypertension.[87] The definition of hypertension was not described in the paper. In the National Registry of Myocardial Infarction 2 Study, 47% of men and 59% of women had a history of hypertension as recorded in medical case notes.[78] In the REGICOR Study, 40% of men and 61% of women had a history of hypertension.[84] The prevalence increased with age so that 38% of men and 53% of women aged less than 65 years had a diagnosis of hypertension rising to 45% of men and 66% of women aged 65-74 years. These sex differences were statistically significant. In the Yorkshire AMI

Study, 25% of men and 36% of women had a diagnosis of hypertension ($p<0.001$).[85] In the Göteborg Study 31% of men and 44% of women had a history of hypertension ($p<0.001$).[79] In the Alberta Health and Wellness Database which used routine coding at discharge to identify comorbid diagnoses, 29% of men and 40% of women had a diagnosis of hypertension at discharge.[80] In the TRACE Study 20% of men and 28% of women had a diagnosis of systemic hypertension.[86] In the Worcester Heart Attack study 54% of women and 40% of men hospitalised with a first AMI had a history of hypertension ($p<0.001$).[56]

2.3.6 Renal impairment

Few of the large epidemiological studies that have examined baseline characteristics and survival in individuals hospitalised with AMI have included renal impairment in their description of baseline characteristics of men and women. Different definitions have been used to measure renal impairment and most studies have categorised patients on the basis of renal function and have not provided sex specific data. The Medicare Study looked the independent effect of chronic kidney disease on case fatality in 559 hospital survivors of an AMI who had been admitted to hospital in 1998 (Table 8).[88] Creatinine clearance was estimated using the Cockcroft-Gault equation. Chronic kidney disease was defined on the basis of a creatinine clearance of less than 60ml/min. The mean age of this cohort was 73.8 years and chronic kidney disease was present in 48.7% of men and 72.7% of women. The Cooperative Cardiovascular Project examined the association between renal insufficiency and case fatality following AMI in 130,099 individuals hospitalised with AMI between 1994 and 1995.[89] Renal impairment was defined according to creatinine clearance and women accounted for 48% of the study sample. Approximately 41% of men and 33% of women had mild or moderate renal impairment (figures are estimated as sex specific data were not reported). The Mayo Clinic Study examined survival in 3106 individuals admitted to coronary care with an AMI between 1988 and 2000.[90] Renal impairment was defined according to creatinine clearance which was estimated using the Cockcroft-Gault equation. Overall, 47% of men and 76% of women had a degree of renal impairment, although the prevalence increased substantially with age. In the Alberta Health and Wellness Database 3% of men and 4% of women hospitalised with an AMI had a diagnosis of chronic renal disease made at discharge.[80] This sex difference was statistically significant. A recent study of individuals admitted to Veterans Affairs Hospitals looked at the independent effect of renal insufficiency and seven month case fatality following hospitalisation with unstable angina and AMI.[91] Sex specific figures

were not reported and only a very small number of women were included in the study which comprised approximately 98% men. Of the 2706 individuals with acute coronary syndrome, only 16% had normal renal function, 43% had mild renal insufficiency and 41% had moderate or severe renal insufficiency. Renal insufficiency was based on the estimated glomerular filtration rate which was calculated using the abbreviated Modification of Diet in Renal Disease Study Equation. The study sample was older relative to other studies of AMI and the prevalence of renal insufficiency increased with age.

2.3.7 Previous AMI

The estimates for the proportion of men and women hospitalised with AMI who have a previous history of AMI vary substantially between different studies. Different methods and definitions have been used to determine which individuals have had a previous AMI. In some studies the diagnosis is based on case note review or on interview and in others on examination of ECGs. In the Northern Sweden MONICA Project 73.5% of men and 75.0% of women who were hospitalised with an AMI were reported to have had a previous AMI (Table 9).[82] The study only included individuals aged 35 to 64 years and previous AMI was diagnosed through examination of case records and on interview with the patient when appropriate. Other studies have reported lower prevalence rates. In the National Registry of Myocardial Infarction 2 Study, 28% of men and 24% of women had a history of previous AMI.[78] Men were more likely than women to have a history of previous AMI at all ages. In the Gőtcborg Study, 32% of men and 28% of women had a previous AMI.[79] The study included an unselected cohort of all AMIs with a median age of 69 years in men and 76 years in women. In the Yorkshire AMI Study which again included all consecutive hospitalisations for AMI, 29% of men and 21% of women had a history of previous AMI.[85] The mean age of men in this study was 68 years compared to 74.9 years in women. In the TRACE Study, 25% of men and 19% of women hospitalised with AMI had a previous history of AMI.[86] The prevalence of previous AMI increased with age especially in women in whom only 8% of those aged less than 55 years had a previous history of AMI rising to 22% in those aged greater than 75 years.

2.3.8 Previous angina and coronary heart disease

A number of studies have included a previous history of angina in their description of baseline characteristics of individuals hospitalised with AMI (Table 10). The estimates of

prevalence vary, partly because studies have used different definitions of angina. Age specific figures are rarely reported. In the National Registry of Myocardial Infarction 2 Study, 18% of men and women had a previous history of angina on admission to hospital with an AMI.[78] Women were slightly less likely than men to have a history of angina in the older age groups. The study excluded individuals aged 90 years and over as well as people transferred to other hospitals. In the Yorkshire AMI Study, 37% of men and women had a previous history of angina as documented in medical case notes.[85] In the Göteborg Study, 45% of men and 51% of women had a history of angina reported at interview.[79] Both the Yorkshire Study and the Göteborg Study included individuals of all ages in a non-selected cohort. In the REGICOR Study, 47% of men and 51% of women hospitalised with a first AMI and aged less than 75 years had a history of angina.[84] The prevalence increased only slightly with age in both sexes. In the Established Populations for the Epidemiologic Studies of the Elderly project. (The EPESE Study) 43% of men and 51% of women had a documented history of angina.[92] This study only included individuals aged 65 years or over. In the Framingham Study, 21% of men and 25% of women with a diagnosis of first AMI that included clinically unrecognised AMI, had a diagnosis of pre-existing angina.[93] In the TRACE Study, 36% of men and 38% of women hospitalised with AMI had a diagnosis of angina.[86] This sex difference was not statistically significant.

2.3.9 Atrial fibrillation

There are a number of studies that have examined the prevalence and prognostic significance of atrial fibrillation in men and women hospitalised with AMI, including clinical trials (Table 12). As with many of the other comorbid diagnoses, it is not always clear from the literature whether the diagnosis preceded the index AMI or arose subsequent to it. It is also difficult to determine sex differences because sex specific data are rarely presented presumably because the data categorisation is usually based on the presence or absence of the comorbid condition. The Cooperative Cardiovascular Project examined prevalence and outcome of atrial fibrillation in 106,780 men and women aged greater than 64 years who were hospitalised following an AMI.[94] Diagnosis of atrial fibrillation was based on the patient's ECG report. A similar proportion of men and women, approximately 22%, had a diagnosis of atrial fibrillation. 47% of men and 51% of women, who had a diagnosis of atrial fibrillation, had this diagnosis on arrival to hospital. Women were therefore more likely to present with atrial fibrillation. This difference was statistically significant, p=0.001. The prevalence of atrial fibrillation increased with age,

though analyses were not sex specific. The TRACE Study found a similar overall prevalence of atrial fibrillation in its study population which comprised 6676 consecutive patients hospitalised with AMI between 1990 and 1992.[95] 23% of women and 20% of men had a diagnosis of atrial fibrillation, either arising before or during hospitalisation. The Worcester Heart Attack Study reported a prevalence of atrial fibrillation of 14.7% in men and 18% in women following hospitalisation with AMI.[96] This figure included new and chronic cases. In the Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan, 12.2% of men and 11.4% of women had atrial fibrillation at baseline.[97] These figures did not include new onset atrial fibrillation. The global use of strategies to open occluded coronary arteries (GUSTO III Trial) reported similar prevalence figures of 11.9% in men and 12.6% in women.[98] A Japanese Study examined the prevalence of atrial fibrillation in 1039 individuals hospitalised with AMI between 1985 and 1995.[99] 10% of men and 9% of women either had a history of atrial fibrillation or developed atrial fibrillation during their admission. The distribution of age in men and women was not described and sex specific data were not reported. Other studies have looked at the risk of developing atrial fibrillation in individuals hospitalised with AMI. The Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-3 Study) examined the incidence of new-onset atrial fibrillation in 17,749 individuals hospitalised with AMI.[100] The study excluded those individuals who had a diagnosis of atrial fibrillation on admission to hospital. Overall 7.2% of men and 10% of women developed atrial fibrillation during their hospital admission ($p<0.001$).

2.3.10 Chronic obstructive Pulmonary Disease

Few studies have included chronic obstructive pulmonary disease (COPD) in their description of baseline characteristics of men and women hospitalised with AMI (Table 11). The Yorkshire AMI Study reported a previous history of COPD in 15% of men and 14% of women who were hospitalised with AMI.[85] In the SPRINT Trial, 7.5% of men and 5.5% of women hospitalised with AMI had a diagnosis of COPD.[101] The prevalence of COPD increased with age and was more common in men. The Cooperative Cardiovascular Project examined the prevalence of COPD and asthma in 54,962 patients hospitalised with AMI between 1994 and 1995 who did not have contraindications to beta-blocker therapy.[102] 18.7% of women and 21% of men had a diagnosis of COPD or asthma and this diagnosis was classified as being severe in 15% of women and 23% of men. The TRACE Trial examined the prevalence of COPD in 6676 individuals hospitalised with AMI between 1990 and 1992.[103] History of COPD was obtained either from medical case

notes or on interview of the patient. 12% of men and 11% of women hospitalised with AMI had a history of COPD. Sex specific data were not reported. A small study in Newcastle Upon Tyne in the UK, examined the prevalence of COPD in 60 consecutive admissions to coronary care with inferior AMI.[104] COPD as defined by forced expiratory volume and vital capacity was found in 46% of patients. Sex specific data were not provided.

2.3.11 Other vascular diseases

Few studies have included other vascular diseases in their description of baseline characteristics of men and women hospitalised following AMI. The Framingham Study reported long term survival and prevalence of pre-existing cardiovascular conditions in 532 men and 296 women who experienced their first AMI during the 34 year follow up period between 1948 and 1982.[93] 9% of men and 11% of women had a diagnosis of intermittent claudication made on the basis of a standardised interview. Intermittent claudication was the most common pre-existing cardiovascular condition after angina. The average age of the individuals was not reported and the diagnosis of AMI included those individuals with a 'silent' AMI. These clinically unrecognised AMIs accounted for 30% of all AMI diagnoses in men and 38% in women. 5% of men and 8% of women had a history of stroke or TIA. The SPRINT Trial examined the prevalence and prognostic significance of peripheral vascular disease in 4258 individuals hospitalised with a first AMI.[105] The prevalence of PVD was similar in men and women with 6.4% of men and 6% of women having a diagnosis of PVD based on clinical history and physical examination.

Table 4 Prevalence of diabetes in men and women hospitalised with AMI

Study	Location	Type of study	Years of study	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/median age	Prevalence in women (age adjusted?)	Mean/median age	Sex difference
Northern Sweden MONICA Study[82]	Northern Sweden	Population-based AMI study. All AMIs. Aged 35-64 years	1989-1995	3,152 (79%)	14.9% not age adjusted	NA	19.7% not age adjusted	NA	Yes. P=0.003
ISIS-3[83]	Multinational in 20 countries	Clinical trial. All AMIs. All ages	1989-1991	36,080 (73%).	Age <60 years, 7% Age 60-69 years, 10% Age ≥70 years, 12%	NA	Age <60 years, 14% Age 60-69 years, 15% Age ≥70 years, 18%	NA	Age <60 years, yes, p<0.001 Age 60-69 years, yes, p<0.001 Age ≥70 years, yes, p<0.001
Yorkshire AMI Study[85]	Yorkshire, UK	Observational case note study. All AMIs	1995	2153 (60%)	11% not age adjusted	68 years	16% not age adjusted	75 years	Yes. P<0.001
Göteborg AMI Study[79]	Sweden	Prospective study. All AMIs All ages	1986-1987	921 (67%)	11% not age adjusted	69 years	15% not age adjusted	76 years	No
National Registry of Myocardial Infarction 2[78]	USA	Prospective observational study. All AMIs. Age 30-89 years	1994-1998	384,878 (60%).	25% not age adjusted	66 years	33% not age adjusted	72 years	NA
Alberta Health and Wellness Databases[80]	Canada	Retrospective routine data study. All AMIs All ages.	1993-2000	22967 (69%)	16% not age adjusted	64 years	22% not age adjusted	73 years	Yes. P<0.001
TRACE Study[86]	Denmark	Clinical trial Consecutive patients. All AMIs. Age 45-86 years	1990-1992	6671 (67%)	9% not age adjusted Age <55 years, 6% Age 55-65 years, 9% Age 65-75 years, 10% Age >75 years,11%	67 years	14% not age adjusted Age <55 years, 11% Age 55-65 years, 11% Age 65-75 years, 15% Age >75 years,15%	72 years	Yes. P<0.001
Worcester Heart Attack Study[56]	Massachusetts, USA	Prospective study. Population-based. First AMIs. All ages	1975-1988 (6-one year periods)	3148 (61%)	16% not age adjusted	64 years	27% not age adjusted	72 years	Yes. P<0.001
REGICOR Study[84]	Gerona, Spain	Clinical registry First AMIs. Aged 25 to 74 years	1978-1997	2769 (84%)	18% not age adjusted Age <65 years, 16% Age 65-74 years, 23%	59 years	46% not age adjusted Age <65 years, 43% Age 65-74 years, 48%	65 years	Yes. P<0.001

Table 5 Prevalence of heart failure of heart failure in men and women hospitalised with AMI

Study	Location	Type of study	Year s of study	No of Events (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
Northern Sweden MONICA Study[82]	Northern Sweden	Population-based AMI study. All AMIs. Aged 35-64 years	1989-1995	3,152 (79%)	6.5% not age adjusted	NA.	7.6% not age adjusted	NA	No. P=0.36
Rochester (Minnesota) Epidemiology Project[87]	Minnesota, USA	Retrospective longitudinal observational. Population-based First AMIs All ages	1960-1979	1013 (66%) first AMIs who survived first 30 days from 1960-1979	25% not age adjusted	22% aged 70 or over	35% not age adjusted	53% aged 70 or over	NA
Yorkshire AMI Study[85]	Yorkshire, UK	Observational case note study. All AMIs. All ages	1995	2153 (60%)	9% not age adjusted	68 years	11% not age adjusted	75 years	No. P=0.08
EPESE Project[91]	New Haven, Connecticut	Longitudinal cohort study. All AMIs Aged ≥65 years	1982-1992	223 (46%)	32.5% not age adjusted	77 years	40.8% not age adjusted	79 years	No. P=0.2
Göteborg AMI Study[79]	Sweden	Prospective study. All AMIs All ages	1986-1987	921 (67%)	18% not age adjusted	69 years	29% not age adjusted	76 years	Yes. P<0.001
National Registry of Myocardial Infarction 2[78]	USA	Prospective observational study. All AMIs. Age 30-89 years	1994-1998	384,878 (60%).	13% not age adjusted	66 years	21% not age adjusted	72 years	NA
REGICOR Study[84]	Gerona, Spain	Clinical registry First AMIs. Aged 25 to 74 years	1978-1997	2769 (84%)	8% not age adjusted Age <65 years, 6% Age 65-74 years, 11%	59 years	19% not age adjusted Age <65 years,14% Age 65-74 years, 23%	65 years	Yes. P<0.001
Alberta Health and Wellness Databases[80]	Canada	Retrospective routine data study. All AMIs All ages	1993-2000	22967 (69%)	17% not age adjusted	64 years	25% not age adjusted	73 years	Yes. P<0.001
TRACE Study[86]	Denmark	Clinical trial Consecutive patients. All AMIs. Age 45-86 years	1990-1992	6671 (67%)	50% not age adjusted Age <55 years, 24% Age 55-65 years, 41% Age 65-75 years, 58% Age >75 years,73%	67 years	60% not age adjusted Age <55 years, 27% Age 55-65 years, 49% Age 65-75 years, 58% Age >75 years,74%	72 years	Yes. P<0.001

Table 6 Prevalence of hypertension in men and women hospitalised with AMI

Study	Location	Type of study	Years of study	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
ISIS-3[83]	Multinational in 20 countries	Clinical trial. All AMIs. All ages	1989-1991	36,080 (73%).	Age <60 years, % Age 60-69 years, % Age ≥70 years, %	NA	Age <60 years, % Age 60-69 years, % Age ≥70 years, %	NA	NA
Rochester (Minnesota) Epidemiology Project[87]	Minnesota, USA	Retrospective longitudinal observational Population-based First AMIs All ages	1960-1979	1013 (66%) first AMIs who survived first 30 days from 1960-1979	56% not age adjusted	22% aged 70 or over	89% not age adjusted	53% aged 70 or over	NA
Yorkshire AMI Study[85]	Yorkshire, UK	Observational case note study. All AMIs. All ages	1995	2153 (60%)	25% not age adjusted	68 years	36% not age adjusted	75 years	Yes. P<0.001
EPESE Project[92]	New Haven, Connecticut	Longitudinal cohort study. All AMIs Aged ≥65 years	1982-1992	223 (46%)	47% not age adjusted	77 years	66% not age adjusted	79 years	Yes. P=0.004
Göteborg AMI Study[79]	Sweden	Prospective study All AMIs. All ages	1986-1987	921 (67%)	31% not age adjusted	69 years	44% not age adjusted	76 years	Yes. P<0.001
National Registry of Myocardial Infarction 2[78]	USA	Prospective observational study. All AMIs. Age 30-89 years	1994-1998	384,878 (60%).	47% not age adjusted	66 years	59% not age adjusted	72 years	NA
REGICOR Study[84]	Gerona, Spain	Clinical registry. First AMIs Aged 25 to 74 years	1978-1997	2769 (84%)	40% not age adjusted Age <65 years, 38% Age 65-74 years, 45%	65 years	61% not age adjusted Age <65 years,53% Age 65-74 years, 66%	59 years	Yes. P<0.001
Alberta Health and Wellness Databases[80]	Canada	Retrospective routine data study. All AMIs. All ages	1993-2000	22967 (69%)	29% not age adjusted	64 years	40% not age adjusted	73 years	Yes. P<0.001
TRACE Study[86]	Denmark	Clinical trial Consecutive patients. All AMIs. Age 45-86 years	1990-1992	6671 (67%)	20% not age adjusted Age <55 years, 14% Age 55-65 years, 21% Age 65-75 years, 24% Age >75 years, 19%	67 years	28% not age adjusted Age <55 years, 22% Age 55-65 years, 28% Age 65-75 years, 29% Age >75 years, 28%	72 years	Yes. P<0.001
Worcester Heart Attack Study[55]	Massachusetts, USA	Prospective study. Population-based. First AMIs. All ages	1975-1988 (6- one year periods)	3148 (61%)	40% not age adjusted	64 years	54% not age adjusted	72 years	Yes. P<0.001

Table 7 Prevalence of other vascular diseases in men and women hospitalised with AMI

Study	Location	Type of study	Years of study	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
Framingham Study[93]	Framingham, USA	Prospective cohort Study. First AMIs. Includes silent AMIs. All ages	1948-1982	828 (64%)	Intermittent claudication -9.4% not age adjusted Stroke /TIA- 5.3% not age adjusted	NA	Intermittent claudication 10.5% not age adjusted Stroke /TIA- 8.1% not age adjusted	NA	NA
Alberta Health and Wellness Databases[80]	Canada	Retrospective routine data study. All AMIs. All ages	1993-2000	22967 (69%)	PVD- 5% not age adjusted	64 years	PVD- 5% not age adjusted	73 years	No. P=0.92
SPRINT Trial	Israel	Clinical trial	1981-1983	4258 (73%)	PVD- 6.4% not age adjusted	NA	PVD- 6% not age adjusted	NA	No.

Table 8 Prevalence of renal impairment in men and women hospitalised with AMI

Study	Location	Type of study	Years of study	Definition of renal impairment	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
Alberta Health and Wellness Databases[80]	Canada	Retrospective routine data study. All AMIs All ages	1993-2000	ICD9 codes- not provided	22967 (69%)	3% not age adjusted	64 years	4% not age adjusted	73 years	Yes. P=0.005
Medicare Study[88]	USA	Retrospective case note study. All AMIs who survived admission All ages	1998	Creatinine clearance ≤ 60ml/min	559 (51%)	48.7% not age adjusted	NA	72.7% not age adjusted	NA-	NA
Cooperative Cardiovascular Project[89]	USA	Retrospective cohort study. All AMIs. Aged ≥65 years	1994-1995	Serum creatinine >1.5 mg/dl	130,099 (52%)	41% not age adjusted	NA	33% not age adjusted	NA	NA
Mayo Clinic Study[90]	USA	Retrospective cohort study. Coronary care admissions. All AMIs. All ages	1988-2000	Creatinine clearance < 75 ml/min	3106 (63%)	47% not age adjusted	NA	76% not age adjusted	NA	P<0.001

Table 9 Prevalence of previous AMI in men and women hospitalised with AMI

Study	Location	Type of study	Years of study	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
Northern Sweden MONICA Study[82]	Northern Sweden	Population-based AMI study. All AMIs. Aged 35-64 years	1989-1995	3,152 (79%)	73.5 % not age adjusted	NA. Age 35-64 years	75.0 % not age adjusted	NA.	No. P=0.46
ISIS-3[83]	Multinational in 20 countries	Clinical trial. All AMIs. All ages	1989-1991	36,080 (73%).	Age <60 years, 16% Age 60-69 years, 24% Age ≥70 years, 26%	NA	Age <60 years, 14% Age 60-69 years, 18% Age ≥70 years, 21%	NA	Age <60 years, yes, p<0.01 Age 60-69 years, yes, p<0.001 Age ≥70 years, yes, p<0.001
Yorkshire AMI Study[85]	Yorkshire, UK	Observational case note study. All AMIs. All ages	1995	2153 (60%)	29% not age adjusted	68 years	21% not age adjusted	75 years	Yes. P<0.001
EPESE Project[92]	New Haven, Connecticut	Longitudinal cohort study. All AMIs. Aged ≥65 years	1982-1992	223 (46%)	29.2% not age adjusted	77 years	20.4% not age adjusted	79 years	No. P=0.132
Göteborg AMI Study[79]	Sweden	Prospective study All AMIs. All ages	1986-1987	921 (67%)	32% not age adjusted	69 years	28% not age adjusted	76 years	No
National Registry of Myocardial Infarction 2[78]	USA	Prospective observational study. All AMIs. Age 30-89 years	1994-1998	384,878 (60%).	28% not age adjusted	66 years	24% not age adjusted	72 years	NA
Alberta Health and Wellness Databases[80]	Canada	Retrospective routine data study.. All AMIs. All ages	1993-2000	22967 (69%)	13% not age adjusted	64 years	10% not age adjusted	73 years	Yes. P<0.001
TRACE Study[86]	Denmark	Clinical trial Consecutive patients. All AMIs. Age 45-86 years	1990-1992	6671 (67%)	25% not age adjusted Age <55 years, 17% Age 55-65 years, 24% Age 65-75 years, 29% Age >75 years, 29%	67 years	19% not age adjusted Age <55 years, 8% Age 55-65 years, 14% Age 65-75 years, 21% Age >75 years, 22%	72 years	Yes. P<0.001

Table 10 Prevalence of previous angina in men and women hospitalised with AMI

Study	Location	Type of study	Year s of study	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
Yorkshire AMI Study[85]	Yorkshire, UK	Observational case note study. All AMIs	1995	2153 (60%)	37% not age adjusted	68 years	37% not age adjusted	75 years	No. P=0.82
EPESE Project[92]	New Haven, Connecticut	Longitudinal cohort study. All AMIs. Aged ≥65 years	1982-1992	223 (46%)	43% not age adjusted	77 years	51% not age adjusted	79 years	No. P=0.286
Göteborg AMI Study[79]	Sweden	Prospective study. All AMIs All ages	1986-1987	921 (67%)	45% not age adjusted	69 years	51% not age adjusted	76 years	No
National Registry of Myocardial Infarction 2[78]	USA	Prospective observational study. All AMIs. Age 30-89 years	1994-1998	384,878 (60%).	18% not age adjusted	66 years	18% not age adjusted	72 years	NA
REGICOR Study[84]	Gerona, Spain	Clinical registry. First AMIs Aged 25 to 74 years	1978-1997	2769 (84%)	47% not age adjusted Age <65 years, 46% Age 65-74 years, 48%	65 years	51% not age adjusted Age <65 years,52% Age 65-74 years, 51%	59 years	No
Framingham Study[93]	Framingham, USA	Prospective cohort Study. First AMIs. Includes silent AMIs. All ages	1948-1982	828 (64%)	20.9% not age adjusted	NA	24.7% not age adjusted	NA	NA
TRACE Study[86]	Denmark	Clinical trial Consecutive patients. All AMIs. Age 45-86 years	1990-1992	6671 (67%)	36% not age adjusted	67 years	38% not age adjusted	72 years	No. P=0.39
Worcester Heart Attack Study[56]	Massachusetts, USA	Prospective study. Population-based. First AMIs. All ages	1975-1988 (6- one year periods)	3148 (61%)	17% not age adjusted	64 years	22% not age adjusted	72 years	Yes. P<0.001

Table 11 Prevalence of chronic obstructive pulmonary disease in men and women hospitalised with AMI

Study	Location	Type of study	Years of study	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
Yorkshire AMI Study[85]	Yorkshire, UK	Observational case note study. All AMIs	1995	2153 (60%)	15% not age adjusted	68 years	14% not age adjusted	75 years	No. P=0.80
Alberta Health and Wellness Databases[80]	Canada	Retrospective routine data study. All AMIs All ages	1993-2000	22967 (69%)	5% not age adjusted	64 years	6% not age adjusted	73 years	Yes. P<0.001
TRACE Study[86]	Denmark	Clinical trial Consecutive patients. All AMIs. Age 45-86 years	1990-1992	6671 (67%)	12% not age adjusted	67 years	11% not age adjusted	72 years	No
Cooperative Cardiovascular Project[102]	USA	Retrospective cohort study. All AMIs. Age >65 years	1994-1995	54,962 (55%)	21% not age adjusted	NA	18.7% not age adjusted	NA	NA
SPRINT Trial[101]	Israel	Clinical trial	1981-1983	5839 (74%)	7.5% not age adjusted	NA	5.5% not age adjusted	NA	NA

Table 12 Prevalence of atrial fibrillation in men and women hospitalised with AMI

Study	Location	Type of study	Years of study	No of AMIs (% men)	Prevalence in men (age adjusted?)	Mean/Median age	Prevalence in women (age adjusted?)	Mean/Median age	Sex difference
EPESE Project[92]	New Haven, Connecticut	Longitudinal cohort study. All AMIs. Aged ≥65 years	1982-1992	223 (46%)	20.0% not age adjusted	77 years	6.8% not age adjusted	79 years	No. P=0.286
Japanese Study[99]	Japan	Prospective study. All AMIs. All ages	1985-1995	1039 (75%)	10% not age adjusted	NA	9% not age adjusted	NA	NA
Cooperative Cardiovascular Project[94]	USA	Retrospective cohort study. All AMIs. Aged >64 years	1994-1996	106780 (51%)	22.3% not age adjusted	NA	21.9% not age adjusted	NA	No.
Worcester Heart Attack Study[96]	Massachusetts, USA	Prospective study. Population-based. First AMIs. All ages	1975-1986 (5-one year periods)	4108 (62%)	14.7% not age adjusted	NA	18% not age adjusted	NA	Yes. P<0.001
TRACE Study[86]	Denmark	Clinical trial Consecutive patients. All AMIs. Age 45-86 years	1990-1992	6676 (67%)	19.9% not age adjusted	NA	22.9% not age adjusted	NA	Yes. P<0.001
GISSI-3 Study[100]	Italy	Clinical trial. All AMIs. Excluded pre-existing atrial fibrillation	1991-1993	17,749	7.2% not age adjusted New onset atrial fibrillation	NA	10% not age adjusted New onset atrial fibrillation	NA	Yes. P<0.0001

2.4 Temporal trends in baseline characteristics of men and women

Age

There are few data describing trends in the baseline characteristic of men and women hospitalised with AMI. Many studies exclude individuals over a certain age or only include those admitted to coronary care units. This introduces bias and does not provide an accurate reflection of the AMI population age structure. Very few studies only include individuals with first events so that they comprise a mix of first and recurrent events which tend towards different age profiles. The Ontario Study described trends in the demographic and comorbidity characteristics of 89,456 patients admitted to hospital between 1992 and 1996.[106] In this study there was an overall trend towards an increasing proportion of older AMI patients. The median age of men and women rose from 68 years in 1992 to 69 years in 1996. Sex specific figures were not reported. In the Nottingham Heart Attack Register the mean age of men and women hospitalised following an AMI increased between 1982 and 1992.[107] The mean age increased from 67.6 years in women and 60.7 years in men in 1982 to 69.7 years in women and 64.8 years in men in 1992. These trends were significant. The proportion of male patients also fell during this time. In 1992 men accounted for 79% of the total population falling to 63% in 1992. In the SPRINT Registry, the mean age on hospitalisation with AMI between 1981-3 and 1992-4, remained relatively stable in men whilst the mean age of women increased by approximately one year, from 67.3 years to 68.4 years.[108] In the Worcester Heart Attack Study, the mean age of individuals hospitalised with AMI increased from 65.4 years in 1975-1978 to 72.5 years in 2001.[109] Sex specific data were not reported. None of these data distinguish between first and subsequent events.

Comorbid diagnoses

The SPRINT Registry examined trends in baseline characteristics of men and women with AMI admitted to coronary care in 1981-3 and 1992-4.[108] The prevalence of diabetes increased in men and women. In 1981-3, 18% of men and 29% of women had a diagnosis of diabetes. By 1992-4, this figure had increased to 23% in men and 35% in women. The prevalence of hypertension remained relatively stable whilst the prevalence of previous angina decreased during the study period. In the Ontario Study the proportion of most patient comorbidities remained relatively stable between 1992 and 1996.[106] The proportion

of individuals with a secondary diagnosis of diabetes with complications rose from 1.6% in 1992 to 2.3% in 1996. The proportion of individuals with a congestive heart failure diagnosis rose slightly from 19.3% to 21.5% over the same time period. Neither the sex specific figures nor the statistical significance of these trends were reported. The National Hospital Discharge Survey examined the prevalence of comorbid diagnoses in hospital discharges for AMI between 1988 and 1997.[53] The study however reported data relating to episodes rather than individuals and reported few sex specific analyses. Overall it found that the prevalence of diagnosed hypertension increased by 62%, a mean annual increase of 6%. By contrast the prevalence of diabetes remained stable. The Worcester Heart Attack Study examined changes over time in the demographic characteristics of individuals hospitalised with AMI.[109] The study found that with the exception of previous angina, the prevalence of comorbid diagnoses increased in hospitalised patients between 1975-1978 and 2001. There was an increase in the prevalence of heart failure, diabetes, hypertension and stroke during this time. For example the prevalence of heart failure increased from 13.9% in 1975-8 to 25.5% in 2001. Hypertension increased in prevalence from 41% to 68.7%. Sex specific data were not reported. The Minnesota Heart Survey examined trends in coronary heart disease hospitalisations and deaths in residents of Minnesota between 1985 and 1990.[55] It also looked at trends in coronary heart disease risk factors through surveys of the Minnesota population between 1985 and 1992. The study found that the coronary heart disease risk factor profile improved over this time. In terms of comorbid diagnoses, only hypertension was included in the interview schedule. The proportion of individuals with a diagnosis of hypertension remained relatively stable in men but decreased significantly in women from 26% in 1985 to 18% in 1992. The study examined the risk factor profile of the general population and not those individuals hospitalised with AMI.

2.5 Short term Survival in men and women following first AMI

One month and in-hospital case fatality

Many studies have examined short term survival following AMI (Table 13). Not all studies have clearly reported sex specific data or have analysed first AMI survival as oppose to first or recurrent.[48;110] In addition, comparison is hindered by a lack of consistency in the end points that are used. Time periods vary from in-hospital case fatality to 28 day and 30 day case fatality. Variation in age between different study groups also limits the comparability of results and age specific case fatality is not always reported.

The Rochester (Minnesota) Epidemiology Project reported 28 day case fatality rates for incident hospitalised AMI between 1979 and 1994 in men and women of all ages.[54] In 1994, 28 day case fatality was 7% in men and 15% in women. Age specific figures were not reported for men and women. The Worcester Heart Attack Study examined incidence and survival in 3,148 individuals hospitalised with a first AMI between 1975 and 1988.[56] Overall unadjusted in-hospital case fatality rates were significantly higher in women (21.7%) than in men (12.7%). After adjusting for age the sex difference narrowed and case fatality was 17.9% in women compared to 15.2% in men. It is not clear whether this difference was statistically significant and age specific rates were not reported. In the Minnesota Heart Survey in 1990, age adjusted 28 day case fatality was 10% in men and 12% in women.[55] Sex differences were not explored and it is not clear whether this difference was statistically significant. Data from the Swedish National Acute Myocardial Infarction Register was used to examine sex differences in survival in men and women aged 30 to 89 years hospitalised with AMI between 1987 and 1995.[111] The Register included all events, not just first events. Overall crude case fatality was 22.6% in men and 27.5% in women. The overall age adjusted odds ratio in women compared to men was 0.98 (95% CI 0.96-1.00). The Northern Sweden MONICA Project reported 28 day case fatality in 2483 men and 669 women aged 35 to 64 years who were hospitalised with an AMI between 1989 and 1995.[82] Unadjusted case fatality was significantly lower in men than in women (12.7% versus 21.2% respectively). The MONICA Breman Study examined 28 day survival in 1710 men and 563 women aged 25-69 years who were admitted to hospital following a first AMI.[112] The unadjusted 28 day case fatality rate was higher in women than in men (23.1% versus 16.1% respectively). Adjusting for age did not eliminate the difference entirely. The National Hospital Discharge Survey was used to examine age adjusted in-hospital case fatality in men and women aged 35 years and over between 1988 and 1997 across the United States of America.[53] Overall unadjusted case fatality was 13.9% in men and 9.3% in women. In 1997 age adjusted case fatality was 4.4% in women and 3.4% in men. Case fatality was higher in women than in men in all age groups except in those aged greater than 84 years. The Myocardial Infarction Triage and Intervention (MITI) registry database recorded data on 4255 women and 8076 women who developed an AMI and were admitted to coronary care in 19 Seattle, Washington area hospitals between 1988 and 1994.[113] In-hospital case fatality was 13.7% in women and 7.8% in men. This difference persisted after adjusting for age and women were 20% more likely to die in the hospital than men. Age specific rates were not reported. In ISIS-3, 35-day case fatality was examined in 9600 women and 26,480 men who had been hospitalised with AMI between 1989 and 1991 and who had clear indications for fibrinolytic therapy.[83]

Overall case fatality was 14.8% in women and 9.1% in men, the unadjusted odds ratio was 1.73. Adjusting for age reduced the odds ratio to 1.20 (1.11-1.29), but did not remove the sex difference in survival. The National Registry of Myocardial Infarction 2 collected data on 384,878 men and women admitted to hospital across the USA with an AMI between 1994 and 1998.[78] Overall in-hospital case fatality was 16.7% in women and 11.5% in men. However, sex-based differences in case fatality varied according to age, so that the effect of sex could not be simply described. The REGICOR Study included all 2769 individuals aged less than 74 years admitted to hospitals in Gerona between 1978 and 1997 with a diagnosis of Q-wave AMI.[84] Unadjusted 28 day case fatality was 18.8% in women and 9.3% in men. The unadjusted female to male odds ratio was 2.27 (1.72-2.99). In a fully adjusted multivariate model, sex differences in survival varied with age. In the Danish Verapamil Infarction Trial carried out between 1979 and 1981, 15 day case fatality was 17% in women and 16% in men.[114] The trial included 738 women and 2335 men aged less than 76 years who had been admitted to hospital following an AMI. The EPESE Cohort included 2182 individuals aged 65 years and over who were living in New Haven in 1982.[92] 103 women and 120 men were hospitalised with an AMI between 1982 and 1992. The overall 30 day case fatality was 21.4% in women and 25.0% in men. Unadjusted female to male relative risk was 0.85 (0.49-1.47). In the Göteborg Study, the in-hospital case fatality rate was 12% in men and 19% in women.[79] The study included all AMIs and the median age was 69 years in men and 76 years in women. The unadjusted female to male relative risk was 1.54 (1.09-2.18).

Table 13 Short-term case fatality following acute myocardial infarction in men and women

Study	Location	Type	Year of study	No of subjects (proportion of men)	Case-fatality in men (time)	Age-specific case-fatality in men	Case-fatality in women	Age-specific case-fatality in women	Adjusted relative risk	Age-sex interaction
Rochester (Minnesota) Epidemiology Project[54]	Olmsted County, Minnesota, USA	Longitudinal observational (retrospective) Population-based. First AMIs	1994	1820 (56%) First events from 1979-1994 All ages	7% at 28 days (1994)	NA	15% at 28 days (1994)	NA	NA	NA
Oxford Myocardial Incidence Study[59]	Oxford, UK	12 month prospective study. All AMIs	1994-5	476 events (72%)	15% * at one month	Age 30-49 years, 2% Age 50-69 years, 18%	44% *	Age 30-49 years, 25% Age 50-69 years, 48%	NA	NA
Worcester Heart Attack Study[56]	Massachusetts, USA	Prospective study. Population-based. First AMIs. All ages	1975-1988 (6- one year periods)	3148 (61%)	15.2%* in-hospital	NA	17.9%* in-hospital	NA	0.90 (0.70-1.16) MV Adjusted odds ratio relative to men	NA
Swedish National AMI Register[111]	Sweden	Retrospective population-based study. First AMIs in that time period. Aged 30-89 years	1987-1995	353,905 (63%)	22.6% at 28 days	Age 30-49 years, 6% Age 55-59 years, 10% Age 65-69 years, 18% Age 75-79 years, 30% Age 85-89 years, 43%	27.5% at 28 days	Age 30-49 years, 10% Age 55-59 years, 12% Age 65-69 years, 19% Age 75-79 years, 28% Age 85-89 years, 40%	0.98 (0.96-1.00) Age adjusted odds ratio relative to women	Yes. Higher case fatality in women than in men aged up to 70 years. Better prognosis in women > 75 years
Northern Sweden MONICA Study[82]	Northern Sweden	Population-based AMI study. All AMIs Aged 35-64 years	1989-1995	3,152 (79%)	12.7% at 28 days	NA	21.2% at 28 days	NA	0.8 (0.6-1.1) Non-significant MV Adjusted odds ratio relative to women	No
MITI Registry[113]	Washington, USA	Prospective CCU study. All AMIs. All ages	1988-1994	12,331 (66%)	7.8% in-hospital	NA	13.7% in hospital	NA	1.22 (1.1-1.4) MV Adjusted odds ratio relative to men	NA

***age standardised**

Continued over…

Table 13 *continued*

Study	Location	Type of study	Year	No of subjects (proportion of men)	Case-fatality in men (time)	Age-specific case-fatality in men	Case-fatality in women	Age-specific case-fatality in women	Adjusted relative risk	Age-sex interaction
MONICA Bremen Study[112]	Bremen, Germany	Population-based AMI study. First AMIs 25-69 years	1985-1990	2,273 (75%)	17%* 28 days	Age 35-39 years, 8% Age 45-49 years, 8% Age 55-59 years, 18% Age 65-69 years, 24%	21% * at 28 days	Age 35-39 years, 8% Age 45-49 years, 8% Age 55-59 years, 18% Age 65-69 years, 24%	1.31 (1.02-1.68) Age adjusted odds ratio relative to men 1.13 (0.9-1.5) MV Adjusted odds ratio relative to men	NA
National Hospital Discharge Survey[53]	USA	Population based AMI study. All AMIs. Aged ≥35 years	1988-1997	NA.	3.4%* in-hospital (1997)	Only in figure format	4.4%* in-hospital (1997)	Only in figure format	1.13 (1.12-1.13) MV Adjusted odds ratio relative to men.	MV Adjusted odds ratio relative to men. 1.28 (1.27-1.30) in age 35 to 64 years and 1.09 (1.08-1.10) in age ≥65 years. Interaction not formally tested.
ISIS-3[63]	Multinational in 20 countries	Clinical trial. All AMIs. All ages	1989-1991	36,080 (73%).	9.1% at 35 days	Age <60 years, 4% Age 60-69 years, 10% Age ≥70 years, 19%	14.8% at 35 days	Age <60 years, 5% Age 60-69 years, 12% Age ≥70 years, 23%	1.20 (1.11-1.29) Age adjusted odds ratio relative to men 1.14 (1.05-1.23) MV Adjusted odds ratio relative to men	NA
Minnesota Heart Survey[55]	Minneapolis-St-Paul, Minnesota, USA	Retrospective case note study. First events. Age 30-74 years	1985-1990	7,032 (70%) All AMIs First events, data not reported	10%* at 28 days (1990)	NA	12%* at 28 days (1990)	NA	NA	NA

***age standardised**

Continued over...

Table 13 *continued*

Study	Location	Type of study	Year	No of subjects (proportion of men)	Case-fatality in men (time)	Age-specific case-fatality in men	Case-fatality in women	Age-specific case-fatality in women	Adjusted relative risk	Age-sex interaction
National Registry of Myocardial Infarction 2[78]	USA	Prospective observational study. All AMIs. Age 30-89 years	1994-1998	384,878 (60%).	11.5% in-hospital (1998)	Age <50 years, 3% Age 55-59 years, 6% Age 65-69 years, 11% Age 75-79 years, 18% Age 85-89 years, 25%	16.7% in-hospital (1998)	Age <50 years, 6% Age 55-59 years, 10% Age 65-69 years, 13% Age 75-79 years, 19% Age 85-89 years, 24%	1.18 (1.16-1.20) Age adjusted odds relative to men.	Age sex interaction, P<0.001. MV adjusted odds ratio 1.07 (1.06-1.08) relative to men for every 5 years decrease in age
Danish Verapamil Infarction Trial[114]	Denmark	Clinical trial. All AMIs. Aged less than 76 years	1979-1981	3073 (76%)	16% at 15 days	NA	17% at 15 days	NA	NA	Age sex interaction, p=0.02. Case fatality higher in young women than in men. Equal in sexes from age 64 years
EPESE Project[92]	New Haven, Connecticut	Longitudinal cohort study. All AMIs Aged ≥65 years	1982-1992	223 (46%)	25% at 30 days	NA	21.4% at 30 days	NA	NA	No
Göteborg AMI Study[79]	Sweden	Prospective study. All AMIs All ages	1986-1987	921 (67%)	12% at 30 days	NA	19% at 30 days	NA	1.12 (0.78-1.61) Age adjusted odds relative to men	NA
REGICOR Study[84]	Gerona, Spain	Clinical registry. First AMIs Aged 25 to 74 years	1978-1997	2769 (84%)	9.3% at 28 days	Age < 65 years,7% Age 65-74 years, 14%	18.8% at 28 days	Age < 65 years,7% Age 65-74 years, 27%	Age <65 years, 0.45 (0.19-1.04) MV adjusted odds relative to men Age 65-74 years, 1.62 (1.01-2.66) MV adjusted odds relative to men	Yes. Case fatality lower in younger women than younger men. Case fatality higher in women than in men aged 65-74 years

*** Age standardised**

One year case fatality

There are fewer studies describing case fatality following AMI after 28 days, and even fewer doing so in men and women separately. In addition, methodologies are not consistent in terms of whether the analyses include or exclude deaths within the first 28 days, one month or in-hospital time period. The study based on the Swedish National Acute Myocardial Infarction Register reported one year age specific case fatality rates in men and women after excluding deaths within the first 28 days (Table **14**).[111] Age standardised case fatality in 1995 at one year was 35% in men and in women. Sex-based differences varied according to age. The Trandoloapril Cardiac Evaluation (TRACE) Study included 4501 men and 2170 women aged between 45 years and 86 years admitted to coronary care units in Denmark following an AMI.[86] One year case fatality was 28% in women and 21% in men. These figures did not exclude early deaths and were not age adjusted. A study carried out on 1551 men and 538 women admitted to hospital in San Diego and Columbia with an AMI reported a one year case fatality of 13% in men and 11% in women.[115] These figures were unadjusted and excluded early in-hospital deaths. The MITI Registry reported case fatality in men and women who admitted to coronary care units in Washington between 1988 and 1994.[113] In this registry, one year case fatality was 24% in women and 16% in men. Case fatality was not age adjusted. In the EPESE Cohort, one year case fatality amongst those who survived the first 30 days was 21% in women and 34.4% in men.[92] The unadjusted female to male relative risk was 0.56 (0.31-1.02). In the Göteborg Study, one year unadjusted case fatality was 36% in women and 25% in men.[79] The unadjusted female to male relative risk was 1.54 (1.09-2.18).

Table 14 One year case fatality following acute myocardial infarction in men and women

Study	Location	Type of study	Year	No of subjects (proportion of men)	1 year Case-fatality in men (time)	Age-specific case-fatality in men	1 year Case-fatality in women	Age-specific case-fatality in women	Adjusted relative risk	Age-sex interaction
Swedish National AMI Register[111]	Sweden	Retrospective population-based study. First AMIs in that time period	1987-1995	353,905 (63%)	35%* one year (1995)	Age 30-49 years, 3% Age 55-59 years, 5% Age 65-69 years, 11% Age 75-79 years, 22% Age 85-89 years, 36%	35%* one year (1995)	Age 30-49 years, 4% Age 55-59 years, 6% Age 65-69 years, 11% Age 75-79 years, 20% Age 85-89 years, 33%	NA	Yes. P<0.0001.
MITI Registry[113]	Washington, USA	Prospective study. All AMIs admitted to CCU. All ages	1988-1994	12,331(66%)	16% one year	NA	24% one year	NA	NA	NA
TRACE Study[36]	Denmark	Clinical trial. All AMIs. Age 45-86 years	1990-1992	6671 (67%)	21% at one year	NA	28% at one year	NA	NA	NA
California and British Columbia Study[115]	USA and Canada	Prospective study. All AMIs. All ages	1979-1984	2089 (74%)	11% at one year excluding early in-hospital deaths	NA	13% at one year excluding early in-hospital deaths	NA	NA	NA
EPESE Project[92]	New Haven, Connecticut	Longitudinal cohort study. All AMIs. Aged ≥65 years	1982-1992	223 (46%)	34.4% at one year excluding deaths in first 30 days	NA	21% at one year excluding deaths in first 30 days	NA	0.44 (0.20-0.99) multivariable adjusted female to male relative risk	No
Göteborg AMI Study[79]	Sweden	Prospective study. All AMIs All ages	1986-1987	921 (67%)	25% at one year	NA	36% at one year	NA	1.06 (0.82-1.37) age adjusted female to male relative risk	NA

*Age standardised

2.5.1 Trends in short term survival in men and women following AMI

Many of the studies that examined short term case fatality following AMI, have also described trends in survival rates over time.[53;54;82;116] Although a number of studies have demonstrated a decline in short term case fatality over time in men and in women, the results of these studies are not consistent. In addition, not all studies have presented sex specific results or have adjusted survival to take account of variation in baseline characteristics and other prognostic factors over time.[117] Many of the studies have examined case fatality in all AMIs and do not distinguish between first and subsequent events.[53;82] Other studies, including many of the MONICA Studies, have included deaths following AMI that have occurred in those individuals who die before reaching hospital.[1;49;51;58] The Rochester (Minnesota) Epidemiology Project reported 28 day unadjusted case fatality rates for incident AMI of 10% in men and 14% in women in individuals hospitalised in 1979 (**Table** 15).[54] In 1994 the equivalent figures were 7% and 15%. No significant time trend was found in men or in women. The case fatality rate decreased over time in people aged less than 75 years old, but did not change in those aged greater than 75 years. Adjusted odds of death were not calculated for men and women separately. The Northern Sweden MONICA Project demonstrated a significant improvement between 1985 and 1994 in short term survival following an acute myocardial infarction.[82] Age standardised 28 day case fatality fell from 15% in men and 26% in women in 1989, to 10% in men and 18% in women in 1994. Previous analyses used multivariate modelling to explore sex differences in changing case fatality and found that after adjusting for other prognostic factors, the trends were only significant in men in whom adjusted odds of death declined by 56% in men between 1985 and 1994, $p<0.0001$.[116] The adjusted odds ratio in women was 0.95, $p=0.390$. The Minnesota Heart Survey demonstrated a decline in 28 day case fatality in men and women.[55] In men case fatality fell from 13% in 1985 to 10% in 1990 (adjusted relative risk 0.74, 95% CI 0.58-0.96). In women the equivalent figures were 15% and 12% (adjusted relative risk 0.84, 95% CI 0.62-1.13). The National AMI Register in Sweden reported declines in 28 day case fatality in men and women between 1987 and 1995.[50] Age standardised case fatality declined from 30% to 23% in men and from 28% to 23% in women. Multivariate modelling was not carried out. Data derived from the National Hospital Discharge Survey demonstrated a significant decline in in-hospital case fatality following AMI in men and in women.[53] Age adjusted in-hospital case fatality fell from 7% to 3.4% in men and from 8.2% to 4.4% in women between 1988 and 1997. The average annual percentage decline in case fatality was greater in older men and women compared to younger men and

women, although these figures were not reported. No clear trends in in-hospital case fatality between 1975 and 1988 were observed in men or women in the Worcester Heart Attack Study.[56] In the ARIC Study, the age adjusted 28 day case fatality rate fell by 4.1% per year in men and by 9.8% per year in women between 1987 and 1994.[57] This decline was statistically significant only among women. The Ontario Myocardial Infarction Database was used to describe 30 day and one year survival in 89,456 patients who were hospitalised between 1992 and 1997 following an AMI.[106] There was a gradual decline in overall 30 day case fatality in men and women during this period. Case fatality fell from 12.8% in men and 20.1% in women in 1992 to 11.6% in men and 19.1% in women in 1996. This trend was significant only in men. The declines were also significant in younger and older age groups, though sex specific analyses were not reported. Risk adjusted rates were not reported for men and women separately.

Table 15. Trends in short-term survival following acute myocardial infarction in men and women

Study	Location	Type of study	Years	No of subjects (proportion of men)	Case-fatality in men at start of study (time)	Case-fatality in men at end of study (time)	Significant change in case-fatality	Adjusted change in case-fatality	Case-fatality in women at start of study	Case-fatality in women at end of study	Significant change in case-fatality	Multivariate Adjusted change in case-fatality	Significant difference between men and women
Rochester (Minnesota) Epidemiology Project[54-56]	Olmsted County, Minnesota, USA	Longitudinal observational (retrospective) Population-based Incident AMI	1979-1994	1820 (56%) First AMIs All ages	10% at 28 days	7% at 28 days	No	NA	14% at 28 days	15% at 28 days	No	NA	NA
ARIC[57] Study	USA	Retrospective observational study. All AMIs. Age 35-74 years	1987-1996	14,842 AMIs (66%)	NA	NA	No -4.1%* per year (-10.5, +2.8)	NA	NA	NA	Yes -9.8%* per year (-2.3, -16.7)	NA	NA
Oxford Myocardial Incidence Study[59]	Oxford, UK	12 month prospective study. All non-fatal definite AMI (all, not first)	1966-7 1994-5	476 events (72%) in 1994-5 No data for 1966-7	27% * at 30 days Age 30-49, 37% Age 50-69, 25%	15% * at 28 days Age 30-49, 2% Age 50-69, 18%	Yes -43% * (73, -14% Age 30-49, -93% (-134, -53) Age 50-69, -29% (-66, 8)	NA	65% * at 30 days Age 30-49, 0% Age 50-69, 55%	44% * at 28 days Age 30-49, 25% Age 50-69, 48%	Yes - 53% * (-87, -19) Age 50-69, -58% (-90, -26)	NA	NA
Northern Sweden MONICA Study[82]	Northern Sweden	Population-based AMI study. All AMIs	1989-1995	3,152 (79%) Aged 35-64 years	15% * at 28 days	10% * at 28 days	Yes -5% * annual decline	NA	26% * at 28 days	18% * at 28 days	Yes -8% *annual decline	NA	No

***Age standardised**

Continued over...

Table 15 ***continued***

Study	Location	Type of study	Years	No of subjects (proportion of men)	Case-fatality in men at start of study (time)	Case-fatality in men at end of study (time)	Significant change in case-fatality	Adjusted change in case-fatality	Case-fatality in women at start of study	Case-fatality in women at end of study	Significant change in case-fatality	Multivariate Adjusted change in case-fatality	**Significant difference between men and women**
National Hospital Discharge Survey[53]	USA	Population based AMI study. All AMIs. Aged ≥35 years	1988-1997	NA	7.0%* in-hospital	3.4%* in-hospital	Yes. P=0.005	NA	8.2%* in-hospital	4.4%* in-hospital	Yes. P=0.02	NA	-
Swedish National AMI Register[111]	Sweden	Retrospective population-based study. First AMIs in that time period Age >19 years	1987-1995	353,905 (63%)	30% * at 28 days	23%* at 28 days	NA	NA	28%* at 28 days	23%* at 28 days	NA	NA	-
Minnesota Heart Survey[55]	Minneapolis-St-Paul, Minnesota, USA	Retrospective case note study. First events. Age 30-74 years	1985-1990	7,032 (70%) All AMIs First events, numbers not reported	13%* at 28 days	10%* at 28 days	Yes. Relative risk 0.74 (0.58-0.96) Adjusted for age and previous AMI	NA	15%* at 28 days	12%* at 28 days	No. Relative risk 0.84 (0.62-1.13). Adjusted for age and previous AMI	NA	-
Ontario Study[186]	Canada	Retrospective routine data linkage study. All AMIs All ages	1992-1996	89,456 (64%)	12.8% at 30 days	11.6% at 30 days	Yes. P<0.05	NA	20.1% at 30 days	19.1% at 30 days	No	NA	-

One year case fatality

Again there are few studies that have reported trends in one year case fatality. The study based on data from the National AMI Register in Sweden found that one year case fatality improved in men and women between 1987 and 1995.[50] Age standardised case fatality fell from 44% in men and 43% in women in 1987 to 35% in both sexes in 1995. Age specific rates were not reported. In the Ontario Myocardial Infarction Database there was a gradual decline in overall one year case fatality in men but not in women between 1992 and 1996.[106] Case fatality fell from 20.3% in 1992 to 19.1% in 1996 in men. In women case fatality remained relatively stable at 29.8% in 1992 and 29.9% in 1996. Virtually all of the improvement in one year survival in men occurred within 30 days of the AMI.

Table 16 Trends in One year Survival following Acute Myocardial Infarction in Men and Women

Study	Location	Type of study	Years	No of subjects (proportion of men)	One year Case-fatality in men at start of study (time)	One year Case-fatality in men at end of study (time)	Significant change in case-fatality	Adjusted change in case-fatality	One year Case-fatality in women at start of study	One year Case-fatality in women at end of study	Significant change in case-fatality	MV Adjusted change in case-fatality	Significant difference between men and women
Swedish National AMI Register[50]	Sweden	Retrospective population-based study. First AMIs in that time period Age>19 years	1987-1995	353,905 (63%)	44%*	35%*	NA	NA	43%*	35%*	NA	NA	-
Ontario Study[106]	Canada	Retrospective routine data linkage. All AMIs All ages	1992-1996	89,456 (64%)	20.3% at 30 days	19.1% at 30 days	Yes. P<0.05	NA	29.8% at 30 days	29.9% at 30 days	No	NA	-

2.6 Longer term Survival in men and women following first AMI

There are many fewer studies examining the longer term prognosis in men and women following AMI than there are examining short term case fatality (**Table** 17). Those that do exist are not consistent in their chosen end points or in their reporting of sex specific data.[56;118;119] For example the original Worcester Heart Attack Study looked at survival between one and 14 years but did not report these data in men and women.[56] The authors did however observe that no significant sex differences in either crude or age adjusted long term case fatality were seen. The Worcester Heart Attack continued and later analyses have reported two year case fatality in men and women survived hospitalisation for AMI between 1975 and 1995.[120] The overall two year case fatality rate was higher in women, 28.9% than in men, 19.6%. The effect of sex varied with age. The Minnesota Heart Survey reported three year case fatality in men and women aged 30 to 74 years between 1985 and 1990.[55] Three year age adjusted case fatality in individuals with a first AMI in 1990 was 18% in men and 24% in women. The REGICOR Study examined three year case fatality in men and women who had survived the first 28 days following their first AMI.[84] Unadjusted three year case fatality was 22% in men and 10% in women. The study only included individuals aged 25 years to 74 years. The TRACE Study examined longer term survival in men and women admitted to coronary care units between 1990 and 1992. Patients were enrolled in the study between 1990 and 1992 and were followed up until 1994.[86] Average length of follow up was not reported. After adjusting for age and excluding deaths occurring within the first 30 days, men had a 20% increased risk of death in the longer term (hazard ratio 1.2, 95% CI 1.1-1.3). A study was carried out using the Alberta Health and Wellness databases which included information on 7158 women and 15809 men admitted to hospital following an AMI between 1993 and 2000.[80] At five years crude case fatality was 38.8% in women and 26.8% in men. A study using the Helsinki Coronary Registry examined five year case fatality in 388 men and 178 women with a first AMI occurring between 1970 and 1971.[121] Five year age adjusted case fatality excluding the first 28 days was 17.3% in women and 26.3% in men. The sex difference was not statistically significant. In the Danish Verapamil Infarction Trial, patients were followed up for ten years.[114] Unadjusted case fatality at ten years excluding deaths within the first 15 days was 58.7% in men and 60.9% in women. After adjustment for age, long term case fatality was similar in men and women.

Table 17 Longer-term Case Fatality following Acute Myocardial Infarction in Men and Women

Study	Location	Type of study	Year	No of subjects (proportion of men)	Case-fatality in men (time)	Age-specific case-fatality in men	Case-fatality in women	Age-specific case-fatality in women	Adjusted relative risk	Age-sex interaction
Minnesota Heart Survey	Minneapolis-St-Paul, Minnesota, USA	Retrospective case note study. First events. Age 30-74 years	1985-1990	7,032 (70%) All AMIs First events, data not reported	18%* at three years (1990)	NA	24%* at three years	NA	NA	NA
TRACE Study[56]	Denmark	Clinical trial. All AMIs. Two to four years follow up	1990-1992	6671 (67%)	NA	NA	NA	NA	1.2 (1.1-1.3) age adjusted in men relative to women at 30 days to three years 1.16 (1.03-1.31) after adjusting for other factors	NA
MITI Registry[10]	Washington, USA	Prospective study. All AMIs admitted to CCU. All ages	1988-1994	12,331(66%)	20% at two years	NA	29% at two years	NA	0.92 (0.84-1.0) MV Adjusted odds ratio relative to men	NA
Worcester Heart Attack Study[56]	Massachusetts, USA	Prospective study. Population-based. First AMIs. All ages	1975- 1995 (6- one year periods)	6826 (62%) First AMIs who survived hospitalisation.	19.6% at two years	<50 years, 6.0% 50-59 years, 8.3% 60-69 years, 17.2% 70-79 years, 28.9% ≥80 years, 51.3%	28.9% at two years	<50 years, 8.9% 50-59 years, 11.5% 60-69 years, 18.4% 70-79 years, 31.0% ≥80 years, 46.0%	Age adjusted hazard ratio for women compared to men 1.40 in < 60 years, 1.05 in 60-69 years and 0.95 in ≥70 years.	Yes. For every ten years decrease in age the age adjusted hazard of death in women increased by 15.4% (4.3-27.6)

***Age standardised**

Continued over…

Table 18 *continued*

Study	Location	Type of study	Year	No of subjects (proportion of men)	Case-fatality in men (time)	Age-specific case-fatality in men	Case-fatality in women	Age-specific case-fatality in women	Adjusted relative risk	Age-sex interaction
Alberta Health and Wellness Databases[86]	Canada	Retrospective routine data study. All AMIs	1993-2000	22967 (69%)	26.8% at five years overall	NA	38.8% at five years overall	NA	0.99 (0.93-1.05) in men relative to women after adjustment for age and other factors	Significant, p=.008
Danish Verapamil Infarction Trial[114]	Denmark	Clinical trial. All AMIs. Aged less than 76 years	1979-1981	3073 (76%)	58.7% at ten years excluding first 15 days	NA	60.9% at ten years excluding first 15 days	NA	0.90 (0.80-1.01) in women relative to men after adjusting for age	Non-significant
Helsinki Coronary Registry	Finland	Registry. First AMIs. Aged <66 years	1970-1971	566 (69%)	26.3%* at five years excluding first 28 days	NA	17.3%* at five years excluding first 28 days	NA	NA	NA
REGICOR Study[84]	Gerona, Spain	Clinical registry. First AMIs Aged 25 to 74 years	1978-1997	2769 (84%)	22% at three years excluding first 28 days	NA	10% at three years excluding first 28 days	NA	1.3 (0.9-1.9) in women relative to men after adjusting for age and other factors	NA

***Age standardised**

2.6.1 Trends in longer term survival in men and women following AMI

There are few studies describing trends in longer term case fatality following AMI. In addition, the time periods chosen are not consistent so that comparison between studies is not easy. The Minnesota Heart Survey reported three year case fatality rates in men and women between 1985 and 1990 (**Table** 18).[55] Age adjusted case fatality following a first AMI declined in men and women during this time. In men case fatality fell from 21% in 1985 to 18% in 1990 and in women from 29% to 24%. Neither of these falls was statistically significant as demonstrated by the relative risk ratios.

Table 18 Trends in Longer-term Case Fatality following Acute Myocardial Infarction in Men and Women

Study	Location	Type of study	Years	No of subjects (proportion of men)	Three year Case-fatality in men at start of study (time)	Three year Case-fatality in men at end of study (time)	Significant change in case-fatality	Adjusted change in case-fatality	Three year Case-fatality in women at start of study	Three year Case-fatality in women at end of study	Significant change in case-fatality	MV Adjusted change in case-fatality	Significant difference between men and women
Minnesota Heart Survey	Minneapolis-St-Paul, Minnesota, USA	Retrospective case note study. First events. Age 30-74 years	1985-1990	7,032 (70%) All AMIs First events, data not reported	21%*	18%*	No. Relative risk 0.85 (0.67-1.08)	NA	29%*	24%*	No. Relative risk 0.81 (0.63-1.03)	NA	No

*** Age standardised**

2.7 Factors affecting survival following AMI in men and women

2.7.1 Age

Survival following AMI

The effect of age on survival following AMI has been extensively discussed in the literature. Age is widely reported to be strongest predictor of survival following AMI in men and women and sex differences in survival have often been attributed to differences in the age distribution of men and women. However many studies adjust for age but do not examine the magnitude of effect of age in men and women.[56;113] Age is not always included in models as a categorical variable so that the interpretation of its effect may not be straightforward. The Swedish National Myocardial Infarction Register Study reported age and sex specific 30 day case fatality rates.[111] Case fatality was only 8% in men and 14% in women aged less than 50 years but rose to 63% in men and 60% in women aged 85-89 years. The TRACE Study examined prognostic factors for 30 day case fatality following AMI in men and women separately.[86] In a multivariate model, a one year increase in age was associated with a 4% increase in the risk of death in men and women.

Determining the effect of age on survival following AMI is hindered by a lack of consistency in the age categorisation applied to the study populations involved and also by the tendency towards describing the effect of age on survival in the whole study population rather than men and women separately. In addition, many studies have reported age adjusted results so that the effect of age cannot be determined or described from the analyses performed.

Short term survival

A number of studies have reported short term age stratified case fatality rates in men and women following AMI.[59;78;83;111;112] In all these studies, case fatality rates rise substantially with increasing age. For example in the National Registry of Myocardial Infarction 2, 30 day case fatality rose steeply with increasing age from 2.9% in men aged less than 50 years to 25.3% in men aged 85-89 years.[78] There was a corresponding increase in women from 6.1% to 24.2%. In the Swedish National Register, 28 day case fatality rose from 5.7% in men aged 30-49 years to 43% in men aged 85-89 years.[111] The corresponding figures in women were 10.1% and 40.2% respectively. Age has been

consistently shown to have a powerful effect on prognosis, though the magnitude of that effect varies according to the study type and population. There are very few studies that have provided data regarding the independent effect of age on survival in men and women after adjusting for other baseline variables. The MONICA Breman Study reported the effect of age after adjusting for other baseline variables and found that every additional year led to an increased risk of 4% in 28 day case fatality.[112] Separate models were not carried out in men and women. The Swedish MONICA Project also examined the independent effect of age on survival, but again not in men and women separately.[82]

Longer term survival

There are few studies that have described the effect of age on longer term survival in men and women following AMI. Those that have examined longer term survival have usually presented their results using Kaplan Meier Survival Curves so that case fatality rates cannot be quantified easily. In the Worcester Heart Attack Study two year case fatality rates in men hospitalised with AMI who survived to discharge, increased from 6.0% in those aged less than 50 years to 51.3% in those aged greater than 79 years.[120] The equivalent figures in women were 8.9% and 46% respectively. There are no studies that report the effect of age on the adjusted risk of longer term case fatality following AMI in men and women.

2.7.2 Sex

Short term survival following AMI

Sex specific data are not always examined or reported. In addition, studies do not consistently examine the independent effect of sex on survival after adjusting for other prognostic factors, so that it may not be clear whether observed sex differences are due to sex differences in baseline characteristics such as age. In the Rochester (Minnesota) Epidemiology Project sex differences in short term survival were not modelled in multivariate analyses, making it difficult to make valid comparisons between men and women.[54] Most studies that have examined short term case fatality in men and women have reported higher unadjusted case fatality in women.[53;54;56;59;82;83;113] Studies that have gone on to adjust for sex differences in age and other prognostic factors have found conflicting results. It is not universally accepted that sex is an independent predictor of short term survival and a number of studies have attributed sex differences in survival to variation in baseline characteristics such as age and comorbid diagnoses.[112] The MITI

registry examined in-hospital survival in men and women admitted to coronary care.[113] Multivariate modelling adjusted for age, sex, history of congestive cardiac failure and of previous AMI. Women were still more likely to die with an odds ratio of 1.22 (95% CI 1.06-1.39).

Studies that have found that sex is not an independent predictor of short term survival

In the MONICA Bremen Study, 28 day case fatality was significantly higher in women (23.1%) than in men (16.1%).[112] Adjusting for sex differences in age reduced but did not eliminate the excess risk seen in women. Controlling for previous use of inotropic medicine and diuretics, during the event receipt of thrombolysis and platelet inhibitors and age in logistic regression analyses resulted in a similar 28 day mortality risk after acute myocardial infarction for both sexes (female/ male odds ratio=1.13, 95% CI 0.86-1.50). In the Worcester Heart Attack Study in hospital survival was similar in men and women after adjusting for prognostic factors including age in a multivariate model (odds ratio 0.90, 95% CI 0.70-1.16).[56] The factors controlled for in the multiple regression models included age, sex, year, medical history, AMI location and type, peak serum creatine kinase levels, congestive heart failure, cardiogenic shock as well as medication and surgical intervention. Age sex interaction terms were not explored in the models. In the Northern Sweden MONICA Project unadjusted case fatality was significantly lower in men than in women (12.7% versus 21.2% respectively). [82] In a multivariate model, the sex difference in 28 day case fatality was largely determined by other variables so that sex was not an independent predictor of outcome. Age sex interactions were explored but none were found to be statistically significant. Multiple logistic regression models included sex, age, diabetes, time to admission, admission to coronary care, thrombolytic therapy and smoking. In the EPESE Study which only included individuals aged 65 years and over hospitalised with AMI, unadjusted 30 day case fatality was 21.4% in women and 25% in men.[92] After adjusting for demographic factors, comorbidity, functional status, psychosocial factors and clinical severity the female to male relative risk was 0.85 (0.41-1.76). Case fatality at 30 days did not therefore differ significantly between the sexes.

Studies that have found that sex is an independent predictor of short term survival

In the National Hospital Discharge Survey, unadjusted and adjusted survival was higher in women than in men except in the very elderly.[53] Multivariate logistic regression was carried out on the whole group and in two age groups; age 35-64 years and age 64 and older. The models included age, sex, hypertension, hyperlipidaemia, diabetes, cardiogenic

shock, revascularisation, heart failure and length of stay. After adjusting for these factors, sex remained a significant predictor of in hospital case fatality with the odds of death 13% greater in women relative to men (odds ratio 1.13, 95% CI 1.12-1.13). The sex difference in survival was greater in younger than in older individuals. In the age group 35 to 64 years, the odds of death were 28% greater in women than in men. In individuals aged 65 and over, this figure declined to 9%. The MITI registry examined in-hospital survival in men and women admitted to coronary care.[113] Multivariate modelling adjusted for age, sex, history of congestive cardiac failure and of previous AMI. Women were still more likely to die with an odds ratio of 1.22 (95% CI 1.06-1.39). In ISIS-3 the unadjusted odds ratio of death among women compared to men was 1.73 (95% CI 1.61-1.86). Adjusting for age reduced this odds ratio to 1.20 (95% CI 1.11-1.29). Adjustment for other differences in baseline characteristics further reduced the odds ratio to 1.14 (95% CI 1.05-1.23). Multiple logistic regression models included the variables: age, sex, time since onset of pain, systolic blood pressure, heart rate, previous AMI and stroke, diabetes, smoking and ECG findings.

Studies that have found an interaction between sex and age in short term survival

In the Swedish National Acute Myocardial Infarction Register the age adjusted odds ratio for 28 day case fatality for women compared to men was 0.98 (95% CI 0.96-1.00). [111] This disguised variation between age groups in men and women. Women aged less than 75 years had a worse prognosis than men. For example, the odds ratio in women aged 30 to 49 years compared to men of the same age was 1.84 (95% CI 1.56-2.18). Conversely, women aged 75 years and over had a better prognosis than men. Formal testing of an age sex interaction was not reported. Case fatality was adjusted only for age and multivariate modelling was not carried out. The National Registry of Myocardial Infarction 2 found that sex-based differences in case fatality varied according to age, and that younger women but not older women had higher case fatality rates than men of the same age.[78] Among patients less than 50 years the case fatality rates were twice as high in women as in men. The difference in the rates decreased with increasing age and was no longer significant after age 74 years. An age sex interaction term was found to be highly significant, $p<0.001$. Multivariate analyses showed that the odds of death were 7% greater in women than in men for every five years decrease in age. In the Danish Verapamil Infarction Trial there was a significant interaction between age and sex for case fatality at 15 days, $p=0.02$.[114] Case fatality was higher in younger women compared to younger men but was similar in men and women from age 64 years. The REGICOR Study examined survival in

men and women following a first AMI, and found a significant interaction between age and sex. Unlike the other studies they found that women aged less than 65 years had a lower risk of death at 28 days than men.[84] The multivariable adjusted odds ratio for women relative to men was 0.45 (0.19-1.04) in individuals aged less than 65 years. Women aged 65 to 74 years however had a higher early risk of death than men of a similar age with an adjusted odds ratio of 1.62 (1.01-2.66). The difference in the results between this and other studies is attributed to differences in study design and methodologies and possibly because of differences in the incidence rate of AMI between Southern European Countries and American or Northern European Countries.

One year case fatality

In the Swedish Acute Myocardial Infarction Register, the effect of sex on case fatality at one year in those individuals who survived the first 28 days, varied according to age.[111] 4.0% of women and 2.9% of men aged less than 50 years were dead within one year (odds ratio 1.37, 95% CI 1.06-1.76). One year case fatality increased to 11% in men and women aged 65 to 69 years. After the age of 69 years, women had a small survival advantage. There was a significant interaction between age and sex ($p<0.0001$). In the MITI Registry, one year case fatality was similar in men and women after adjusting for age and other clinical and treatment variables.[113] In the Göteborg Study, unadjusted one year case fatality was 25% in men and 36% in women.[79] After adjusting for age, sex was no longer a significant predictor of outcome with an age adjusted relative risk of 1.06 (0.82-1.37). Early deaths were not excluded and the authors concluded that the increased case fatality seen at one year could be accounted for by older age of women. In the EPESE Cohort Study, women were almost twice as likely to survive one year compared to men both before multivariable adjustment (relative risk 0.56, 95% CI 0.31-1.02) and after controlling for other prognostic factors (relative risk 0.44, 95% CI 0.20-0.99).[92] One year survival excluded deaths within the first 30 days.

Longer term case fatality

In the TRACE Study the effect of sex was examined using Cox's Proportional Hazard models to the end of the study period, after excluding the first 30 days.[86] Average follow up was between two and four years. After adjusting for age, men had a significantly increased risk of death in the longer term, hazard ratio 1.20 (1.10-1.31). When other factors including body mass index, previous AMI or angina, creatinine, heart failure, diabetes, thrombolytic therapy and hypertension were taken into account, the risk of death

remained elevated in men compared to women with a hazard ratio of 1.16 (1.03-1.31). The authors therefore concluded that men had an increased longer term mortality relative to women that was not explained by variation in age and other factors. In the Worcester Heart Attack Study, no significant sex differences in either crude or age adjusted long term survival were seen.[56] Future analyses however on an extended database did however reveal sex differences in two year case fatality following discharge with AMI.[120] There was a significant interaction between age and sex and only women younger than 60 years had a higher mortality rate than men of a similar age. The age adjusted hazard ratio of death for women compared to men was 1.40 in those younger than 60 years of age, 1.05 in those aged 60-69 years and 0.95 in those at least 70 years old. This relationship was not altered by adjusting for other factors including demographic characteristics, clinical history and treatment. The hazard of death for women compared to men increased by 15.4% for every ten year decrease in age. In the MITI Study the two years unadjusted case fatality rates were 29% in women and 20% in men.[113] The adjusted hazard ratio for death in women compared to men was 0.92 (0.84-1.00). After excluding early in-hospital deaths there was a trend towards improved survival in women. The age adjusted hazard ratio was 0.87 (0.79-0.96). In the Alberta Study which looked at five year survival, sex was not a significant predictor of five year case fatality but did demonstrate a significant interaction with age so that its effect could not be simply described.[80] Higher unadjusted case fatality in women was confined to those aged less than 65 years who were at a significantly higher risk even after adjustment. In the Danish Verapamil Infarction Trial the overall age adjusted hazard ratio for women versus men was 0.90 (0.80-1.01).[114] There was no interaction between age and sex for long term case fatality.

2.7.3 Socioeconomic deprivation

Short term case fatality

There are few studies that have examined the relationship between socioeconomic deprivation and survival following AMI in men and women and the literature that does exist is not consistent in its findings. Most studies that have examined the relationship between socioeconomic deprivation and survival following AMI have looked at short term case fatality.[122] Many studies have not reported sex specific data or have excluded women from the study population.[122-124] A number of studies examining case fatality in men and women have included socioeconomic factors in multivariate models but have not reported their independent effects.[92] The Glasgow MONICA Coronary Event Register examined

the effect of socioeconomic group on short term survival on 2568 men and 1059 women aged 25 to 64 years admitted to hospital following an AMI.[75] They found no social class variation in in-hospital case fatality in men or women. There was however a socioeconomic gradient in the proportion of men and women reaching hospital alive with a decreasing proportion of men and women in more deprived quarters reaching hospital alive. In the FINMONICA Myocardial Infarction Register Study the age adjusted mortality rate ratios for death within 28 days showed three times higher mortality rates in the low income category compared with the high income category.[77] The findings were similar in women. Actual case fatality rates were not reported. Data from the Ontario Myocardial Infarction Database was used to examine the effect of socioeconomic status on one year case fatality following AMI.[122] The study found that income was a consistent predictor of case fatality and that this effect was substantial. The effect was consistent amongst age groups. Although the study included men and women and adjusted for the effect of sex, it did not examine the effects of income in men and women separately.

2.7.4 Diabetes

There are a number of studies that have examined the impact of diabetes on survival following AMI in men and women. Most studies have looked at diabetes as a predictive variable in multivariate analyses examining survival following AMI, whereas a smaller number have only included those individuals with a diagnosis of diabetes and AMI.[125]

Short term case fatality

A limited number of studies have found that women are at an increased risk of death after AMI compared to men with diabetes.[125-128] Not all these studies have disentangled the effects of sex and the effects of diabetes and any interaction between them, on case fatality. The Worcester Heart Attack Study examined sex differences in short and longer term survival following AMI in 1354 men and 1280 women between 1975 and 1999.[125] Unadjusted in-hospital case fatality rates were higher in women than in men. Average in-hospital case fatality was 14.9% in men and 21.3% in women. Women with diabetes remained at a significantly increased risk of in-hospital death compared to men with diabetes after adjusting for age, comorbidities and AMI associated characteristics. The adjusted odds ratio was 1.37 (1.08-1.75). Compared to the referent group of men without diabetes, women without diabetes had an increased risk of in-hospital death with an adjusted odds ratio of 1.06 (0.90-1.24). Women with diabetes had an increased risk of 1.24 (1.02-1.51) when compared to women without diabetes whilst men with diabetes had an

increased risk of 1.05 (0.85-1.29) when compared to men without diabetes. In the Secondary Prevention Reinfarction Israeli Nifedipine (SPRINT) Study, diabetes was a significant predictor of in-hospital death after AMI in women but not in men.[126] After adjusting for age as well as clinical variables, the relative odds of death in women with diabetes compared to women without diabetes was 1.92 (1.4-2.55). In men there was an increased risk of 24% which was not significant. The MONICA Project in New South Wales examined 28 day case fatality in 3643 men and 1679 men admitted to hospital following a first AMI between 1985 and 1994. The age adjusted 28 day case fatality rate for women with diabetes (25%) was significantly higher than for women without diabetes (16%). The age adjusted relative risk was 1.56 (1.19-2.04). The difference in men was also significant (25% with diabetes and 20% without diabetes, relative risk 1.25, 1.02-1.53).[129] However, after adjusting for age, year of diagnosis, smoking, hypercholesterolaemia and hypertension, the increased risk associated with diabetes was no longer statistically significant in men. The authors therefore concluded that the effect of diabetes on short term case fatality was therefore greater in women than in men. Other studies have found no significant difference in the effect of diabetes in men and women on survival following AMI.[130-132] In the National Registry of Myocardial Infarction 2, women were at increased risk of in-hospital death after adjusting for clinical and treatment variables.[131] The adjusted odds of death in women compared to men was similar in people with diabetes, odds ratio 1.25 (1.17-1.35) and people without diabetes, odds ratio, 1.32 (1.25-1.39). Diabetes had a similar effect on case fatality in men, odds ratio 1.45 (no CI), and in women, odds ratio 1.38 (no CI). In the Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI) Study which examined one year case fatality in men and women with diabetes, sex was not an independent predictor of outcome after adjusting for other factors.[130]

Longer term case fatality

There are far fewer studies that have examined the impact of diabetes on long term survival following AMI in men and women. These studies have not been consistent in their results but have generally shown a greater impact of diabetes in women than in men on long term case fatality following AMI.[128;132-134] In the Framingham Study men and women who had survived an AMI were followed up for 34 years.[128] Diabetes was an important factor in determining survival. In individuals with diabetes, the age adjusted risk of fatal coronary heart disease was increased more in men than in women. The age adjusted relative risk for fatal coronary heart disease was 1.8 (1.2-2.9) in men and 2.6 (1.4-4.7) in men. The Determinants of Myocardial Infarction Onset Study included 1935 men

and women hospitalised with AMI between 1989 and 1993.[135] During an average follow up period of approximately four years, the risk of dying in patients with diabetes compared with patients without diabetes was almost two times higher among women compared to men. In the Worcester Heart Attack Study the differences in post-discharge survival between men and women with diabetes declined during the ten year follow up period.[125] There were no significant differences in long term survival rates between men and women with diabetes after adjusting for other prognostic factors. In the SPRINT Study the risk of death up to ten years after an AMI was higher among women with diabetes who were treated with insulin than men with diabetes who were treated with insulin.[133] However long term case fatality was similar in men and women treated with oral hypoglycaemic agents. One study has shown that the effect of diabetes is stronger on long term than short term case fatality, and that the impact accelerates over time.[134] Sex specific results were not reported.

Diabetes is the most widely studies comorbid condition in relation to AMI survival. There are fewer studies that have examined the independent effects of other comorbid conditions on the prognosis following AMI in men and women.

2.7.5Heart failure

Short term case fatality

There are far more studies that have looked at the development of heart failure following AMI than there are that have examined the association between pre-existing heart failure and AMI survival. The occurrence of heart failure in patients with AMI has been consistently recognised as a significant and powerful predictor of prognosis, with individuals who develop heart failure experiencing poorer survival than those who do not. The National Registry of Myocardial Infarction database 2 and 3 included data on 605,500 patients hospitalised with AMI between 1994 and 2000. Patients with a previous history of heart failure were excluded from the study.[136] Of those hospitalised with AMI, 29% developed heart failure during their admission. The unadjusted in-hospital case fatality rate for patients with AMI complicated by heart failure was 24% compared to 6.2% in patients without heart failure. After adjusting for clinical and demographic factors, the odds of dying remained significantly elevated in patients with heart failure (adjusted odds ratio 3.8, 95% CI 3.7-3.9), compared to those without heart failure. Sex specific data were not presented and gender effects were not examined. In the Worcester Heart Attack Study, heart failure developed in approximately 38% of patients with AMI over the 20 year study

period.[137] In 1993 to 1995 the in-hospital case fatality rate in patients with heart failure was 17.7% compared to 7% in those without heart failure. The multivariable adjusted odds of dying in those with heart failure was 2.71 (2.31-3.18) compared to those without heart failure. Again sex specific analyses were not reported, although sex was included in the multivariate models. Both of these studies included first and recurrent AMIs.

Longer term case fatality

The Rochester Epidemiology Project examined the development of new onset heart failure in 1915 individuals with a first AMI and no prior history of heart failure.[138] Of these, 41% developed new onset heart failure during an average of over six years follow up. Survival was examined at one and five years after the onset of heart failure. In those patients who developed heart failure, male sex was associated with a 38% increase in the risk of death compared to female sex after adjusting for age and other prognostic factors. Survival was not compared between those who did and did not develop heart failure.

2.7.6Chronic obstructive pulmonary disease

There are few studies that have included COPD in their description of baseline characteristics or in their analysis of prognostic factors following hospitalisation for AMI. No studies have examined the prognostic significance of a COPD diagnosis on outcome in men and women separately. The Cardiovascular Cooperative Project examined one year case fatality in 54,962 patients hospitalised with AMI.[102] Of these, 21% of men and 18.7% of women had a diagnosis of COPD or asthma. In 23% of men and 15% of women the diagnosis of COPD or asthma was severe. Unadjusted one year case fatality was 23.3% amongst those with a diagnosis of severe COPD or asthma compared to 10% in those without COPD or asthma. Sex specific figures were not reported. The TRACE Study examined the relationship between COPD and survival following AMI.[103] Unadjusted case fatality was 13.7% at 30 days, 27.8% at one year and 57.1% at five years in patients with a diagnosis of COPD compared to 12% at 30 days, 22.5% at one year and 42.5% at five years in those without a diagnosis of COPD. The overall unadjusted relative risk of COPD was 1.49 (1.35-1.65). In multivariate analyses, COPD was an independent predictor of long term case fatality after adjusting for other factors. The relative risk was 1.15 (1.04-1.28). Sex specific analyses were not carried out. Sub-analyses were performed to examine the interaction of a COPD diagnosis with congestive heart failure. These analyses revealed that COPD was a predictor of long term case fatality following AMI only in those patients without a diagnosis of congestive heart failure. The SPRINT Study examined the

relationship between COPD and outcome and found that it was not a significant predictor of five year survival after adjusting for other factors.

2.7.7 Atrial fibrillation

Many of the studies that have described the incidence or prevalence as well as the prognostic significance of atrial fibrillation are clinical trials. The study populations of clinical trials tend to be younger and fitter and are rarely generalisable to the general population. A number of studies, such as GISSI-3, have distinguished between new-onset atrial fibrillation and chronic atrial fibrillation.[100] Previous studies have reported conflicting findings regarding the prognostic significance of atrial fibrillation and AMI and there is some evidence to suggest that this may depend upon the time of atrial fibrillation onset. Both the GUSTO I Trial and the Cooperative Cardiovascular Project found that patients with atrial fibrillation on arrival to hospital had only a small risk of mortality whereas those who developed atrial fibrillation during hospitalisation had a substantially increased risk of death.[94;139] A Japanese Study that examined 1039 patients hospitalised with AMI also found that the onset time of atrial fibrillation was a important parameter in determining the impact of atrial fibrillation on prognosis.[99] None of these studies have reported sex specific analyses.

Short term case fatality

The Cooperative Cardiovascular Project examined the prevalence and prognostic significance of atrial fibrillation in AMI.[94] The study was confined to individuals aged greater than 64 years. Patients with atrial fibrillation had higher in-hospital, 30 days and one year case fatality. Overall case fatality was 29.3% at 30 days and 48.3% at one year in patients with atrial fibrillation compared to 19.1% and 32.7% in those without atrial fibrillation. Sex specific data were not reported. When adjusted for other prognostic factors, atrial fibrillation increased the odds of death by 20% at 30 days and by 34% at one year. The TRACE Study examined the occurrence and prognostic significance of atrial fibrillation following AMI.[95] Unadjusted in-hospital case fatality was 18% in patients with atrial fibrillation which was significantly higher than in patients without atrial fibrillation. After adjustment for baseline characteristics, the presence of atrial fibrillation increased in hospital case fatality by 50% (odds ratio 1.5, 95% CI 1.2-1.8).

Longer term case fatality

There are fewer studies examining the association between atrial fibrillation and longer term survival following AMI. In the TRACE Study, five year case fatality excluding in-hospital deaths was elevated in individuals with atrial fibrillation when compared to those without this diagnosis (hazard ratio 1.3, 95% CI 1.2-1.4).[95] Again, sex specific analyses were not reported. The SPRINT Trial examined the relationship between paroxysmal atrial fibrillation and long term survival following AMI.[140] Patients with paroxysmal atrial fibrillation who survived hospitalisation had approximately two-fold higher five year case fatality rates when compared to those without paroxysmal atrial fibrillation (43.5% versus 25.4% at five years). The multivariate adjusted relative risk associated with paroxysmal atrial fibrillation was estimated to be 1.28 (95% CI, 1.12-1.46).

2.7.8 Hypertension

Many of the studies that have examined prognosis following AMI have included hypertension in their description of baseline characteristics and analysis of potential independent prognostic factors. However, as for other baseline characteristics, few of these studies have reported sex specific analyses. In addition the definition of hypertension varies, may be based on different criteria and is not always described.

Short term case fatality

The Rochester, Minnesota Study examined the relationship between hypertension and survival following AMI in 1321 individuals diagnosed with first AMI between 1960 and 1975.[141] 30 day case fatality rates were elevated in individuals with hypertension. The age adjusted 30 day case fatality rate was 13% in normotensive and treated hypertensive, 16% in borderline and 19% in untreated hypertensive patients. Sex specific data were not reported.

Longer term case fatality

The Framingham Heart Study examined the relationship between pre-existing hypertension and the risk of adverse outcomes after initial AMI.[142] Mean follow up was 7.85 years. Median survival was 12.19 years, 8.8 years and 4.18 years among normotensive, untreated hypertensives and treated hypertensives respectively. After excluding deaths within 30 days, and adjusting for other prognostic factors, untreated and treated hypertensives had an increased risk of death (hazard ratios relative to normotensive group, 1.19 and 1.69

respectively). The Survival and Ventricular Enlargement (SAVE) Clinical Trial examined and compared outcomes in 906 patients with hypertension and 1325 patients without hypertension.[143] All patients had survived an AMI and had left ventricular systolic dysfunction. Mean follow up was 42 ± 10 months. Case fatality was higher in patients with hypertension than in those who were normotensive, 27.4% versus 19.3%. After adjusting for known risk factors, patients with hypertension had a significant increase in the risk of death (hazard ratio 1.25, 95% CI 1.02-1.53). Sex specific results were not reported.

2.7.9Renal impairment

It is only relatively recently that studies have examined the relationship between renal impairment and outcome following AMI. Survival of patients with renal failure is considerably worse than survival of patients without renal failure and patients with other comorbid diagnoses. There is however a lack of data describing the impact of renal impairment on survival following AMI in men and women separately as studies have usually categorised risk in terms of the degree of renal impairment rather than on the basis of sex. In addition many of the multivariate models that have been used to examine the prognostic significance of factors thought to affect survival have included sex. For renal failure, the interpretation of these findings is complicated by the fact that sex is incorporated into the estimation and definition of glomerular filtration rate, creatinine clearance and elevated creatinine levels. This may bias the results of any multivariate analyses that further adjust for the effects of sex.

Short term case fatality

Data from the Mayo Clinic and the Veterans Affairs Hospital at the University of San Francisco illustrated the significant excess mortality risk faced by those with renal impairment who had experienced an AMI.[90] Renal function was estimated according to creatinine clearance and stratified into five groups. In-hospital case fatality rates were 2% in patients with normal renal function, 6% in those with mild renal failure, 14% in those with moderate renal failure and 21% in those with severe renal failure. The adjusted risk of death followed a similar gradation of risk with mild renal failure being associated with an odds ratio of 1.9 (1.1-3.1) and severe renal failure an odds ratio of 5.1 (2.2-12.1) relative to normal renal function. Sex specific data were not reported. Data pooled from the Thrombolysis In Myocardial Infarction (TIMI) trial 10A, 10B, and 14 trials, were used to examine the association between impaired renal function and 30 day case fatality in

individuals hospitalised following an AMI who had been treated with thrombolysis.[144] The study found that impaired renal function was associated with increased case fatality after adjusting for other prognostic factors. Renal impairment was measured using creatinine levels and creatinine clearance. For both measures there was a stepwise increase in case fatality among patients with normal, mildly and severely impaired renal function. The odds ratio for death in individuals with severe renal impairment relative to normal renal function was 3.81 (95% CI 2.57-5.65), as measured by creatinine clearance. No sex specific data were reported. Renal impairment has also been shown to relate to one year case fatality. The Cooperative Cardiovascular Project also found that renal impairment was an independent predictor of death following an AMI. Unadjusted one year case fatality was 24% in those with normal renal function, 46% in those with mild renal impairment and 66% in those with moderate renal impairment.[89] A study carried out in Boston and Framingham, Massachusetts, examined one year case fatality in 562 individuals hospitalised following AMI between 1991 and 1992.[145] 22% of these individuals had a raised creatinine level. One year case fatality was 46% in these individuals compared to 15% in those with a normal creatinine level. After multivariate adjustment, one year case fatality remained elevated in individuals with raised creatinine with a hazard ratio of 2.40 (1.55-3.72).

Longer term case fatality

There are few studies that have examined the longer term prognosis of individuals hospitalised with AMI who also have renal failure. The United States Renal Data System was used to identify those individuals on renal replacement therapy who were hospitalised with a first AMI between 1977 and 1995.[146] Case fatality in these individuals was 51.8% at two years and 70.2% at five years. The Mayo Study followed-up individuals hospitalised with AMI for up to five years and found an increased long term risk of death in individuals with renal dysfunction who were hospitalised with AMI.[90] The adjusted hazard ratio was 5.4 in patients with end stage renal disease compared to those with normal renal function. Again there was a gradation of risk of death associated with the degree of renal impairment and individuals with mild renal insufficiency had 2.4 times the risk of death compared to those individuals with normal renal function.

2.7.10 Other vascular diseases

As for COPD there is a lack of data describing the prevalence and prognostic significance of other vascular diseases in men and women following hospitalisation with AMI. The

SPRINT Trial, which was carried out between 1981 and 1983, reported a peripheral vascular disease prevalence of approximately 6% in men and women hospitalised with a first AMI.[105] In-hospital, one year and five year case fatality rates were significantly higher amongst those with a diagnosis of PVD compared to those without a diagnosis of PVD. One year and five year case fatality rates excluded in-hospital deaths. Case fatality in those individuals with a diagnosis of PVD was 24% in-hospital, 12% at one year and 33% at five years. The same figures in those without a diagnosis of PVD were 13%, 7% and 22% respectively. The multivariate adjusted odds of death for in-hospital case fatality following AMI in patients with PVD relative to those without PVD were 1.37 (1.03-1.83). PVD was not independently associated with longer term (mean follow-up 5.5 years) case fatality. Sex specific figures were not reported.

2.7.11 Previous coronary heart disease

Short term case fatality

A number of studies have included a previous history of angina in their description of baseline characteristics of individuals hospitalised with AMI and analysis of prognostic factors. Studies have tended to use different definitions of angina and age and sex specific figures are rarely reported. It has been estimated that approximately one half of individuals hospitalised with AMI have a history of angina pectoris.[147] Studies examining the prognostic significance of previous angina in individuals hospitalised with AMI have reported conflicting results.[148-152] A number of studies have suggested that myocardial preconditioning may occur.[151-153] Myocardial preconditioning is a phenomenon in which brief episodes of ischaemia and reperfusion protect the myocardium against prolonged ischaemic damage.[153] In the Thrombolysis in Myocardial Infarction (TIMI) 4 Study, previous angina was found to have a beneficial effect on in-hospital outcome after AMI, although this effect was not statistically significant and sex specific figures were not reported.[152] The Japanese Acute Coronary Syndrome Study found that preinfarction angina had a beneficial effect on in-hospital outcome, but only in individuals with anterior AMI.[154] In the Göteborg Study, the in-hospital case fatality rate was similar in individuals with and without a previous history of angina and angina was not an independent predictor of death during the in-hospital period.[147] However individuals with previous chronic angina did have a worse one year prognosis than individuals without previous chronic angina. In the SPRINT Registry a history of previous chronic angina was associated with a higher in-hospital case fatality rate in individuals hospitalised with a first AMI (16% versus 12%, $p<0.0001$).[149] The literature regarding the effect of previous angina on short

term case fatality following AMI is therefore conflicting. There is evidence to suggest that the effect of previous angina on short term survival may depend upon how long the individual has had angina for, the site of infarct as well as the age of the patient.[151;154;155]

Longer term case fatality

Fewer studies have examined the relationship between previous angina and longer term prognosis following AMI. In the TIMI 4 Study, although previous angina improved in-hospital outcome, there was no long term benefit of this diagnosis.[152] In the SPRINT Registry a history of previous angina was associated with higher five year case-fatality rates (26% versus 19%, p<0.0001).[149] The Framingham Study also reported higher long term case fatality rates in individuals with a previous history of angina.[93] After adjusting for the effect of age, this association was significant only in men in whom the risk of coronary death was increased by 49% in individuals with a previous history of angina. It is therefore apparent that there is very little literature that has examined the relationship between previous angina and short and long term in individuals hospitalised with a first AMI.

2.7.12 Previous AMI

Short term case fatality

Many studies have described the prevalence of a previous AMI and have also adjusted for the potential effects of a previous AMI on prognosis following a subsequent AMI.[78;82;83;85;147;151] However few studies have examined the independent effect of a previous AMI on survival in men and women following hospitalisation with a subsequent AMI. The Northern Sweden MONICA Project included previous AMI in its multivariate analyses of in-hospital survival which were carried out in men and women separately.[82] Previous AMI was not a significant independent predictor of outcome although the p-value and odds ratio were not reported.

Longer term case fatality

Very few studies have examined the prognostic effect of previous AMI on survival following a subsequent AMI. A Japanese Study carried out between 1981 and 1990 examined prognosis in 350 individuals hospitalised with an anterior AMI and found that previous AMI was not a significant predictor of outcome at five years.[151]

2.8 Incidence of and trends in incidence of second acute myocardial infarction

Whilst there is a considerable literature examining the incidence of first AMI, there is little known about trends in the incidence of and prognosis after second infarction. No studies have reported the incidence rates of second AMI in men and women. A number of studies have looked at of the risk of re-infarction during an in-hospital stay,[83;113;156;157] and the short-term incidence of re-infarction has been examined in some clinical trials.[157-160] The GUSTO I and III trials described re-infarction rates in 52,662 men and women with an ST-segment elevation AMI who received fibrinolysis.[157] It reported an in-hospital re-infarction rate of 4.3% (Table 19). The GISSI-2 Study analysed re-infarction rates amongst hospital survivors of AMI treated with thrombolysis.[159] The post-discharge to six-month incidence rate of AMI was 2.9% overall. None of the trials reported sex-specific figures though the independent effect of sex examined in multivariate models looking at predictors of subsequent AMI. The Framingham Heart Study compared one, five and ten-year re-infarction rates in subjects with Q-wave and non-Q-wave infarctions.[161] The study included 227 men and 136 women with a first AMI and a mean duration of follow-up of 5.1 years. The five-year re-infarction rates were 20.6% in Q-wave and 32.4% in non-Q-wave infarctions. The numbers of re-infarctions was small and sex-specific figures were not reported. The First Danish Verapamil Infarction Trial Database examined ten year reinfarction rates in 5993 patients hospitalised with AMI who survived to day 15.[160] The ten year re-infarction rate was 49.8% in men and 45.6% in women. This difference was not statistically significant. The Rochester Study examined reinfarction rates in 1013 men and women hospitalised with a first AMI, who survived the first 30 days, between 1960 and 1979.[87] The rates of reinfarction were higher in men than in women. The five year age adjusted reinfarction rate per 100 person-years was 7.3% in men and 5.9% in women in the 1970-1979 cohort. The Göteborg Study reported one year reinfarction rates in 621 men and 300 women hospitalised with AMI between 1986 and 1987.[79] 17% of men and 15% of women were hospitalised with a recurrent AMI in the year subsequent to their index admission.

All of these studies have looked at re-infarction rate within a defined and usually short time period, rather than incidence rate of subsequent AMI. The numbers are consequently small and sex-specific data rarely reported. A number of studies including many of the MONICA Studies and the ARIC Study have looked at population incidence of recurrent events (Table 20). The ARIC Study examined trends in incidence of recurrent AMI in men

and women between 1987 and 1996.[62] They reported significant declines in the incidence of recurrent events in residents aged 35-74 years. The incidence rate fell by 1.9% in men and 2.1% in women. The Toulouse MONICA Study described the AMI recurrence rates, between 1985 and 1993, in individuals aged 35 to 64 years.[58] In men, age-standardised rates for recurrent AMI declined by 1.9%, and in women, increased by 1.4%. Neither trends reached statistical significance. The National Health and Nutrition Examination Survey Epidemiological Follow-up Study examined trends in incidence and recurrence rates of AMI in two cohorts, between 1971 and 1992.[60] They reported a 21.9% decline in recurrent AMI rate in white men but a 35.2% increase in white women. Both trends were statistically significant.

Table 19 Incidence of recurrent or second AMI

Study	Type of study	Location	Year	No of subjects (proportion of men)	No of second AMIs (proportion of men)	Age group (years)	Overall incidence (%). Time	Overall incidence in men . Time	Overall incidence in women. Time
GUSTO I & III Studies[157]	Clinical trial	Multinational	1990-7	52,662 first AMIs (69%)	2,258 (67%)	Age 52-73 years	4.3% in-hospital	NA	NA
GISSI-2 Study[159]	Clinical trial	Italy	1990 (Published)	8,907 first AMIs (82%)	260	61 years (overall mean)	2.9% at 6 months in hospital survivors	NA	NA
SPRINT Trial[158]	Clinical trial	Israel	1981-3	3,695 first AMIs (76%)	220 (72%)	NA	6.0% at one year in hospital survivors	5.7% at one year	6.9% at one year
MITRA & MIR Studies[156]	Registries	Germany	1994-8	22,613 first AMIs	1071 (59%)	NA	4.7% in hospital	4.3% in hospital	5.7% in-hospital
Framingham Heart Study[161]	Cohort study	USA	1971-1987	363 first AMI (63%)	68 (59%)	NA	Q-wave, 21% at 5 years Non-Q-wave, 32% at 5 years Q-wave, 27% at 10 years Non-Q-wave, 45% at 10 years	NA	NA
Gilpin et al[162]	Prospective study	USA	1979-1989	3,666 AMIs All AMIs	171 (70%) recurrent non-fatal AMIs	62 years (overall mean)	4.7% at one year	NA	NA
First Danish Verapamil Infarction Trial Database[160]	Clinical trial	Denmark	1979-1981	5993 (72%) AMIs All AMIs who survive first 15 days	1046 (78%) recurrent non-fatal AMIs	<76 years	48.8% at ten years	49.8% at ten years	45.6% at ten years
Rochester Study[87]	Cohort study	USA	1960-1969 cohort 1970-1979 cohort	1013 AMIs. All AMIs who survive first 30 days	280 hospitalised reinfarctions	All ages	NA	7.3 /100 person years	5.9 /100 person years
Göteborg AMI Study[79]	Sweden	Prospective study	1986-1987	921 (67%) All AMIs All ages	148 (70%) hospitalised reinfartions	Median age in men-69 years Median age in women - 76 years	NA	17% at one year	15% at one year

Table 20 Trends in the incidence of second or recurrent AMI

Study	Location	Type of study	Years of study	No of Events (% men)	Incidence in men at start of study period	Incidence in men at end of study period	Change in men	Incidence in women at start of study period	Incidence in women at end of study period	Change in women
ARIC Study[57]	USA	Observational study. Definite and probable AMI. First and recurrent events Retrospective Age 35-74 years	1987-1996	14,842 events All events, not first (66%)	410 per 100,000*	410 per 100,000*	-1.9%* decrease per year in recurrent AMI. Significant	190 per 100,000*	180 per 100,000*	2.1% * decrease per year. Significant
Toulouse MONICA Study[58]	France	Coronary event register. All events including first and recurrent and out of hospital deaths. Age 35-64 years	1985-1993	3,174 (85%) All events, not first	47 per 100,000*	44 per 100,000*	-1.9% decline (crude) Non-significant	5 per 100,000*	3 per 100,000*	-1.4% decline (crude) Non-significant
NHANES 1 Epidemiological Follow up Study[60]	United States	Two cohort Study.	One cohort, 1971-1982 Second cohort, 1982-1992	20,643 individuals in cohort. 941 first AMI (60%) Age NA	NA	NA	-21.9%* decline in white men. (crude). Significant	NA	NA	+35.2% increase in white women (crude). Significant

***Age standardised**

2.9 Factors predicting a subsequent AMI

A number of studies, including clinical trials, have attempted to examine the independent predictors of re-infarction. Many of these have looked at in-hospital re-infarction.[156;157] In the GUSTO I and III Trials, the most important predictors of in-hospital re-infarction were age, time to fibrinolysis, previous coronary heart disease and anterior AMI.[157] Sex was also a significant predictor with women being more likely to experience re-infarction, after adjusting for other factors. In the SPRINT Trial, women were again more likely to experience a recurrent AMI by one year, though this increased risk did not reach statistical significance in a multivariate model.[158] Significant predictors of re-infarction included age, previous angina, diabetes, heart failure and peripheral vascular disease. In the Maximum Individual Therapy in Acute Myocardial Infarction (MITRA) and the Myocardial Infarction Registry (MIR), female sex was independently associated with an increased risk of re-infarction during the in-hospital period (odds ratio 1.14, 95% CI 1.05-1.32).[156] Other predictive factors included age and previous AMI. None of these studies examined predictive factors in men and women separately and in general the predictive ability of the multivariate models were low, for example 63% of re-infarctions in the GUSTO I and III Studies were correctly identified.[157] The Rochester Study was unable to identify any factors that were significant predictors of subsequent infarction.[87]

2.10Survival following a second or recurrent AMI

There are few data describing prognosis following a recurrent AMI and no data looking specifically at prognosis following second AMI. Some of the MONICA Studies have looked at survival following a recurrent AMI, however these have mainly included out-of-hospital deaths and have not reported the prognosis of recurrent hospitalised AMI.[58;163] Other studies have examined a prior history of AMI or ischaemic heart disease as an independent predictor of prognosis. These studies provide an estimate of the excess risk associated with previous AMI, but do not provide an estimate of absolute risk or of how this risk might vary according to age, sex and socio-economic deprivation status. The SPRINT Trial examined the in-hospital case fatality of individuals who experienced a second AMI within one year of their first AMI.[158] The overall in-hospital case fatality rate was 31%. In those individuals with a second AMI who survived hospitalisation, the one year case fatality rate was 11.8% and the five year case fatality rate was 40.1%. Sex specific data were not reported. In the MITRA and MIR Study, the authors examined in-

hospital case fatality in those individuals hospitalised with an AMI who experienced a recurrent AMI during their index hospital admission.[156] Sex specific data were not reported. The overall in-hospital case fatality rate for individuals who experienced a re-infarction was 41.2%. The Study by Gilpin et al examined case fatality at one year in 3,666 individuals hospitalised with an AMI.[162] Of these, 171 (4.7%) experienced a recurrent AMI within a one year time period. Case fatality was higher in this group, and at one year was 16.4% compared to those who had not experienced a recurrent AMI. The one year follow up was taken from the time of the index admission and not from hospitalisation with the recurrent AMI. Sex specific data were not reported. The GUSTO I and III Studies carried out similar analyses and compared 30 day case fatality in those individuals hospitalised with an AMI who did and did not experience hospitalisation with a recurrent AMI.[157] Overall 30 day case fatality was 11.3% in those with reinfarction compared to 3.5% in those without reinfarction. Sex specific data were again not reported.

2.11 Factors affecting survival following a second AMI

Very few studies have examined factors that predict survival following a second or recurrent AMI. The 60 Minutes Myocardial Infarction Project examined in-hospital case fatality in 2854 individuals hospitalised with reinfarction between 1992 and 1994, and compared it to the in-hospital case fatality observed in 12,126 individuals hospitalised with first AMI.[164] Case fatality was higher in individuals hospitalised with a recurrent AMI compared to those hospitalised with a first AMI (23% versus 15% respectively). Multivariate analyses were not used and sex specific figures were not reported. A number of studies have however looked as subsequent AMI as a predictor of death following a first event. In the SPRINT Trial which examined case fatality in individuals hospitalised with a second AMI, multivariate modelling was used to determine whether re-infarction was an independent predictor of case fatality following a first AMI.[158] However, the study did not examine the independent predictors of case fatality following a second AMI.

Table 21 Survival following admission to hospital with a second or recurrent AMI

Study	Location	Type of study	Year	No of subjects (proportion of men)	Case-fatality in men (time)	Age-specific case-fatality in men	Case-fatality in women	Age-specific case-fatality in women	Adjusted relative risk	Age-sex interaction
SPRINT Trial[158]	Clinical trial	Israel	1981-3	3,695 first AMIs (76%) 220 (72%) second AMIs	31% in hospital in men and women	NA	31% in hospital in men and women	NA	NA	NA
GUSTO I & III Studies[157]	Clinical trial	Multinational	1990-7	52,662 first AMIs (69%) 2,258 (67%) recurrent AMIs	11.3% for 30 day case fatality from first AMI in men and women	NA	11.3% for 30 day case fatality from first AMI in men and women	NA	NA	NA
MITRA & MIR Studies[156]	Registries	Germany	1994-8	22,613 first AMIs. 1071 (59%) second AMIs	41.2% in-hospital in men and women	NA	41.2% in-hospital in men and women	NA	NA	NA
Framingham Heart Study[161]	Cohort study	USA	1971-1987	363 first AMIs (63%) 68 second AMIs	59% overall	NA	NA	NA	NA	NA
Gilpin et al[162]	Prospective study.	USA	1979-1989	3,666 AMIs (all, not first) 171 (70%) recurrent AMIs	16.4% at one year from first AMI in men and women	NA	16.4% at one year from first AMI in men and women	NA	NA	NA
The 60 Minutes Myocardial Infarction Project[164]	Prospective study	Germany	1992-1994	11,901 first AMIs (67%) 2,584 recurrent AMIs (72%)	23% in-hospital in men and women with recurrent AMI	NA	23% in-hospital in men and women with recurrent AMI	NA	NA	NA

3 AIMS AND OBJECTIVES

3.1 Aims

In the light of the findings of the literature review, a study was developed with the following aim:

- To compare the baseline characteristics, survival and health service burden of men and women hospitalised with a first and second acute myocardial infarction in Scotland between 1990 and 2000.

The aim translated into the following objectives:

3.2 Objectives

- To describe and compare the age and socio-economic characteristics of men and women admitted to hospital with a first and a second acute myocardial infarction 1990-2000.

- To describe the incidence of hospitalisations for first and second AMI in men and women between 1990 and 2000.

- To determine and compare the nature and extent of comorbidity in men and women admitted to hospital with a first and a second acute myocardial infarction 1990-2000.

- To analyse, describe and compare short and longer term survival and trends in survival in men and women following an admission to hospital with a first and a second acute myocardial infarction 1990-2000.

- To examine and compare the independent effect of sex on short and longer term survival in different age groups in individuals admitted to hospital with a first and a second acute myocardial infarction 1990-2000.

- To determine and compare the independent effect of factors thought to influence survival in men and women following an admission to hospital with a first and a second acute myocardial infarction 1990-2000.

- To describe the burden of first and second acute myocardial infarctions on the Scottish National Health Service in men and in women 1990-2000.

4 METHODS

4.1 Data sources

Data were obtained from the Information and Statistics Division of the National Health Service in Scotland (ISD Scotland). ISD Scotland manage the Scottish Record Linkage System on behalf of NHS Scotland. This system links together computerised hospital records (Scottish Morbidity Records) and death registration records that belong to the same patient.[165]

4.1.1Scottish Morbidity Records

The Scottish Morbidity Record (SMR) schemes record hospital discharge data at an individual level. The main records kept under these schemes include all discharges from acute hospitals (SMR01), maternity units (SMR02), psychiatric units (SMR04) and neonatal discharges (SMR11). This study involved the analysis of SMR01 data. SMR01 data is generated when a patient is discharged from hospital; changes consultant, is transferred to another hospital or dies. SMR01 relates to both inpatients and day cases who are discharged from non-psychiatric, non-obstetric wards in Scottish hospitals. It includes data on both emergency and elective admissions. The data is abstracted from case notes and then transcribed onto an SMR01 form. The Information and Statistics Division of the Common Services Agency (CSA) hold this information on computer at a National level. The data collected includes a principal diagnosis and up to five secondary diagnoses as well as up to four operative procedures. The World Health Organisation (WHO) International Classification of Diseases (ICD) system is used to classify both principal and secondary discharge diagnoses.[166] The tenth revision (ICD-10) has been available since the mid-1990's and was introduced by the CSA in April 1996. The data in this study are therefore based on diseases coded using the ninth revision (ICD-9) from January 1st 1990

to March 31st 1996 and the tenth revision (ICD-10) from 1st April 1996 to 31st December 2001.

4.1.2Death certificate data

The General Register Office for Scotland records the causes of death for all Scottish residents.[167] The codes used to classify these deaths are allocated using the WHO International Classification of Diseases.[166] Prior to 1996, a team of trained nosologists coded the causes of death manually. They selected the underlying cause and up to three other causes considered to have contributed to death as outlined on the death certificate.

4.1.3Linked Database

In Scotland, computerised hospital records, cancer registration records and death registration records belonging to the same patient are linked together in the Scottish Record Linkage System. Heasman first demonstrated the potential for linking individual patient records together in 1968. As record linkage had to be carried out for each analysis, it was initially expensive and slow. A joint project between ISD and the CSA started in May 1989 and led to the development of a new record linkage system. The linked data set holds hospital discharge records for non-psychiatric, non-obstetric specialties (SMR1) together with Cancer Registry records (SMR6) and Registrar General's death records from 1981 until the present day. Ad hoc linkages can also be carried out dating back to 1968.[165]

Methods of linking

Methods of probability matching have been developed and refined in Oxford, Scotland and Canada over the last thirty years, and are used by the Record Linkage System to allow for inaccuracies in the identifying information. When records are linked, two records are compared and a decision is made as to whether they belong to the same individual. A computer algorithm calculates a score for each pair of records that is proportional to the likelihood that they belong to the same person. The common core of identifying items includes: surname, first initial, sex, year, month and day of birth and postcode. Surnames are changed to coded format in order to avoid the effects of differences in spelling. The huge volume of data would mean that it would be impossible to compare every record with all the other records and blocking is used to cut down the number of comparisons required. Only those records that have a minimum level of agreement in identifying items are

compared. Probability matching then allows mathematically precise assessment of the implications of the levels of agreement and disagreement between records.[168]

4.1.4 Accuracy of data

The linkage process is largely automatic as a threshold score based on probability matching dictates the decision as to whether the records belong together. Clerical checking has shown that both the false positive rate and the false negative rate are around one per cent. It is the responsibility of the Quality Assessment and Accreditation Unit (QAA) of ISD to monitor the quality of SMR data, by assessing accuracy, completeness, consistency and fitness for purpose. The QAA have carried our regular audits that have involved sample sizes of between 7,500 and 9,500 records. Between 2000 and 2002, the national average accuracy at a three-digit level was 88% for the main diagnosis. Acute myocardial infarction was coded with an accuracy rate of 84%. Coding of secondary diagnoses was less accurate with an overall accuracy rate of 77%. The most frequently observed omissions included diabetes, hypertension, cardiac dysrythmias, asthma, angina and chronic ischaemic heart disease. The accuracy of recording data for non-clinical data items was 97%. A number of other studies have looked at the accuracy of SMR1 data with variable results. Kohli *et al* compared SMR1 data and case-notes of patients discharged with upper gastro-intestinal diagnoses from Greater Glasgow Health Board hospitals in 1987. In a sample of 778 cases, they found a crude agreement of 73.6% between primary diagnosis and the case-note diagnosis.[169] Coding of secondary diagnoses was much poorer and there was a significant underestimation of arthritis.

4.1.5 Organisation and Extraction of data

At present the linked data is stored as a conventional flat file of records. The records for each individual are stored adjacently in chronological order and marked with a unique personal identifier. Different types of record are stored in their original unlinked format and are preceded by several fields of linkage information. This increases the range of analyses that are possible. The dataset is complex and requires tailored FORTRAN programs to access the data. The staff in ISD use FORTAN programming to produce specific data sets. In collaboration with staff at ISD, a data spec was written which detailed the nature of the data required for this study. This is included as Appendix 1.

4.2 Data extracted for present study

Information available

For this study, all adults (aged 16 and over) with a first and second principal diagnosis of acute myocardial infarction admitted to Scottish hospitals between 1986 and 2000, were identified along with any subsequent deaths related to these admissions occurring up until December 31st 2001.

The ICD9 code used to identify acute myocardial infarction patients included: **410- acute myocardial infarction.** The ICD10 diagnoses used included: **I21 and I22 .**

This information available allowed patients to be followed up for a minimum of one year to the end of the study (31st December 2001). Only the first and second episode of acute myocardial infarction leading to a hospital admission per patient was analysed. Each patient record provided information on age, sex, postcode of residence, date of admission and death, if it occurred.

Postcode sectors were used to derive Carstairs socio-economic deprivation scores, which were used to categorise patients into deprivation categories. Resident postcodes were used to assign a Carstairs deprivation category from one (least deprived) to five (most deprived) to each individual. These categories are derived from 1991 census data on four variables: overcrowding, the proportion of residents unemployed, who do not have a car, or belong to a low occupational social class.

Secondary diagnoses in positions two to six were examined in order to determine the most frequent co-diagnoses. These were then recoded into categorical variables. Information on prior hospital admission came from retrospective linkage back to 1981. This identified those patients who had been admitted to hospital for any other reason, within five years prior to their admission for acute myocardial infarction. In order to consistently obtain a five-year history of prior admission to hospital for each patient, the principal analyses in this study were confined to patients admitted between January 1990 and December 2000. A new comorbidity variable was created which combined prior admission and secondary diagnosis so that the final variable indicated either a prior admission or a secondary diagnosis or both for the following diagnoses:

Atrial fibrillation, cancer, cerebrovascular disease, coronary heart disease (excluding AMI), diabetes, hypertension, peripheral vascular disease, renal failure and respiratory disease. Coronary heart disease excluding AMI was not extracted as a secondary admission but was included as a comorbidity variable from prior admission because it was a relatively common co-diagnosis. The ICD9 and ICD10 codes used to define these diagnoses are also detailed in Appendix 1.

Definition of first admission

A "first admission" was defined as the first admission with a principal diagnosis of AMI between 1990 and 2000. These individuals had no admission with AMI in the previous ten years. Patients with a hospitalisation related to AMI in the previous ten years were excluded from these analyses.

Definition of second admission

A 'second admission' was defined as an admission to hospital with a principal diagnosis of AMI in an individual who had been admitted only once in the previous ten years with the same diagnosis.

4.3 Statistical analyses

All tests of statistical significance were two tailed. All analyses were undertaken using the Statistical Package for Social Scientists (SPSS Inc, Chicago, Illinois 60611) and Confidence Interval Analysis for Windows (CIA, 1998).

4.3.1 Descriptive analyses

Baseline data relating to men and women were compared using chi square tests and chi square tests for trend for categorical data and t tests for continuous data. Population data were used to derive population-based discharge rates per 100,000 individuals for first and second AMI stratified by sex, age group and year of admission. Annual age and sex specific population denominators were obtained from the General Registrar for Scotland. Linear regression was used to test the significance of the observed trends in population discharge rates and numbers. Length of stay was examined in men and women between 1990 and 2000. Mean and median length of stay was also calculated along with interquartile range. Occupied bed days per 1000 population were calculated for men and

women between 1990 and 2000. For each year the number and proportion of men and women who underwent in-hospital revascularisation was calculated. In-hospital revascularisation was subdivided into coronary artery bypass graft surgery and coronary angioplasty. The annual proportion of all emergency medical admissions in Scotland accounted for by first and second AMI was also calculated for men and women. In order to examine temporal trends in the baseline characteristic of men and women hospitalised with a first and second AMI, the overall time period was divided into three approximately equal time periods, 1990-1992, 1993-1196 and 1997-2000. This categorisation was chosen on the basis that the number of men and women admitted to hospital with a first AMI was roughly equivalent in the three time periods because of a decline in the annual number and rate of admissions over time. Age distribution and distribution of comorbid diagnoses was then examined and compared in these three time periods. The annual mean age of men and women was also determined. The chi square test for trend was used to determine the presence of any significant association between time period and the proportion of men and women with each comorbid diagnosis.

4.3.2 Survival analyses

Case fatality rates at 30 days, six months, one year, two years and five years were compared in men and women who were categorized into five age groups. The age categories chosen were consistent with previous studies. Survival time was calculated as the time from either first or second admission for AMI, to death from any cause; or censored at 31/12/2001. Age and sex specific survival rates were calculated for the follow up periods using the actuarial life table method. This takes account of admission dates and periods of follow-up, which differ between patients. Crude survival rates were stratified by sex, by age and sex, by deprivation category and sex, and by co-morbidity and sex. Kaplan-Meier survival curves were drawn in order to graphically illustrate the probability of survival for men and women. Stratified analyses were also performed in order to compare survival of men and women in different age groups, deprivation quintiles and for men and women with each comorbid diagnosis. The log rank test was used to test the null hypothesis that men and women are samples from the same population as regards survival experience. This involves calculating the observed and expected number of deaths in both groups at separate time intervals and summing these. Median survival was also calculated using the Kaplan-Meier survival method.

4.3.3Cox's proportional hazards

Cox's proportional hazard models were then used to determine whether sex, age, socio-economic deprivation and comorbidity were independently associated with survival at one year and five years excluding those deaths that occurred during the first 30 days following admission. The Cox's proportional hazards model compares the hazard functions for each level of the model. This was carried out using a forward stepwise Cox regression. The method started by including sex only and added in the most significant variable at each step until there were no other significant variables that could be added. This was carried out by keeping sex, the variable of interest, in the model. Cox proportional hazard models were also carried out in men and women separately in order to examine any sex differences in the independent effect of variables on survival. Interaction terms between sex and year of admission were tested and found to be non-significant. Interaction terms between sex and other variables were included in the models and tested for significance. Because there was a significant interaction between age and sex, age was then recoded into three age categories, <65 year olds, 65-74 year olds and >74 year olds and Cox's proportional hazard models were then carried out in these three groups. Sex was kept in the models and forward stepwise Cox regression carried out. As no significant departure from linear trend was found, age was modelled as a continuous variable within these age group models. For each variable entered into a model, the lowest class was set at unity. After fitting the final model, the assumptions were checked. The assumptions underlying a Cox's proportional hazards model are:

1. Proportional hazards, the ratio of hazard functions for two individuals with different covariates does not vary with time.

2. Linearity, the relationship between the covariates and the hazard function should be linear in the log space.

3. Survival times should be independent, as should survival times and censoring times and the censoring should not be affected by the covariates.

These were checked by looking at a log-log plot for each categorical covariate in the model, which should demonstrate parallel lines if the hazards are proportional.

4.3.4 Logistic regression

Multiple logistic regression was used to calculate the adjusted odds ratio for the probability of death within 30 days of a first and second admission for AMI. As for Cox proportional hazards, forward stepwise regression was performed. Sex was kept in the model and other significant variables were added sequentially. Age was included as a categorical variable and categorised into the five groups used in the descriptive and survival analyses. Logistic regression was also carried in men and women separately and in the three different age groups used in the Cox proportional hazards. In these age group models, age was modelled as a continuous variable, as no significant departure from linear trend was found. For each variable entered into a model, the lowest class was set at unity.

Adequacy of fit was assessed using the Hosmer Lemeshow Goodness-of Fit-Test.

5 FIRST AMI: BASELINE CHARACTERISTICS

5.1 Results of descriptive analyses

This section describes the baseline characteristics of men and women who are admitted to hospital following a first acute myocardial infarction. In order to examine differences in survival between men and women, it is essential to have a clear understanding of their age, socio-economic status and co-existing medical conditions. Differences in these variables may contribute to discrepancies in survival between men and women. It is therefore difficult to examine the independent effect of sex on survival without first accounting for any differences in baseline characteristics that might influence survival.

5.1.1 Overall

Between January 1st 1990 and December 31st 2000, a total of 110,226 individuals aged 16 years and over, were admitted to Scottish hospitals following a first acute myocardial infarction. 45,600 were women who comprised 41.4% of the total cohort.

5.1.2 Age

Table **22** shows the distribution of age in men and women admitted to hospital following their first AMI. Mean age on admission to hospital was 72.1 years in women and 64.6 years in men. Women were on average seven and a half years older than men at the time of first admission to hospital. A two-sample t-test to compare the mean ages of men and women was highly significant, $p<0.001$. The age distribution of men and women differed significantly with almost twice the proportion of men aged less than 65 years compared to women (47.6% versus 24.2%, $p<0.001$). The distribution of age was relatively normal in men and women and can be summarised using a histogram as seen in Figure 1 and by the median, quartiles and extremes shown in Table **22**. There was a marked variation in age which ranged from 18 to 104 years in both men and women. The distribution of age was clustered around the median with 50% of women aged between 65 and 81 years and 50% of men aged between 56 and 74 years.

Table 22 Descriptive statistics for age of men and women following a first hospital admission for acute myocardial infarction

i. Age group distribution

Number of cases (%)	MEN	WOMEN	BOTH
Age-group <55 years	13897 (21.5%)	3592 (7.9%)	17489 (15.9%)
55-64 years	16866 (26.1%)	7454 (16.3%)	24320 (22.1%)
65-74 years	19283 (29.8%)	13639 (29.9%)	32922 (29.9%)
75-84 years	11940 (18.5%)	14538 (31.9%)	26478 (24.0%)
>84 years	2640 (4.1%)	6377 (14.0%)	9017 (8.2%)
Total	64626 (58.6%)	45600 (41.4%)	110226 (100%)

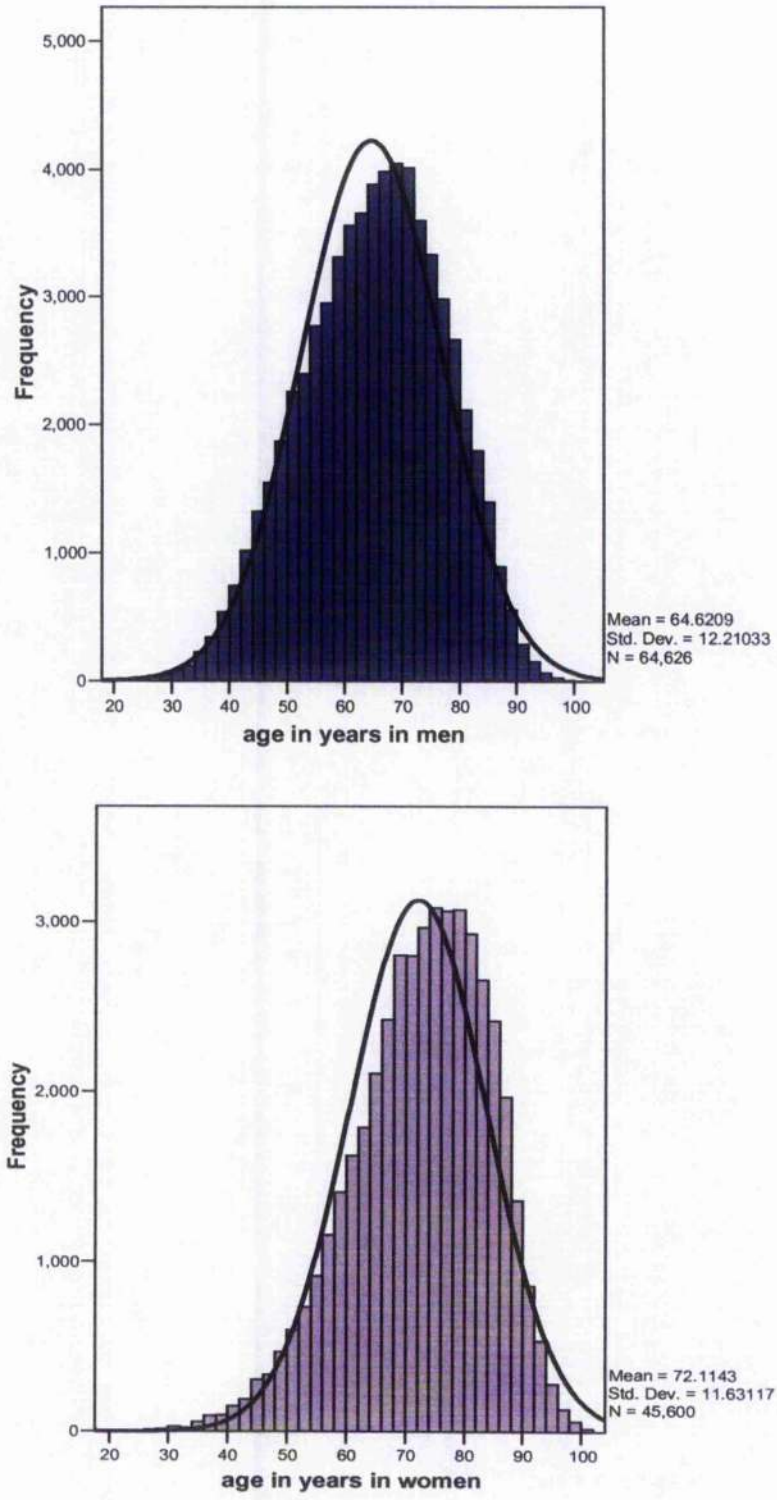
ii. Summary Statistics

	Mean (95%CI)	SD	MEDIAN	MIN	MAX	RANGE	IQR
Men	64.6 (64.5-64.7)	12.2	65	18	104	86	18
Women	72.1 (72.0-72.2)	11.6	73	18	104	86	16

iii. Percentiles

	PERCENTILE						
	5	**10**	**25**	**50**	**75**	**90**	**95**
Men	44	48	56	65	74	80	84
Women	51	56	65	73	81	86	89

Figure 1 Histograms showing age distribution in men and women with a first admission for acute myocardial infarction



5.1.3Deprivation and sex

Overall 41.9% of individuals admitted to hospital with a first AMI came from the two most deprived deprivation categories. Table 23 and Figure 2 show the distribution of deprivation in men and women. There was a socioeconomic gradient in men and women and the proportion of individuals in more deprived categories was higher than the proportion in less deprived categories. A chi square test for trend was highly significant, $p<0.001$ after excluding the relatively small number of individuals not assigned to a deprivation category. Figure 3 shows the distribution of deprivation in men and women in the Scottish population at the time of the population census in 1991. Unlike the AMI cohort, the proportion of men and women in each deprivation category is roughly similar.

Table 23 Distribution of deprivation in men and women

	MEN	WOMEN	ALL
Deprivation categories			
I- least deprived	10,799 (16.7%)	7,318 (16.0%)	18,117 (16.4%)
II	12,668 (19.6%)	8,624 (18.9%)	21,292 (19.3%)
III	12,764 (19.8%)	9,064 (19.9%)	21,828 (19.8%)
IV	12,954 (20.0%)	9,439 (20.7%)	22,393 (20.3%)
V- most deprived	13,560 (21.0%)	10,275 (22.5%)	23,835 (21.6%)
uncoded	1,881 (2.9%)	880 (1.9%)	2,761 (2.5%)

Figure 2 Distribution of deprivation in men and women hospitalised with first AMI

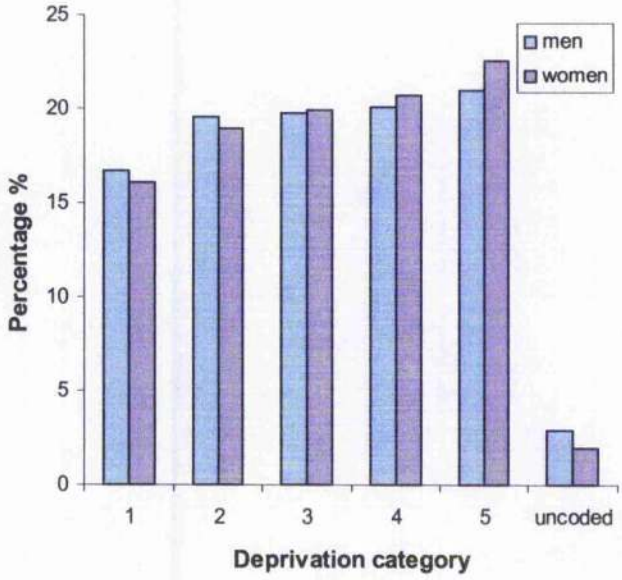
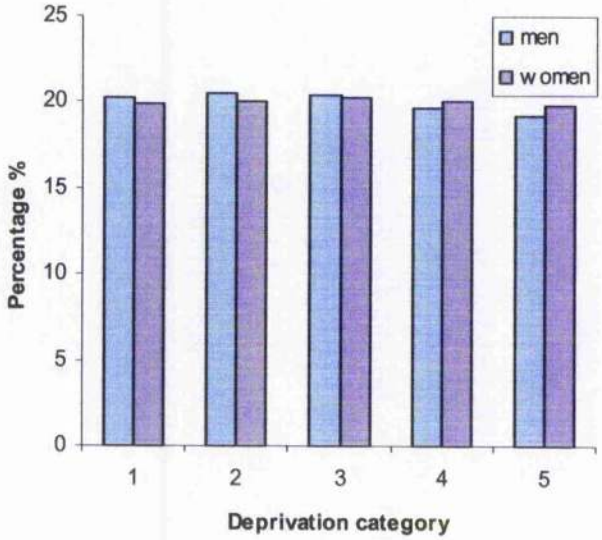


Figure 3 Distribution of deprivation in men and women in Scotland 1991



5.1.4Deprivation and age

There was a marked difference in the distribution of age groups between deprivation categories in individuals admitted to hospital following a first AMI. As shown in Table 24, the most deprived individuals were younger than the least deprived individuals. 32.9% of those in the least deprived category were aged less than 65 years, compared to 43.7% of those in the most deprived category. There was a significant trend of decreasing age with increasing deprivation and this was statistically significant (Chi square test for trend $p<0.001$).

Table 24 Age distribution within deprivation quintiles

	Deprivation category					
Age group	**1-least deprived**	**2**	**3**	**4**	**5-most deprived**	**uncoded**
<55 years	2403 (13.3%)	3025 (14.2%)	3399 (15.6%)	3585 (16.0%)	4539 (19.0%)	538 (19.5%)
55-64 years	3556 (19.6%)	4378 (20.6%)	4652 (21.3%)	5154 (23.0%)	5877 (24.7%)	703 (25.5%)
65-74 years	5238 (28.9%)	6443 (30.3%)	6624 (30.3%)	6770 (30.2%)	7029 (29.5%)	818 (29.6%)
75-84 years	4929 (27.2%)	5477 (25.7%)	5325 (24.4%)	5219 (23.3%)	4948 (20.8%)	580 (21.0%)
>84 years	1991 (11.0%)	1969 (9.2%)	1828 (8.4%)	1665 (7.4%)	1442 (6.0%)	122 (4.4%)
Total	18117 (100%)	21292 (100%)	21828 (100%)	22393 (100%)	23835 (100%)	2761 (100%)

5.1.5Deprivation, age and sex

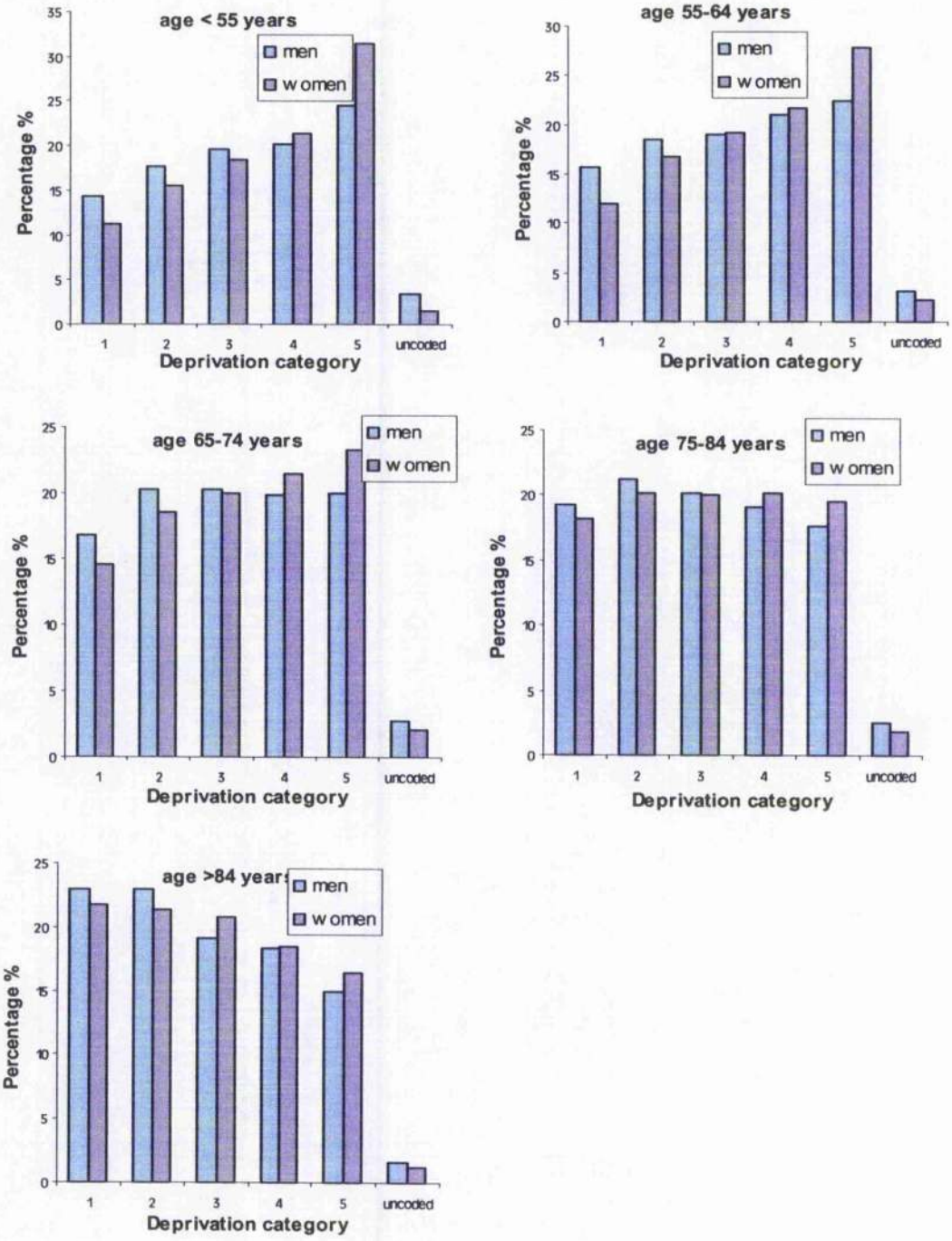
Table 25 shows the distribution of age by sex and deprivation category. The difference in the distribution of age according to deprivation category was seen in both men and women, although women were on average older than men. The socio-economic gradient seen across age groups was greater in women than in men. Individuals aged 55 years and under accounted for only 5.5% of women in the least deprived category compared to 11% of women in the most deprived category. In men the figures were 18.5% and 25.1%. There was a trend across deprivation categories so that more deprived men and women were younger than less deprived men and women. The differences were significant (Chi square test for trend $p<0.001$ in men and women). Figure 4 shows the distribution of deprivation categories by age group and by sex. The interaction between deprivation and sex seen in

all patients was seen in all age groups but was more marked in younger age groups. The excess of women in deprived categories was not therefore confined to certain age groups.

Table 25 Age distribution by sex and deprivation category

		Deprivation category					
Men	**Age group**	**1-least deprived**	**2**	**3**	**4**	**5-most deprived**	**uncoded**
	<55 years	1996 (18.5%)	2467 (19.5%)	2732 (21.4%)	2816 (21.7%)	3407 (25.1%)	479 (25.5%)
	55-64 years	2657 (24.6%)	3134 (24.7%)	3224 (25.3%)	3530 (27.3%)	3794 (28.0%)	527 (28.0%)
	65-74 years	3248 (30.1%)	3920 (30.9%)	3898 (30.5%)	3839 (29.6%)	3851 (28.4%)	527 (28.0%)
	75-84 years	2293 (21.2%)	2541 (20.1%)	2405 (18.8%)	2284 (17.6%)	2112 (15.6%)	305 (16.2%)
	>84 years	605 (5.6%)	606 (4.8%)	505 (4.0%)	485 (3.7%)	396 (2.9%)	43 (2.3%)
Women	**Age group**						
	<55 years	407 (5.5%)	558 (6.5%)	667 (7.4%)	769 (8.1%)	1132 (11.0%)	59 (6.7%)
	55-64 years	899 (12.3%)	1244 (14.4%)	1428 (15.8%)	1624 (17.2%)	2083 (20.3%)	176 (20.0%)
	65-74 years	1990 (27.2%)	2523 (29.3%)	2726 (30.1%)	2931 (31.1%)	3178 (30.9%)	291 (33.1%)
	75-84 years	2636 (36.0%)	2936 (34.0%)	2920 (32.2%)	2935 (31.1%)	2836 (27.6%)	275 (31.3%)
	>84 years	1386 (18.9%)	1363 (15.8%)	1323 (14.6%)	1180 (12.5%)	1046 (10.2%)	79 (9.0%)

Figure 4 Distribution of deprivation categories by age group and sex



5.1.6Co-morbidity

Almost a half (47.3%) of all individuals admitted to hospital following their first AMI had either a hospital admission in the five years prior to their AMI admission, or had a secondary diagnosis falling into one or more of the categories listed (Table 26). Previous coronary heart disease excluded AMI and was based solely on previous admissions and did not include secondary diagnoses. A higher proportion of women had a recorded comorbidity than men (51.5% versus 44.3%). Heart failure was the most commonly recorded comorbidity and was more frequently coded in women than in men. All individual comorbid conditions other than coronary heart disease and peripheral vascular disease were more commonly recorded in women than in men.

Table 26 Distribution and comparison of comorbid diagnoses by sex

Comorbidity	Men	Women	All
Any	28615 (44.3%)	23474 (51.5%)	52089 (47.3%)
Diabetes	5178 (8.0%)	4350 (9.5%)	9528 (8.6%)
Cancer	3729 (5.8%)	2929 (6.4%)	6658 (6.0%)
Respiratory	6119 (9.5%)	4698 (10.3%)	10817 (9.8%)
Cerebrovascular disease	4248 (6.6%)	3456 (7.6%)	7704 (7.0%)
Peripheral vascular disease	4455 (6.9%)	2914 (6.4%)	7369 (6.7%)
Atrial fibrillation	3736 (5.8%)	3378 (7.4%)	7114 (6.5%)
Hypertension	5978 (9.3%)	5432 (11.9%)	11410 (10.4%)
Renal failure	1641 (2.5%)	1515 (3.3%)	3156 (2.9%)
Heart failure	9340 (14.5%)	8810 (19.3%)	18150 (16.5%)
Coronary heart disease	4507 (7.0%)	3158 (6.9%)	7665 (7.0%)

5.1.7Comorbidity, age and sex

Each comorbid condition was examined according to age group and sex. Figure 5 shows the distribution of age group by comorbid condition in men and in women and Table 27 shows the results of the chi square tests of association between age group and sex within each comorbid diagnosis.

Comorbid diagnoses that decreased in prevalence with increasing age

The prevalence of diabetes was greatest in the middle aged groups and declined in the elderly. Prevalence of diabetes was greater in women than in men in all age groups. The observed trends were significant in men and in women, $p<0.001$. Hypertension showed a marked reduction in the elderly, especially in men. Again, hypertension was more common in women than in men of all ages.

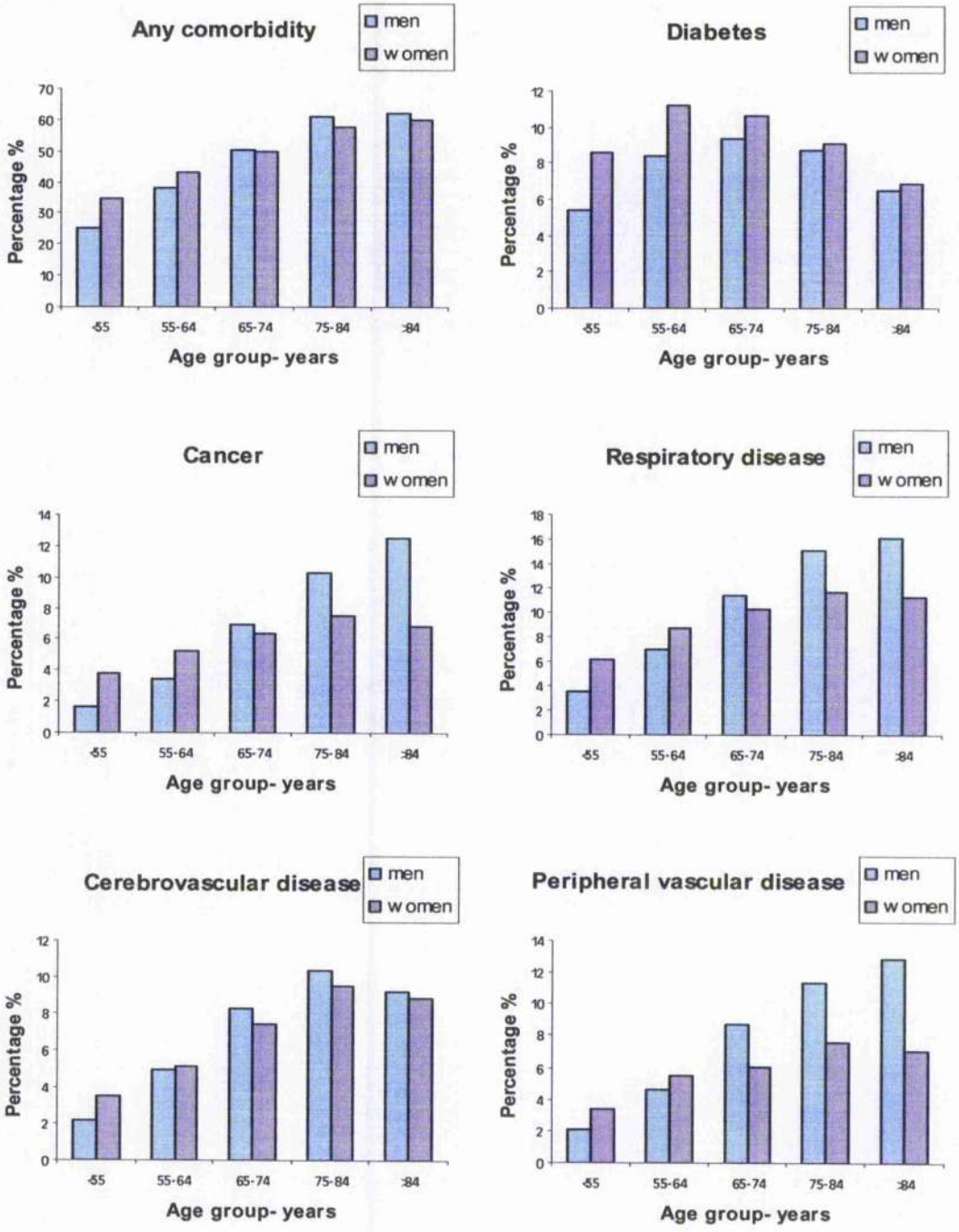
Comorbid diagnoses that increased in prevalence with increasing age

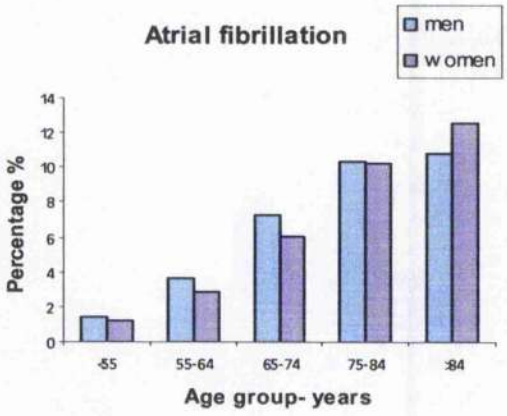
The prevalence of a previous or co-existing heart failure diagnosis increased significantly with age in men and in women, $p<0.001$. Only 5.6% of men and 6.7% of women aged less than 55 years had a heart failure diagnosis coding compared to 27.6% of men and 30.4% of women aged 85 years and over. Heart failure was more common in women than in men in all age groups, except in individuals aged 75-84 years. The prevalence of atrial fibrillation increased with age in men and in women and was slightly more common in men than in women apart from in the very elderly age group. Cerebrovascular disease increased in prevalence with age in men and women up to the age of 75-84 years and declined thereafter. The proportion of individuals with a previous history of coronary heart disease increased only marginally with age and was slightly greater in men than in women except in those aged less than 55 years.

Comorbid diagnoses that displayed an interaction between age and sex

A cancer diagnosis displayed an interaction between age and sex. Cancer was more commonly coded in younger women than in younger men and less commonly coded in older women than in older men. For example, 3.8% of women aged less than 55 years were coded for cancer compared to 1.7% of men. However, 12.6% of men aged >84 years were coded for cancer compared to 6.8% of women. Respiratory disease showed a similar pattern and increased more with age in men than in women. 16.1% of men aged greater than 84 years had a respiratory diagnosis compared to 11.3% of women. Peripheral vascular disease increased dramatically in prevalence with age in men but not in women leading to an age sex interaction. 12.9% of men aged greater than 84 years had a diagnosis of peripheral vascular disease compared to 7.1% of women. Renal failure displayed a similar pattern although the differences between men and women were less marked in all age groups.

Figure 5 Distribution of comorbid diagnosis by age and sex




Atrial fibrillation
men
women
Percentage %
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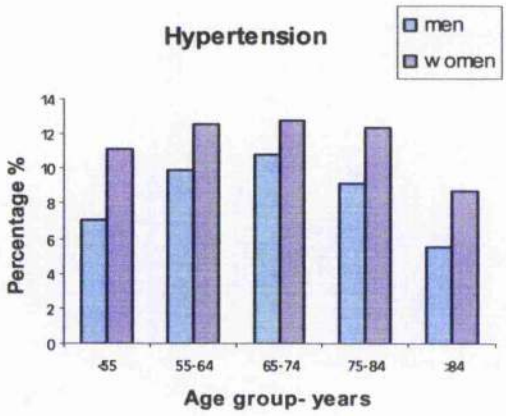
>84
Age group- years


Hypertension
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Percentage %
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75-84
>84
Age group- years


Renal failure
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Percentage %
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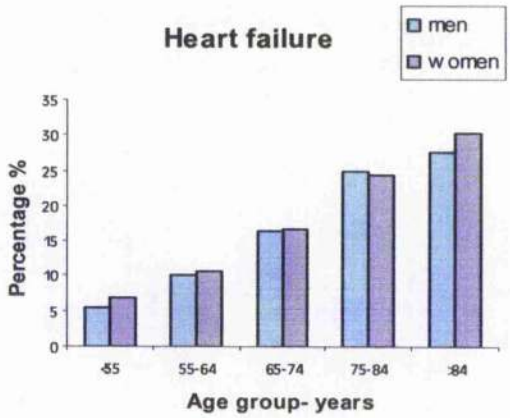
65-74
75-84
>84
Age group- years


Heart failure
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Percentage %
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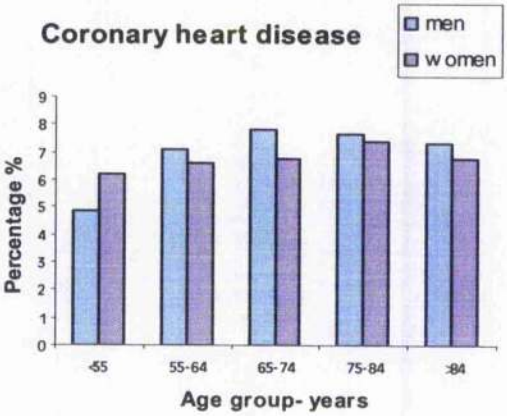
>84
Age group- years


Coronary heart disease
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Percentage %
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65-74
75-84
>84
Age group- years

Table 27 Tests of association between sex and age group within comorbid diagnoses

	CHI SQUARE TEST		CHI SQUARE TEST FOR TREND	
Comorbidity	**Men**	**Women**	**Men**	**Women**
Diabetes	P<0.001	P<0.001	P<0.001	P<0.001
Cancer	P<0.001	P<0.001	P<0.001	P<0.001
Respiratory disease	P<0.001	P<0.001	P<0.001	P<0.001
Cerebrovascular disease	P<0.001	P<0.001	P<0.001	P<0.001
Peripheral vascular disease	P<0.001	P<0.001	P<0.001	P<0.001
Atrial fibrillation	P<0.001	P<0.001	P<0.001	P<0.001
Hypertension	P<0.001	P<0.001	P=0.001	P<0.001
Renal failure	P<0.001	P<0.001	P<0.001	P<0.001
Heart failure	P<0.001	P<0.001	P<0.001	P<0.001
Coronary heart disease	P<0.001	**P=0.038**	P<0.001	**P=0.039**

5.1.8Comorbidity, deprivation and sex

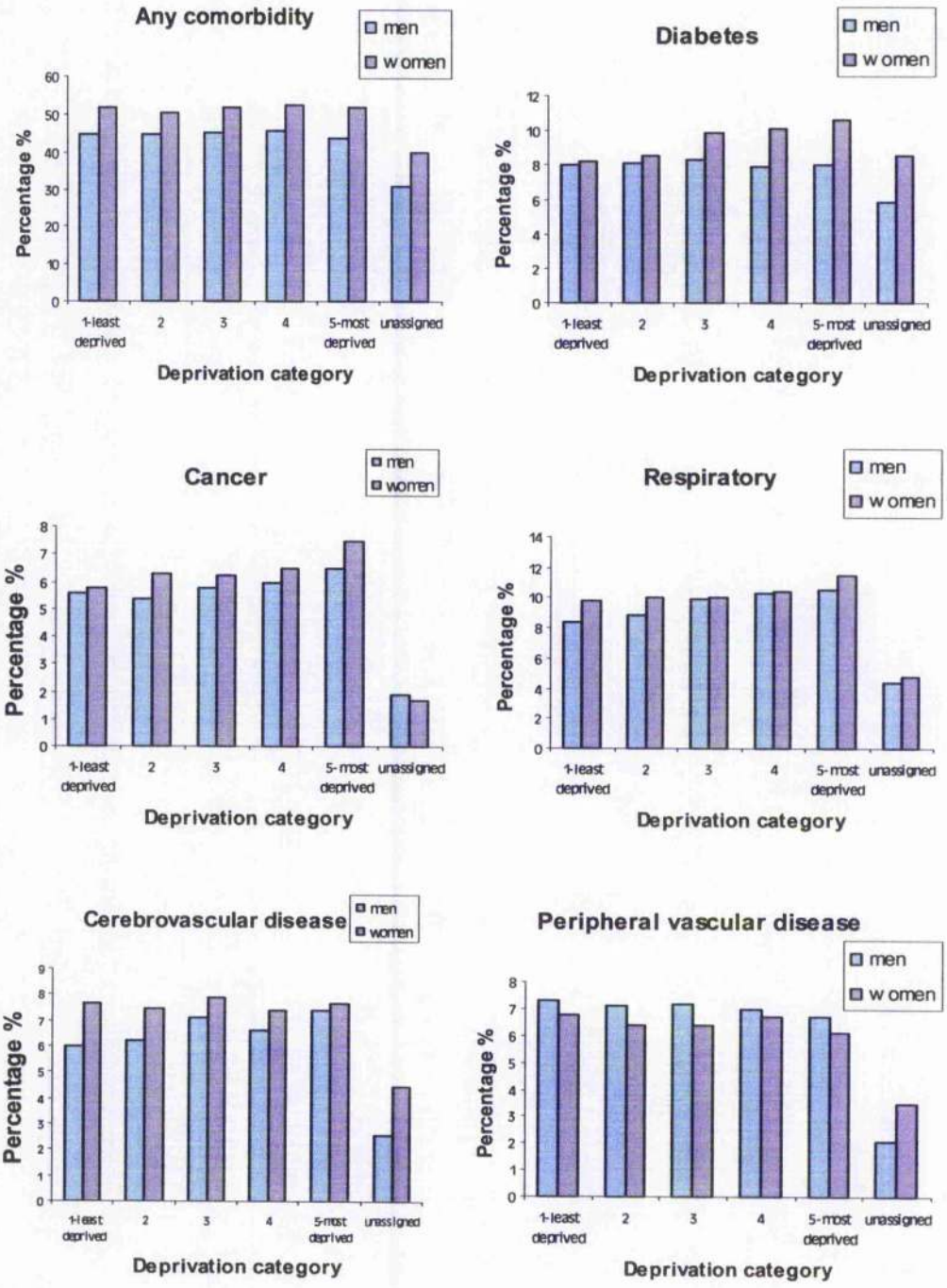
Describing the distribution of deprivation categories for each comorbid diagnosis in men and in women provided more information about the relationship between deprivation and specific comorbid diagnoses (Figure 6). Table 28 shows the results of the chi square tests of association between sex and deprivation within comorbid diagnoses. Individuals who had not been assigned to a deprivation category were excluded from these tests. Variation by deprivation category was not as marked as that observed between age groups.

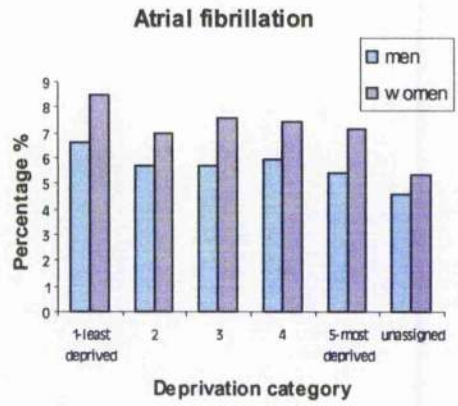
The proportion of women with a comorbid diagnosis of diabetes varied by deprivation category (p<0.001). There was a clear socio-economic gradient so that 8.2% of women in the least deprived category had a comorbid diagnosis of diabetes, rising to 10.6% in the most deprived category. This trend was highly significant, p<0.001. There was no difference across the deprivation categories in men. Cancer and respiratory disease also

displayed a relationship with deprivation and were more commonly coded in more deprived categories in men and women. These trends were highly significant, $p<0.001$.

Coronary heart disease displayed significant variation across deprivation categories in men and in women. The most deprived were more likely to have a coding for previous coronary heart disease and this gradient was similar in men and women. For example, 6.5% of men and 6.3% of women in the least deprived category were coded for coronary heart disease compared to 8.0% of men and 8.1% of women in the most deprived category. In men, cerebrovascular disease was more commonly coded in more deprived categories than in least deprived categories. This trend was not seen in women. Peripheral vascular disease showed no evidence of trend or variation according to deprivation category in men or in women. Hypertension showed a reverse pattern compared to other comorbid diagnoses and was more likely to be coded in least deprived men compared to most deprived men, $P<0.001$. This pattern was not evident in women.

Figure 6 Distribution of deprivation categories by comorbid diagnosis and sex




Atrial fibrillation
men
women
Percentage %
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1-least deprived
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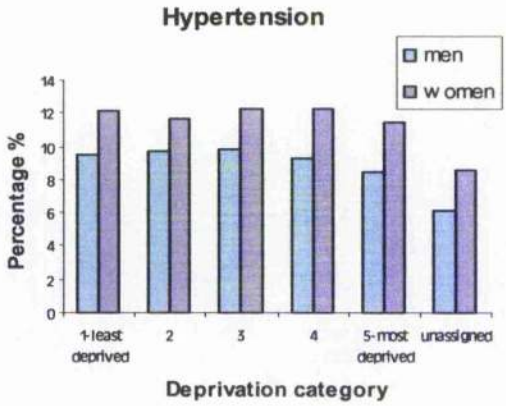
5-most deprived
unassigned
Deprivation category


Hypertension
men
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Percentage %
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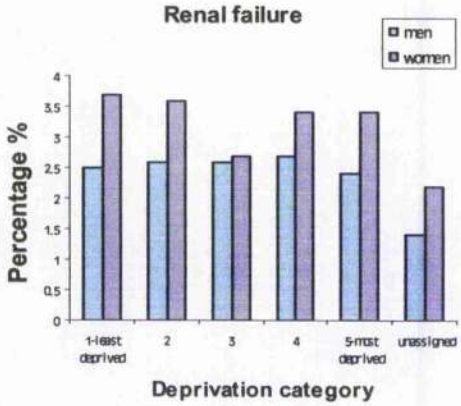
5-most deprived
unassigned
Deprivation category


Renal failure
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women
Percentage %
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1-least deprived
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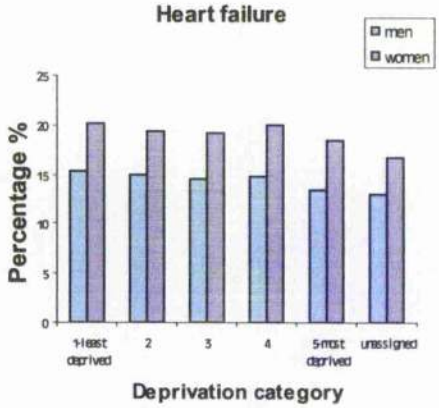
5-most deprived
unassigned
Deprivation category


Heart failure
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Percentage %
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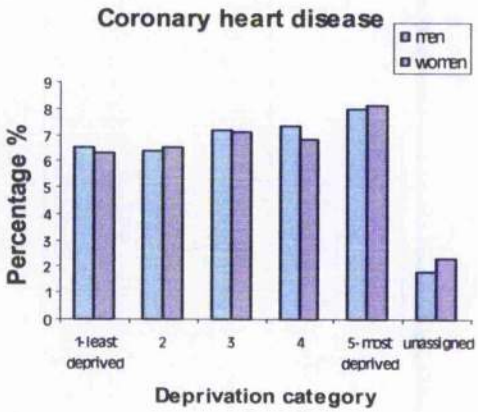
5-most deprived
unassigned
Deprivation category


Coronary heart disease
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Percentage %
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1-least deprived
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5-most deprived
unassigned
Deprivation category

Table 28 Tests of association between sex and deprivation within comorbid diagnoses

	Chi Square Test		Chi Square Test for Trend	
Comorbidity	**Men**	**Women**	**Men**	**Women**
Diabetes	***P=0.759***	P<0.001	***P=0.825***	P<0.001
Cancer	P=0.001	P<0.001	P<0.001	P<0.001
Respiratory disease	P<0.001	P=0.001	P<0.001	P<0.001
Cerebrovascular disease	P<0.001	***P=0.772***	P<0.001	***P=0.909***
Peripheral vascular disease	***P=0.442***	***P=0.273***	***P=0.104***	***P=0.169***
Atrial fibrillation	P=0.001	P=0.002	P=0.001	P=0.011
Hypertension	P=0.002	***P=0.311***	P=0.001	***P=0.473***
Renal failure	***P=0.508***	P=0.006	***P=0.880***	***P=0.300***
Heart failure	P<0.001	P=0.018	P<0.001	P=0.036
Coronary heart disease	P<0.001	P<0.001	P<0.001	P<0.001

5.2 Discussion of first AMI baseline characteristics

There is a large literature surrounding the epidemiology of AMI. Despite this there is a lack of data relating to the comparison of men and women with AMI. Most of the literature that does exist compares survival rates between the sexes and examines possible explanations for differences in these. There are very few studies that have examined the baseline characteristics including comorbid diagnoses in men and women hospitalised with AMI in an unselected population cohort. Many of those studies that have carried out detailed comparisons between men and women hospitalised with AMI include clinical trials such as ISIS-3,[83] SPRINT,[108] TIMI II[170]or GUSTO IIb[171] or studies that have excluded older[82;112;172;173] or younger individuals.[92;174] All of these studies are subject to selection bias and the individuals are not therefore typical of AMI patients in the general population. There is consequently difficulty regarding the generalisability of their results. In addition the vast majority of studies include first and recurrent AMI and do not differentiate between these. The baseline characteristics including age and prevalence of comorbid diagnoses differ between individuals with first and recurrent events and this issue is rarely, if ever, explored. This discussion is therefore carried out with reference to those studies that have examined the distribution of comorbid diagnoses in men and women hospitalised with AMI. It is not restricted to first AMI for which there is a very limited literature.

5.2.1Age and sex

Between 1990 and 2000, 45,600 women were hospitalised in Scotland with a first AMI, accounting for 41.4% of all hospitalisations. This differs from clinical trials where women tend to be enrolled in small numbers if at all but is consistent with other population based studies. In the Worcester Heart Attack Study and the Rochester Epidemiology Project, women accounted for 39% and 44% respectively of the study cohorts of first AMIs, which is similar to this Scottish cohort.[54;56] The mean age of Scottish men and women on admission to hospital was 64.6 years and 72.1 years respectively. Again this is consistent with other studies in which women hospitalised with an AMI are generally six to ten years older than men. In the Worcester Heart Attack Study men and women were 63.9 years and 71.7 years respectively at the time of hospitalisation with their first AMI.[56] It was not possible to determine the mean age of men and women in the Rochester Epidemiology Project from the published report.[54] In the Ontario Myocardial Infarction Database,

women accounted for 36% of all individuals hospitalised with an AMI.[106] The study included all AMIs as oppose to first AMIs. The mean age of these individuals was 69 years in 1996, though again it was not possible to determine the mean age of men and women from the published report. Some of the other large studies like ARIC and NHANES-I excluded patients over the age of 74 years and do not therefore allow a valid comparison of age with population based studies.[60;62] The age and sex characteristics of the patients in this study compare well to smaller studies carried out in the UK. In the Yorkshire AMI Study, 39% of the study population were women with a mean age of 74.9 years compared to 68 years in men.[85] In the Nottingham Heart Attack Register, women accounted for 37% of the study cohort in 1992 and had a mean age of 69.7 years compared to 64.8 years in men.[107] The current study and other studies have therefore consistently shown that women develop clinical manifestations of coronary artery disease later than men. The male to female ratio of coronary artery disease declines with increasing age, possibly due to women undergoing the menopause and acquiring an increasing burden of cardiovascular risk factors. In the Framingham Study AMI incidence in women was roughly half that of men in individuals aged greater than 65 years.[81] The proportion of men and women in an AMI cohort will then depend upon the age and sex structure of the population of origin.

5.2.2 Socioeconomic characteristics

There was a socioeconomic gradient in both men and women, with increasing numbers of admissions seen in the more deprived categories, especially in women. An interaction was observed so that there were more men than women observed in the least deprived categories but more women than men in the most deprived categories. This interaction was also present within each age group. A similar interaction is seen in the whole Scottish population but is not apparent within age groups. There are few publications with which to compare these data. This is because there are few population based studies that examine first AMI and those that do exist have not examined the distribution of socioeconomic deprivation in men and women and in different age groups. The studies that have included some measure of socio-economic deprivation, have used different classification systems and are not therefore directly comparable to the Scottish data. In the National Registry of Myocardial Infarction 2, women, especially younger women were substantially more likely to be receiving Medicaid than men.[78] Medicaid is a program that pays for medical assistance for people with low incomes. In the North Karelia and Kupio Study income was associated with an adverse cardiovascular risk but only in women. [175] Income was the only

socioeconomic factor that seemed to differentiate between men and women in terms of cardiovascular risk. There has been very little analysis or discussion in the literature around the relationship between socioeconomic deprivation and coronary heart disease in men and women. Young women have a relatively low risk of developing the disease and those that do develop coronary heart disease are therefore likely to have a particularly adverse risk profile, which in turn is related to the level of socioeconomic deprivation. Diabetes for example has been found to be more common in people from areas of high socioeconomic deprivation.[176] Diabetes has also been shown to have a greater impact on the relative risk of developing coronary heart disease in men than in women.[81;128;177]

5.2.3 Comorbid diagnoses

Few studies have examined the prevalence of comorbid diagnoses in men and women of all ages. Whilst a number of studies have looked at the prevalence of other cardiovascular diagnoses in men and women separately, they have generally excluded individuals in older age groups and have not included other comorbid diagnoses in their description of baseline characteristics. Very few studies have described the distribution of risk factors and comorbid diagnoses by age group within men and women separately. Slightly more women than men had either a prior admission within five years of the index event, or a secondary diagnosis falling into one or more of the chosen categories (51.5% of women versus 44.3% of men). This is not surprising given that women were on average seven and a half years older than men. However not all comorbid diagnoses increased in prevalence with age and younger patients had a relatively high rate of coded comorbid diagnoses.

Diabetes

Overall 8.0% of men and 9.5% of women in this study had a diagnosis of diabetes. This is lower than the rates reported by most other studies. In the current study, it is likely that diabetes is under recorded as a secondary diagnosis in hospital discharge forms and that those individuals with a primary diagnosis of diabetes in a prior admission represent the more severe end of a spectrum. However the reported prevalence of diabetes in men and women hospitalised with AMI varies substantially between different studies. In the National Registry of Myocardial Infarction 2 Study, 25% of men and 33% of women had a diagnosis of diabetes.[78] This is higher than the rates reported by most other studies. For example 11% of men and 16% of women in the Yorkshire AMI Study had a diagnosis of diabetes.[85] The overall prevalence of diabetes reported by different studies is higher in

women than in men hospitalised with AMI, which is in keeping with the results from this study.[78-80;82;85] The prevalence of diabetes in the general population is not significantly different in white men and women.[177] In this study women were more likely to have a diagnosis of diabetes in all age groups though the prevalence was greatest in the middle age groups and declined in the elderly. The sex difference was greatest in younger age groups. Few studies have looked at age specific prevalence of diabetes in men and women hospitalised with AMI. Those that have are mainly clinical trials, the results of which are difficult to extend to the general population. The National Registry of Myocardial Infarction 2 Study found that younger women were more likely than younger men to have a history of diabetes, but that this sex difference was minimal in older age groups.[78] This is in keeping with the results of this study. Diabetes is linked to obesity which is more common in women and might contribute to the increased prevalence seen in women. As mentioned previously young women have a relatively low risk of developing coronary heart disease and those that do are likely to have particularly adverse risk profiles. In addition diabetes has a greater impact on the relative risk of coronary heart disease in women than in men.[81;177]

Heart failure

Heart failure was the most commonly recorded comorbid diagnosis in this study. More women than men had a recorded diagnosis of heart failure (19.3% versus 14.5%). This finding is in keeping with the rates reported by other studies, for example in the National Registry of Myocardial Infarction 2 Study, 21% of women and 13% of men had a history of congestive cardiac failure. Prevalence of heart failure varies between different studies but has been found to be consistently higher in women than in men.[78-80;85;87] Some of the variation in reported prevalence rates is likely to arise as a result of the different criteria used to define heart failure and also because prevalence is measured at different time points during the index admission. In the current study the prevalence rate is likely to include in the numerator those individuals who develop heart failure in the post-infarct period, prior to discharge or death. The prevalence of heart failure increased significantly with age in men and women, which again is in-keeping with other studies. In the REGICOR Study, 11% of men and 23% of women aged 65-74 years hospitalised with an AMI between 1990 and 1992 had a diagnosis of heart failure.[84] In the current study the equivalent figures were 16% and 17% in men and women respectively. Given that the age specific prevalence rates of heart failure in the current study were similar in men and women it is likely that the overall excess in women can be explained by the fact that

women were on average older than men and that the prevalence of heart failure increases with age.

Hypertension

More men than women had a recorded diagnosis of hypertension (11.9% versus 9.3%). This is substantially lower than the rates reported by other studies and is likely to have arisen as a result of poor coding in hospital discharge forms and medical case notes. Prevalence rates reported by other studies vary considerably. It is often difficult to determine from these studies whether the diagnosis of hypertension was based on a history of hypertension or on clinical examination of the AMI patient. Hypertensive patients can become normotensive after developing an AMI and this would decrease the estimated prevalence. In the REGICOR Study, 61% of women and 40% of women had a diagnosis of hypertension based on clinical examination following hospitalisation with an AMI.[84] Hypertension was more commonly coded in women than in men and this is in keeping with the results of other studies.[56;78-80] Hypertension is believed to develop at similar rates in men and women in the general population, and to exert similar effects on the risk of coronary artery disease in both sexes.[177] Elderly hypertensive women outnumber hypertensive men because men die at a younger age than women.[178] In the current study the prevalence of hypertension reached a peak in middle age groups and declined in the elderly. Few other studies have examined prevalence of hypertension in different age groups and those that have, have largely excluded the very elderly.[84;86] This finding may reflect a greater likelihood of diagnosing and treating cardiovascular risk factors like hypertension in younger people compared to older people rather than a real difference in the prevalence of this diagnosis.[179]

Renal impairment

Renal failure was coded in a small proportion of men and women (2.5% of men versus 3.3% of women). There are few studies with which to compare these figures. In NHANES III the population prevalence rate of chronic renal insufficiency was 2.2% in men and 2.7% in women aged 20-74 years.[180] In the current study a renal failure diagnosis is likely to represent individuals with relatively severe renal disease. In the Framingham Offspring Study, 8.9% of men and 8.0% of women had an elevated serum creatinine level and the prevalence increased steeply with age.[181] 20% of this Framingham cohort had pre-existing cardiovascular disease. In the current study prevalence of renal failure also increased substantially with age, especially in men, 6.9% of whom had a diagnosis of renal

failure over the age of 84 years. There is a growing literature regarding renal failure and AMI, but few studies have reported sex specific data. Furthermore the diagnostic criteria used are not consistent and the reported prevalence rates vary markedly between studies. For example, the Mayo Clinic Study found that 47% of men and 76% of women hospitalised with AMI had a degree of renal impairment.[90] These figures were based on creatinine clearance which is a sensitive marker and likely to pick up mild cases. In contrast, the Alberta Health and Wellness Database found that only 3% of men and 4% of women hospitalised with AMI had a diagnosis of renal failure based on discharge coding.[80] These figures are comparable to those found in this study and are likely to represent individuals with severe disease.

Previous angina and coronary heart disease

In this study a previous diagnosis of coronary heart disease was present in 7.0% of men and 6.9% of women hospitalised following a first AMI. The prevalence was slightly higher in men than in women in all age groups, except in those aged less than 55 years. Prevalence remained relatively stable with age in both sexes. The prevalence of previous angina in individuals hospitalised with AMI reported by other studies varies considerably. In the Worcester Heart Attack Study, 17% of men and 22% of women hospitalised with a first AMI had history of angina based on review of medical notes.[56] Other studies, especially those looking at all AMIs as oppose to first AMI, have reported higher rates of previous angina in individuals hospitalised with AMI.[84;86;92] For example the Göteborg Study found a prevalence of previous angina of 45% in men and 51% in women.[79] Some of these differences may be the result of the different methodologies employed by studies. It is likely that the prevalence of previous angina will be higher in those studies where description of baseline characteristics is based on interview and case notes, compared to those where prevalence is based solely on discharge coding or case notes.

Atrial fibrillation

Overall, 5.8% of men and 7.4% of women in this study had a diagnosis of atrial fibrillation. The prevalence of atrial fibrillation increased substantially with age and was slightly more common in men than in women except in the very elderly. Overall the prevalence of atrial fibrillation was greater in women than in men because of the relatively small number of men compared to women in the older age groups. These figures are lower than those reported by most studies. In the Worcester Heart Attack Study, 14.7% of men and 18% of women had a diagnosis of atrial fibrillation following admission to hospital

with AMI.[96] As in the current sstudy, the prevalence of atrial fibrillation increased significantly with age. In the Worcester Heart Attack Study, AMI patients with atrial fibrillation were more likely to develop heart failure.[96] People with heart failure are more likely to develop atrial fibrillation and the association between heart failure and atrial fibrillation is clearly complex and has not been explored in this study.[99;100;139]

Chronic obstructive airways disease

In this study, the prevalence of respiratory disease which comprised mainly chronic obstructive airways disease was similar in men and women (9.5% in men versus 10.3% in women). There was an interaction between age and sex so that respiratory disease was more common in younger women than in men but more common in older men than in older women. There are very few data with which to compare these findings. In the SPRINT Trial, 7.5% of men and 5.5% of women hospitalised with AMI had a diagnosis of COPD. The prevalence increased with age but the analyses were not sex specific. The relatively higher prevalence of COPD in younger women may reflect the stronger association in women than in men between cigarette smoking and the risk of developing coronary artery disease.[177] The incidence of coronary heart disease is relatively low in younger women and those that do develop the disease are likely to have particularly adverse risk profiles.

Cancer

Slightly more women than men had a diagnosis of cancer (6.4% versus 5.8%). The prevalence of a cancer diagnosis was greater in younger women than in younger men. This is likely to represent breast cancer. Rates increased substantially with age, more so in men than in women so that the diagnosis was more common in men than in women in older age groups. This is likely to represent the lung and bowel tumours seen in these age groups.

Other vascular diseases

Overall the rates of PVD and CVD were similar in men and women in the current study (6.9% of men and 6.4% of women had a diagnosis of PVD and 6.6% of men and 7.6% of women had a diagnosis of CVD). The prevalence of PVD and CVD increased with age, especially PVD in men. This was coded in 12.9% of men and 7.1% of women aged greater than 84 years. CVD was coded in 9.2% of men and 8.9% of women. There are very few data with which to compare these results, especially for CVD. The prevalence of PVD seen in this study was similar to that reported by the SPRINT Trial which found that 6.4%

of men and 6% of women hospitalised with AMI had a diagnosis of PVD.[105] The Framingham Study also reported prevalence of intermittent claudication and stroke or TIA in men and women, though their study included those individuals with a diagnosis of 'silent' AMI, which inflated the denominator, especially in women.[93] In the Framingham Study 9.4% of men and 10.5% of women presenting with a first AMI had a diagnosis of intermittent claudication, and 5.3% of men and 8.1% of women had a history of stroke or TIA. These prevalence figures were not age adjusted and the excess prevalence in women may have been largely or wholly explained by older age of the women. In the current study the prevalence of PVD and CVD was higher in younger women than in men but greater in older men than in women. This finding is again in keeping with other comorbid diagnoses and the hypothesis that as younger women have a relatively low risk of developing coronary heart disease compared to men, they are likely to have particularly adverse risk profiles and high prevalence rates of comorbid disease.

5.2.4Summary

In the current study women were on average more than seven years older than men at the time of hospitalisation with their first AMI. They accounted for approximately 40% of all hospitalisations for first AMI. Both men and women were more likely to come from a more deprived than from a less deprived area, though this was especially true of younger women. Almost half of all men and women had one or more comorbid diagnosis and this prevalence rate increased dramatically with age. Younger women had high levels of comorbid disease relative to men. This is relevant to their hospitalisation with AMI which would be relatively unusual in the absence of cardiovascular risk factors and comorbid disease that serve to counteract the protective effects of the premenopause.[81;177;182]

6 Temporal trends in baseline characteristics of individuals admitted to hospital following a first AMI 1990-2000

6.1 Results

When examining temporal trends in survival following AMI, it is important to consider the baseline characteristics of men and women which may vary over time. Variation over time in baseline characteristics such as age and comorbid diagnoses may contribute to or even explain, observed changes in survival. This section therefore describes the distribution of age and comorbid diagnoses in men and women between 1990 and 2000.

6.1.1Age

For ease of comparison, year of admission was categorised into three time periods as described in the methods. The age distribution of men and women admitted to hospital following a first AMI has experienced modest changes (Table 29). The proportion of younger individuals aged less than 65 years has decreased and the proportion of older individuals aged 75 years and over has increased. This pattern is present in men and women. In men for example, the proportion of individuals aged 55 to 64 years fell from 27.3% in 1990-1992 to 24.5% in 1997-2000, whilst the proportion of individuals aged greater than 84 years increased from 3.3% to 5.1%. In women the proportion of individuals aged 55 to 64 years fell from 17.4% in 1990-1992 to 14.8% in 1997-2000, whilst the proportion of individuals aged greater than 84 years increased from 11.7% to 16.2% in 1997-2000. These trends were all highly significant, $p<0.001$. The average age of men and women on admission also increased between 1990-1992 and 1997-2000 In men the median age increased from 65 to 66 years and in women from 72 to 74 years. Figure 7 shows a scatterplot of mean age on admission in men against year of admission. A linear trend line has been fitted to the data. The sample correlation coefficient R^2 suggests that 67% of the variability in mean age can be explained by its relationship with year of admission, so that there is a strong relationship between the two variables. The strength of the relationship is even greater in women in whom the R^2 is 80%.

Table 29 Temporal trends in age distribution of men and women

iv. Age group distribution

Number of cases (%)	Men			Women		
Year of admission	**1990-1992**	**1993-1996**	**1997-2000**	**1990-1992**	**1993-1996**	**1997-2000**
Age-group <55 years	4293 (21.2%)	5072 (21.2%)	4532 (22.2%)	1166 (8.1%)	1283 (7.5%)	1143 (8.0%)
55-64 years	5535 (27.3%)	6316 (26.4%)	5015 (24.5%)	2495 (17.4%)	2848 (16.7%)	2111 (14.8%)
65-74 years	6021 (29.7%)	7325 (30.6%)	5937 (29.0%)	4425 (30.9%)	5140 (30.1%)	4074 (28.6%)
75-84 years	3748 (18.5%)	4264 (17.8%)	3928 (19.2%)	4556 (31.8%)	5393 (31.6%)	4589 (32.3%)
>84 years	664 (3.3%)	931 (3.9%)	1045 (5.1%)	1667 (11.7%)	2398 (14.1%)	2312 (16.2%)
Total	20261	23908	20457	14309	17062	14229

v. Summary Statistics

	Men			Women		
Year of admission	**1990-1992**	**1993-1996**	**1997-2000**	**1990-1992**	**1993-1996**	**1997-2000**
Mean age (years)	64.4 (64.2-64.6)	64.6 (64.4-64.7)	64.9 (64.8-65.1)	71.5 (71.3-71.7)	72.2 (72.0-72.4)	72.7 (72.5-72.9)
Standard deviation	11.9	12.2	12.5	11.4	11.6	11.9
Median age (years)	65	65	66	72	73	74
Interquartile range	17	17	18	16	16	16

Figure 7 Mean age on admission to hospital following a first AMI in men 1990-2000

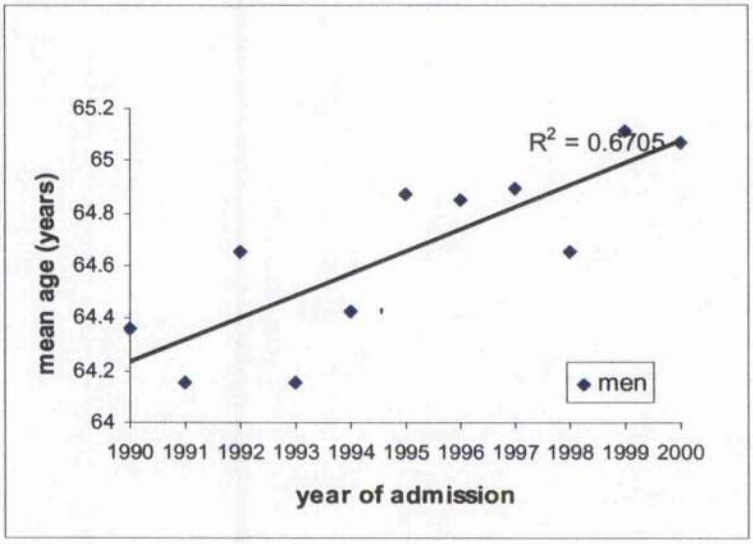
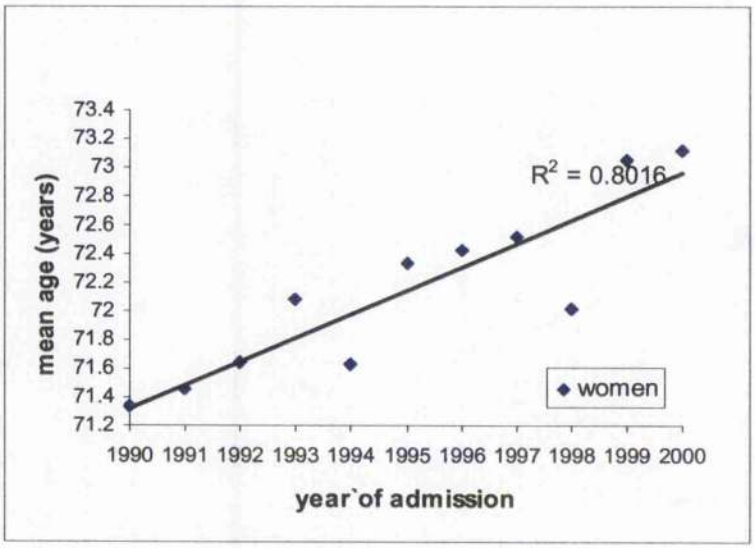


Figure 8 Mean age on admission to hospital following a first AMI in women 1990-2000



Comorbidity

Overall the proportion of men and women coded with each comorbid diagnosis, increased between 1990-1992 and 1997-2000. These trends were all significant, $p<0.001$. In 1990-1992, 37.1% of men and 43.6% of women had at least one comorbid diagnosis. By 1997-2000 this figure had increased to 51.6% of men and 59.8% of women.

The magnitude of change over time varied by diagnosis and by sex. Hypertension, renal failure, atrial fibrillation, respiratory disease and diabetes exhibited the greatest relative increases. The proportion of individuals with a secondary or prior diagnosis of atrial fibrillation almost doubled in men and women. In 1990-1992, only 3.8% of men and 5.1% of women had a comorbid diagnosis of atrial fibrillation. By 1997-2000 this had increased to 7.7% and 10.2% in men and women respectively. The proportion of individuals coded with hypertension more than doubled during the study period, rising from 5.4% in men and 7.4% in women in 1990-1992 to 14.1% in men and 18.2% in women in 1997-2000. Cancer and coronary heart disease exhibited the most modest rises over the study period. In 1990-1992, 6.0% of men and 5.9% of women had experienced a previous admission with coronary heart disease. By 1997-2000 this had increased to 7.9% of men and 8.3% of women.

Table 30 Temporal trends in prevalence of comorbid diagnoses in men and women hospitalised with a first AMI

	Proportion of individuals with comorbid diagnosis (%)					
	Men			**Women**		
Comorbidity	**1990-1992**	**1993-1996**	**1997-2000**	**1990-1992**	**1993-1996**	**1997-2000**
Diabetes	5.8	7.6	10.7	8.0	9.4	11.3
Cancer	4.7	5.6	7.0	4.7	6.5	8.0
Respiratory disease	7.5	9.5	11.3	7.6	10.3	13.0
Cerebrovascular disease	5.5	6.6	7.6	6.6	7.3	8.9
Peripheral vascular disease	5.7	7.0	7.9	5.6	6.4	7.2
Atrial fibrillation	3.8	5.8	7.7	5.1	7.1	10.2
Hypertension	5.4	8.3	14.1	7.4	10.5	18.2
Renal failure	1.6	2.2	3.9	2.2	3.1	4.7
Heart failure	11.6	14.5	17.2	16.2	19.8	21.8
Coronary heart disease	6.0	7.1	7.9	5.9	6.7	8.3
Any comorbidity	37.1	44.1	51.6	43.6	51.2	59.8

Age group

The proportion of men and women with comorbid conditions increased over the time period for most diagnoses and in most age groups. The changes were broadly similar in men and women and were more likely to be significant in older age groups. Figure 9 shows the distribution of comorbid diagnoses by age group and time period for men and women.

The proportion of men with a diagnosis of diabetes increased across all the age groups between 1990-1992 and 1997-2000. 4.2% of men aged less than 55 years had a diagnosis of diabetes but by 1997-2000 this had risen to 7.2%. Other age groups demonstrated similar relative increases. The increase was greatest in the 65-74 year old age group in whom the prevalence was highest. In 1990-1992 the proportion of men aged 65-74 years with a diabetes diagnosis was 6.3% but by 1997-2000 this had risen to 13%. These trends were all highly significant. Relative increases were not as great in women in whom the prevalence of diabetes was higher. In 1990-1992 the prevalence of diabetes in women aged 65-74 years was 8% and by 1997-2000 this had risen to 13.3%. Prevalence of diabetes did not increase significantly in women aged less than 55 years.

The proportion of men and women with a diagnosis of cancer increased significantly in all individuals aged 55 years and over, except in men aged greater than 84 years in whom there was no clear trend, p=0.762. Relative increases were greater in women in whom the prevalence of cancer almost doubled in some age groups. The proportion of women aged 55-64 years with a cancer diagnosis increased from 3.5% in 1990-1992 to 7.4% in 1997-2000. In men the increases in prevalence were significant but were smaller in magnitude.

Cerebrovascular disease and peripheral vascular disease demonstrated similar and more modest changes which were not significant in the younger age groups in men or in women. For example the proportion of men aged 75-84 years with a diagnosis of cerebrovascular disease increased from 9.2% in 1990-1992 to 12.3% in 1997-2000. The equivalent figures in women were 6.2% and 8.6%.

The prevalence of heart failure increased substantially in men and women during the study period. 21.3% of women aged 75-84 years had a diagnosis of heart failure in 1990-1992 and by 1997-2000 this had risen to 27.1%. A similar increase was seen in men in whom

the equivalent figures were 20.3% and 28.4%. All these trends were highly significant (Table 31).

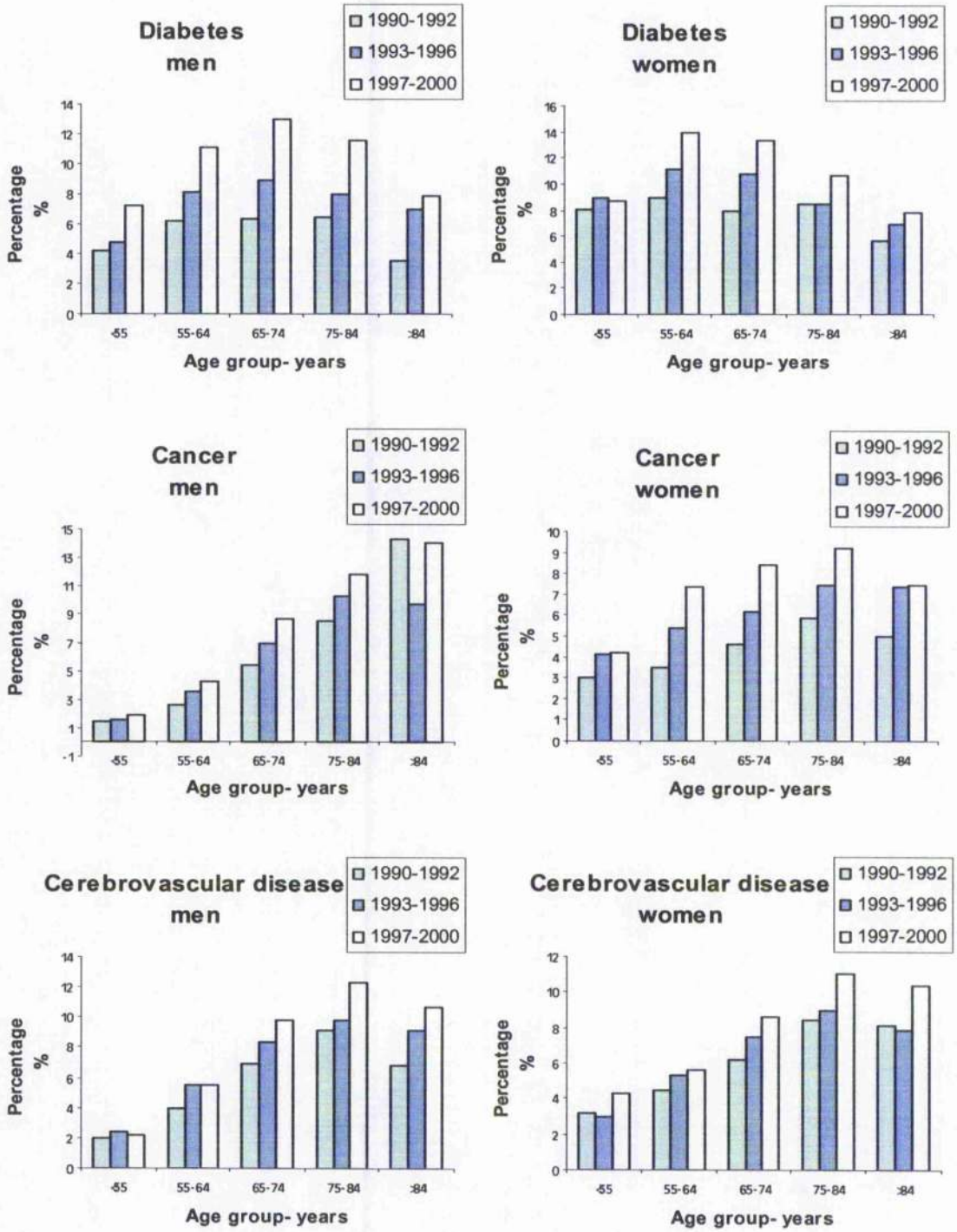
Coding for atrial fibrillation also increased substantially during the study time. In 1990-1992 only 4.4% of women aged 65-74 years had a diagnosis of atrial fibrillation but by 1997-2000 this had risen to 8.2%. Again increases were seen across all age groups and in men and women. Relative increases were greater in older age groups so that in men aged 85 years and over the prevalence increased from 5.4% in 1990-1992 to 14.4% in 1997-2000.

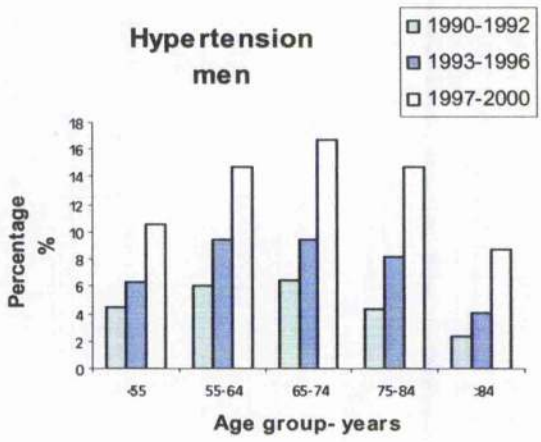
Hypertension also demonstrated substantial increases in prevalence between 1990-1992 and 1997-2000. These changes were apparent across all the age groups and in men and women. For example the proportion of women aged 75-84 years with a diagnosis of hypertension increased from 6.6% in 1990-1992 to 20.1% in 1997-2000. The equivalent figures in men were 4.3% and 14.8%.

The prevalence of men and women with a diagnosis of renal failure was relatively small but increased during the study period, especially in the elderly age groups. In 1990-1992 3.8% of men aged greater than 84 years had a diagnosis of renal failure but by 1997-2000 this had increased to 10%. The equivalent figures in women were 4.4% and 7.8%. Trends in previous coronary heart disease were smaller in magnitude when compared to other diagnoses, especially in the younger age groups. The prevalence of previous coronary heart disease declined slightly in younger women, falling from 6.9% in 1990-1992 to 5.4% in 1997-2000 in individuals aged less than 55 years. Modest increases were seen in older age groups. In men the prevalence of previous coronary heart disease increased across all the age groups though these trends were only significant in individuals aged greater than 64 years.

Overall the proportion of men and women with at least one comorbid diagnosis increased substantially in men and women of all ages across the study period. In 1990-1992 20.8% of men aged less than 55 years had at least one comorbid diagnosis but by 1997-2000 this had increased to 30.8%. The equivalent figures in women were 31.2% and 39.3%. In the elderly age groups the increases were greater in magnitude. 54.2% of men aged greater than 84 years had at least one comorbid diagnosis in 1990-1992 but by 1997-2000 this figure had risen to 70.1%. The equivalent figures in women were 50.9% and 67.7%.

Figure 9 Distribution of comorbid diagnoses by age group and time period for men and women




Hypertension men
1990-1992
1993-1996
1997-2000
Percentage %
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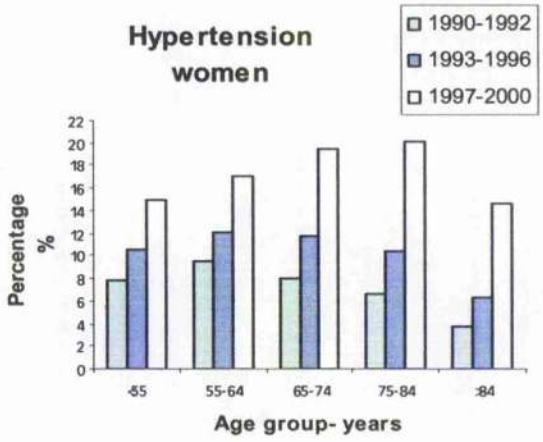
Age group- years


Hypertension women
1990-1992
1993-1996
1997-2000
Percentage %
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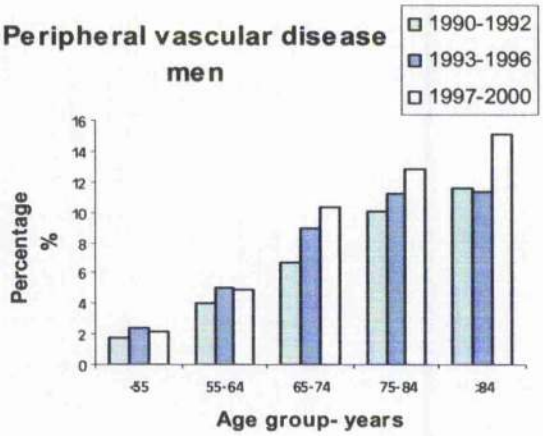
Age group- years


Peripheral vascular disease men
1990-1992
1993-1996
1997-2000
Percentage %
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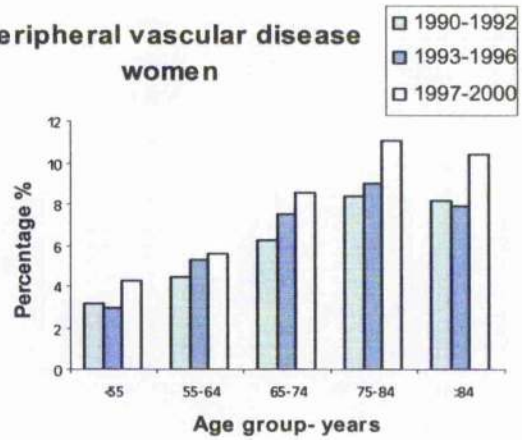
Age group- years


Peripheral vascular disease women
1990-1992
1993-1996
1997-2000
Percentage %
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12
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55-64
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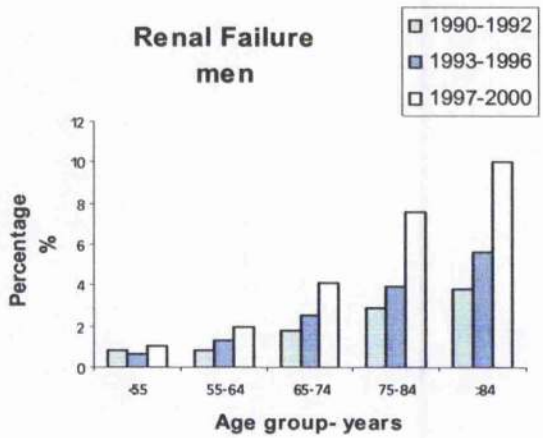
75-84
:84
Age group- years


Renal Failure men
1990-1992
1993-1996
1997-2000
Percentage %
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55-64
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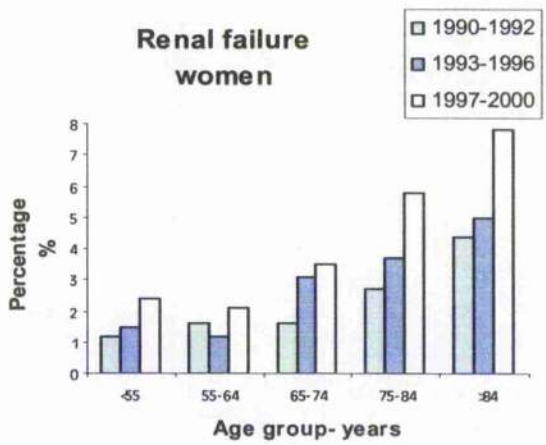
:84
Age group- years


Renal failure women
1990-1992
1993-1996
1997-2000
Percentage %
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4
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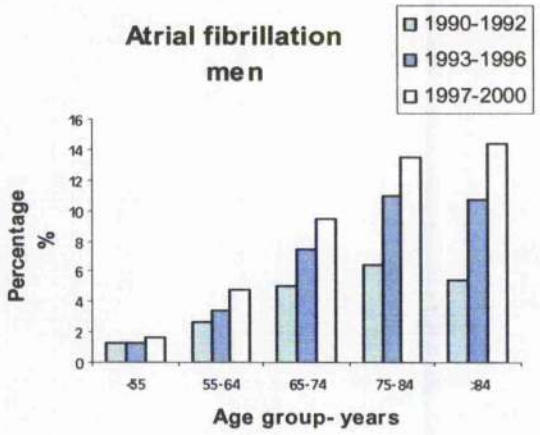
-55
55-64
65-74
75-84
:84
Age group- years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men
1990-1992
1993-1996
1997-2000
Percentage
%
Age group- years
-55
55-64
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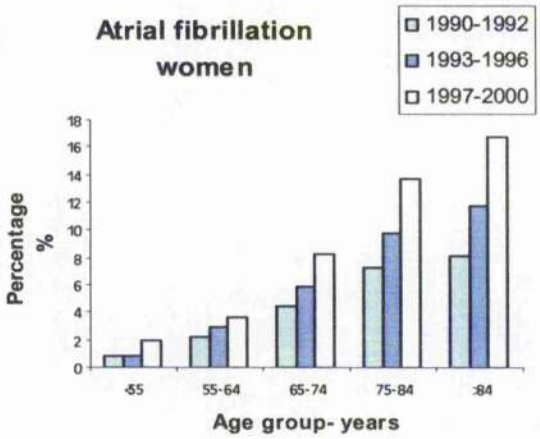
75-84
:84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1990-1992
1993-1996
1997-2000
Percentage
%
Age group- years
-55
55-64
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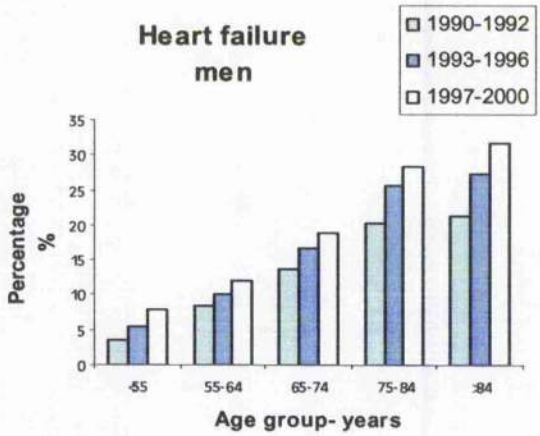
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1990-1992
1993-1996
1997-2000
Percentage
%
Age group- years
-55
55-64
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75-84
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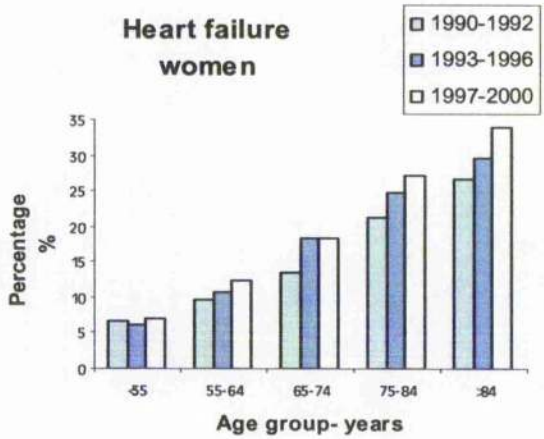
Heart failure
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1990-1992
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1997-2000
Percentage
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Age group- years
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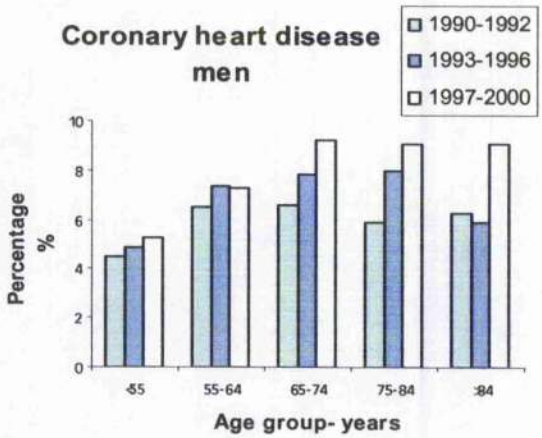
Coronary heart disease
men
1990-1992
1993-1996
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Percentage
%
Age group- years
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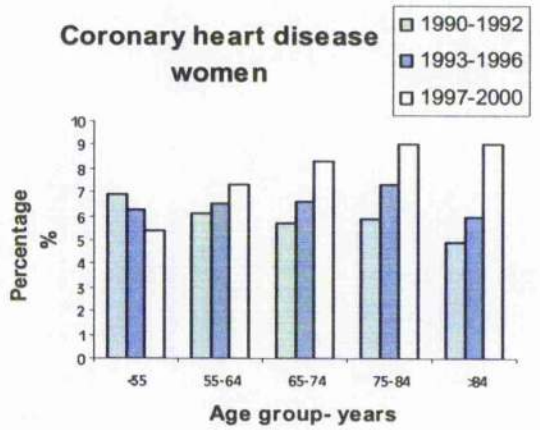
Coronary heart disease
women
1990-1992
1993-1996
1997-2000
Percentage
%
Age group- years
-55
55-64
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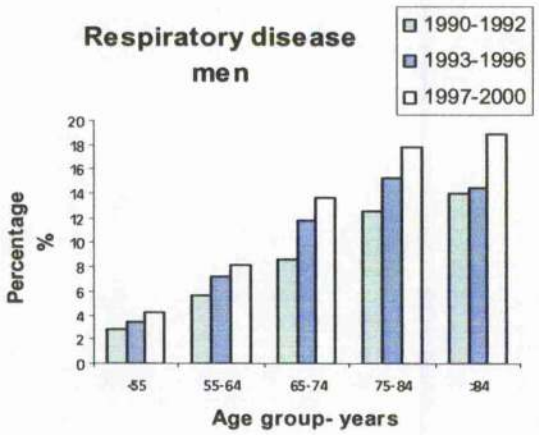
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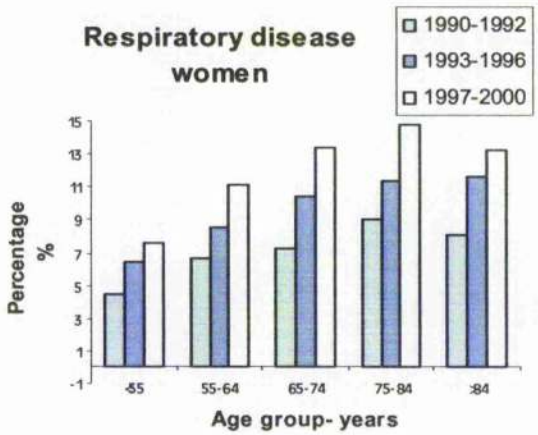
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Respiratory disease women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
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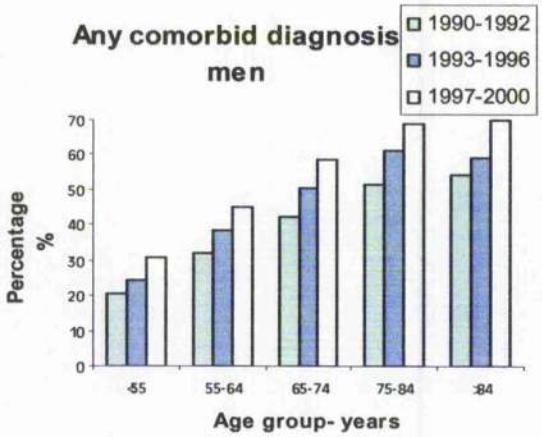

Any comorbid diagnosis men
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84

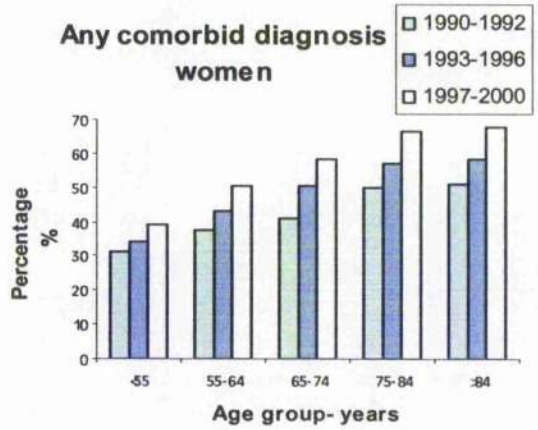

Any comorbid diagnosis women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84

Table 31 Chi square test for trend between year of admission and comorbid condition within age groups

	Chi Square Test for Trend, p value									
	Age <55 years		**55-64 years**		**65-74 years**		**75-84 years**		**>84 years**	
Comorbidity	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
Diabetes	P<0.001	P=0.605	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P=0.001	P=0.009
Cancer	P=0.094	P=0.129	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P=0.762	P=0.003
Respiratory disease	P<0.001	P=0.002	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P=0.004	P<0.001
Cerebrovascular disease	P=0.522	P=0.145	P<0.001	P=0.085	P<0.001	P<0.001	P<0.001	P<0.001	P=0.006	P=0.009
Peripheral vascular disease	P=0.378	P=0.101	P=0.020	P=0.151	P<0.001	P<0.001	P<0.001	P<0.001	P=0.019	P=0.081
Atrial fibrillation	P=0.042	P=0.020	P<0.001	P=0.10	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001
Hypertension	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001
Renal failure	P=0.113	P=0.020	P<0.001	P=0.190	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001
Heart failure	P<0.001	P=0.768	P<0.001	P=0.003	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001
Coronary heart disease	P=0.092	P=0.131	P=0.088	P=0.151	P<0.001	P<0.001	P<0.001	P<0.001	P=0.017	P<0.001
Any diagnosis	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001

6.2 Discussion regarding temporal trends in baseline characteristics of first AMI

Whilst many studies have looked at temporal trends in AMI survival, there are very few studies that have examined temporal trends in baseline characteristics of individuals hospitalised following AMI and none that have included only first AMIs and have reported sex specific analyses in a population based study. Three of the studies that have examined trends in the incidence of first AMI are ARIC, NHANES 1 Epidemiological Follow-up Study and the Minnesota Heart Survey, all of which have an upper age limit of 74 years. Given that age and comorbid diagnoses are significant predictors of outcome, it is important to consider whether the baseline characteristics of men and women have changed over time and whether this may have contributed to any observed changes in survival.

6.2.1Age

In this study the average age of men and women at the time of hospitalisation with their first AMI, increased significantly between 1990 and 2000. The median age of men increased from 65 years to 66 years and the median age of women from 72 years to 74 years. Correspondingly the proportion of individuals aged 65 years and over increased, in men from 51.5% in 1990 to 53.3% in 2000 and in women from 74.4% in 1990 to 77.1% in 2000. More than half of all men and three quarters of all women are now aged 65 years or over at the time of hospitalisation with their first AMI. Just less than a quarter of men and one half of women are aged greater than 74 years. There are very few studies with which to compare these data. In the Nottingham Heart Attack Register, mean age on admission increased from 67.6 years in women and 60.7 years in men in 1982 to 69.7 years in women and 64.8 years in men in 1992.[107] The age of men in Nottingham was similar to men in this study, whilst the women in Nottingham were younger than women in this study. These hospitalisations included first and recurrent AMI events and you might therefore expect the average age of men and women to be greater than in a cohort of only first AMI admissions. The only other study that has reported temporal trends in mean age of men and women hospitalised with AMI is the SPRINT Study. In this study the mean age of men remained relatively stable between 1981-3 and 1992-4, whilst the mean age of women increased slightly from 67.3 years in 1981-3 to 68.4 years in 1992-4.[108] The SPRINT Registry only included those individuals who were admitted to coronary care units who are

likely to be younger than an unselected cohort. The Ontario Study reported an increase in median age for individuals hospitalised with an AMI between 1992 and 1996 but did not report sex specific data.[106]

6.2.2 Comorbidity

In this study, the proportion of men and women who had at least one comorbid diagnosis increased in men and women of all ages between 1990 and 2000. In 1990-1992, 37% of men and 44% of women had one or more comorbid diagnoses. By 1997-2000, this figure had risen to 52% in men and 60% in women. Absolute changes were greatest in older age groups in men and women. The diagnoses that demonstrated the greatest relative increase in prevalence were hypertension, atrial fibrillation and renal failure. The proportion of men and women with comorbid conditions increased over the time period for all diagnoses except previous coronary heart disease. There are a number of possible explanations for this. A comorbid diagnosis of coronary heart disease was based on different coding criteria than the other comorbid diagnoses. It was based on a principal diagnosis of coronary heart disease that occurred within five years prior to the index admission. Unlike other comorbid diagnoses it did not include secondary diagnoses coded in the index admission. Some of the trends observed therefore could be due to changes in coding practice and an increasing likelihood that secondary diagnoses are accurately recorded. The audit reports relating to Scottish Morbidity Data however do not support this hypothesis.[183] Alternatively, the observed changes could reflect real differences in the characteristics of individuals hospitalised with first AMI, who may be becoming older and sicker over time. If that is the case then it is not clear why the proportion of individuals with a previous diagnosis of coronary heart disease would remain stable in younger age groups. Interestingly the Worcester Heart Attack Study has recently reported a similar finding.[109] In this study, which included individuals hospitalised with AMI between 1975 and 2001, those who were hospitalised during recent study years were older and had a higher prevalence of comorbid diagnoses, with the exception of previous angina. Sex specific data were not reported. The SPRINT Study reported a decline in the prevalence of prior angina in men and women hospitalised with AMI between 1981-2 and 1992-4.[108]

As for temporal changes in age, there are few studies that have described trends in comorbid diagnoses in men and women hospitalised with AMI. Of those that have, none of them have reported age and sex specific analyses following hospitalisation with first AMI. Only the SPRINT Study has reported the results of sex specific analyses and this is

in a study population comprising individuals with first and recurrent AMIs who were admitted to coronary care units.

In this Scottish study, the prevalence of diabetes increased in men and women across all age groups. The prevalence of diabetes increased in men from 5.8% in 1990-1992 to 10.7% in 1997-2000 and in women from 8.0% to 11.3%. The relative increases were greater in younger individuals compared to older individuals and in men compared to women. There are a number of possible explanations for these changes. The increase in prevalence may not reflect a real change in the prevalence of the disease and may have arisen as a result of a change in coding practice, improved recognition, or because of the lower diagnostic threshold for diabetes that was introduced by the American Diabetes Association in 1997.[184;185] Alternatively the increase in prevalence may reflect a real change in prevalence that has in part arisen because of increasing levels of obesity that are now found in Scotland.[186] A number of other studies have demonstrated an increase in the prevalence of diabetes in individuals hospitalised with AMI, including the Worcester Heart Attack Study, the SPRINT Study and the Ontario Study.[106;108;109] The SPRINT Study reported an increase in the prevalence of diabetes in men from 18% in 1981-3 to 23% in 1992-4. In women the prevalence rose from 29% in 1981-3 to 35% in 1992-4.[108]

In this study, the prevalence of hypertension more than doubled in men and women during the study period. In men the prevalence of hypertension increased from 5.4% in 1990-1992 to 14.1% in 1997-2000, and in women from 7.4% in 1990-1992 to 18.2% in 1997-2000. As with diabetes, it is not clear whether these changes reflect an underlying change in population disease prevalence or whether they are due to better coding and diagnosis. The literature regarding changing prevalence of hypertension has not been consistent in its findings. The Worcester Heart Attack Study also reported an increase in the prevalence of hypertension in individuals hospitalised with AMI, from 41% in 1975-8 to 68.7% in 2001.[109] However, in the SPRINT Study the prevalence of hypertension remained relatively stable in men and women.[108]

Between 1990-1992 and 1997-2000, the prevalence of heart failure in the current study increased substantially in men and women hospitalised in Scotland with a first AMI. The prevalence increased from 11.6% in men and 16.2% in women in 1990-1992 to 17.2% in men and 21.8% in women in 1997-2000. These figures are similar to those observed in the Ontario Study in which 19.3% of individuals hospitalised with AMI in 1992 had a diagnosis of congestive heart failure.[106] This figure rose to 21.5% in 1996. The Worcester

Heart Attack Study also reported an increasing prevalence of heart failure in those patients who were hospitalised in recent study years compared to those hospitalised during the early study years.[109] The overall prevalence of heart failure increased from 13.9% in 1975-1978 to 25.5% in 2001. In this study the prevalence was based on secondary coding as well as prior admission and it is therefore likely that a proportion of the heart failure cases developed subsequent to the first AMI. In this report from the Worcester Heart Attack Study however, the prevalence was based on past medical history. Further analyses carried out by the Worcester Heart Attack Study reported a modest decline in the incidence rate of heart failure between 1975 and 1995 in individuals hospitalised with AMI.[137] In the current study a true increase in the prevalence of heart failure may have arisen as a result of a number of factors. These would include increasing age and increasing numbers of women as well as an increasing prevalence of hypertension and diabetes, both of which would increase the likelihood of developing heart failure.[187;188]

6.2.3 Summary

In the current study the average age of men and women hospitalised with a first AMI increased by over a year between 1990 and 2000. Over the same period the prevalence of comorbid illness also increased. Whilst some of these changes may reflect changes in coding and diagnostic threshold, it seems likely that they will also reflect a real increase in certain diagnoses. An improvement in the detection and treatment of disease is probably also important and may contribute to a reduction in the severity of disease in individuals hospitalised with AMI and an improvement in their survival rates.

7 FIRST AMI: BURDEN OF DISEASE

7.1 Results

The aim of this section is to describe the changing burden of first AMI in men and in women on the hospital sector of the National Health Service in Scotland over the period 1990-2000. 'Burden' includes numbers of hospitalisations, population hospitalisation rates, length of stay and bed days as well as in-hospital revascularisation rates. Analysis of temporal trends in these measures allows us to place AMI in context to the overall burden on the National Health Service in Scotland and also to examine and compare the contribution of AMI in men and women over time.

7.1.1 Population rates for admission to hospital following a first AMI 1990-2000

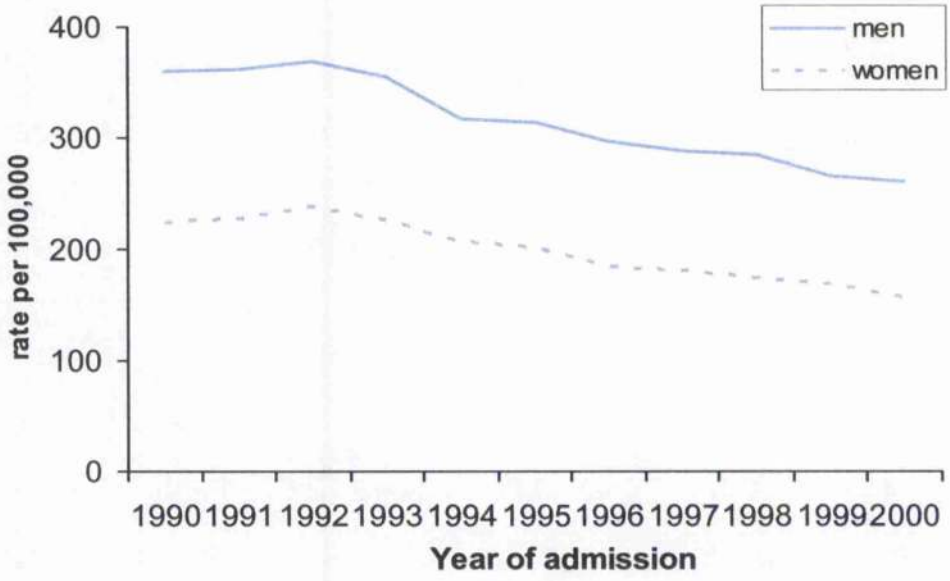
Sex

Between 1990 and 2000, the population discharge rate for first AMI fell by 28% in men, from 361 to 260 per 100,000, and by 30% in women, from 225 to 157 per 100,000 (Table 32). These trends were highly significant in men and women, $p<0.001$.

Table 32 Annual number of cases and population rates per 100,000 for men and women admitted to hospital following a first AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	6687	4657	361	225
1991	6730	4715	363	227
1992	6844	4937	368	238
1993	6630	4686	356	225
1994	5913	4313	317	207
1995	5848	4208	313	202
1996	5517	3855	296	185
1997	5365	3772	288	181
1998	5293	3645	284	175
1999	4958	3531	266	169
2000	4841	3281	260	157
Crude % change	-28	-30	-28	-30
Average annual change (95% CI)	¯217 (¯260-¯175)	¯ 181 (¯ 214- ¯ 149)	¯ 12.7 (¯ 15- ¯ 10)	¯ 8.8 (¯ 10- ¯ 7)

Figure 10 Population rates in men and women for admission to hospital following a first AMI



Age and sex

Examination of age and sex specific temporal trends in population rates revealed important differences between age groups and between men and women. These are shown in, Table 33, Table 34, Table 35, Table 36, Table 37 and Figure 11. The greatest absolute changes in the number of individuals admitted to hospital following a first AMI occurred in those aged 55 to 74 years, and were greater in men than in women. Between 1990 and 2000, the number of men aged 55-64 years with a discharge diagnosis of first AMI decreased by 656, a relative decline of 36%. In women the number of first AMI diagnoses in individuals aged 55-64 years, declined by 404, a relative decline of 50%. These trends were all highly significant.

Smaller absolute and relative changes were seen in men and women aged <55 years. In this age group, population rates for AMI hospitalisation declined by 24% in men and 28% in women. These trends were all significant. Men and women aged greater than 84 years displayed an increase in the absolute number of hospitalisations. This did however translate into a modest decline in population rates of 10% in women and 25% in men.

The sex differences in population rates for first AMI hospitalisation declined with increasing age so that the large discrepancy seen in younger people was no longer as apparent in men and women aged 75 and over.

Table 33 Annual number of cases and population rates per 100,000 for men and women aged <55 years admitted to hospital following a first AMI

Aged < 55 years	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	1432	383	110	29
1991	1447	386	111	29
1992	1414	397	108	30
1993	1460	355	112	27
1994	1279	326	98	24
1995	1173	315	90	24
1996	1160	287	89	22
1997	1155	285	89	21
1998	1220	307	95	23
1999	1082	273	84	21
2000	1075	278	84	21
Crude % change	-25	-27	-24	-28
Average annual change (95% CI)	¯ 44 (¯ 60- ¯ 27)	¯ 13 (¯ 17- ¯ 9)	¯ 3 (¯ 4- ¯ 2)	¯ 1 (¯ 1.3- ¯ 0.7)

Table 34 Annual number of cases and population rates per 100,000 for men and women aged 55-64 years admitted to hospital following a first AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	1816	814	711	286
1991	1862	825	732	292
1992	1857	856	731	304
1993	1758	795	690	283
1994	1543	747	606	266
1995	1591	670	624	239
1996	1424	636	561	229
1997	1360	609	535	220
1998	1261	589	490	211
1999	1234	503	473	178
2000	1160	410	441	145
Crude % change	-36	-50	-38	-49
Average annual change (95% CI)	¯ 77 (¯ 91- ¯ 64)	¯ 42 (¯ 51- ¯ 33)	¯ 32 (¯ 37- ¯ 26)	¯ 15 (¯ 18- ¯ 11)

Table 35 Annual number of cases and population rates per 100,000 for men and women aged 65-74 years admitted to hospital following a first AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	1963	1435	1038	578
1991	2027	1459	1056	586
1992	2031	1531	1045	610
1993	2059	1409	1044	555
1994	1855	1348	926	525
1995	1725	1261	868	499
1996	1686	1122	852	449
1997	1605	1081	813	435
1998	1581	1087	799	439
1999	1378	973	696	395
2000	1373	933	690	379
Crude % change	-30	-35	-34	-34
Average annual change (95% CI)	¯ 72 (¯ 91- ¯ 54)	¯ 61 (¯ 74- ¯ 47)	¯ 41 (¯ 48- ¯ 33)	¯ 24 (¯ 28- ¯ 19)

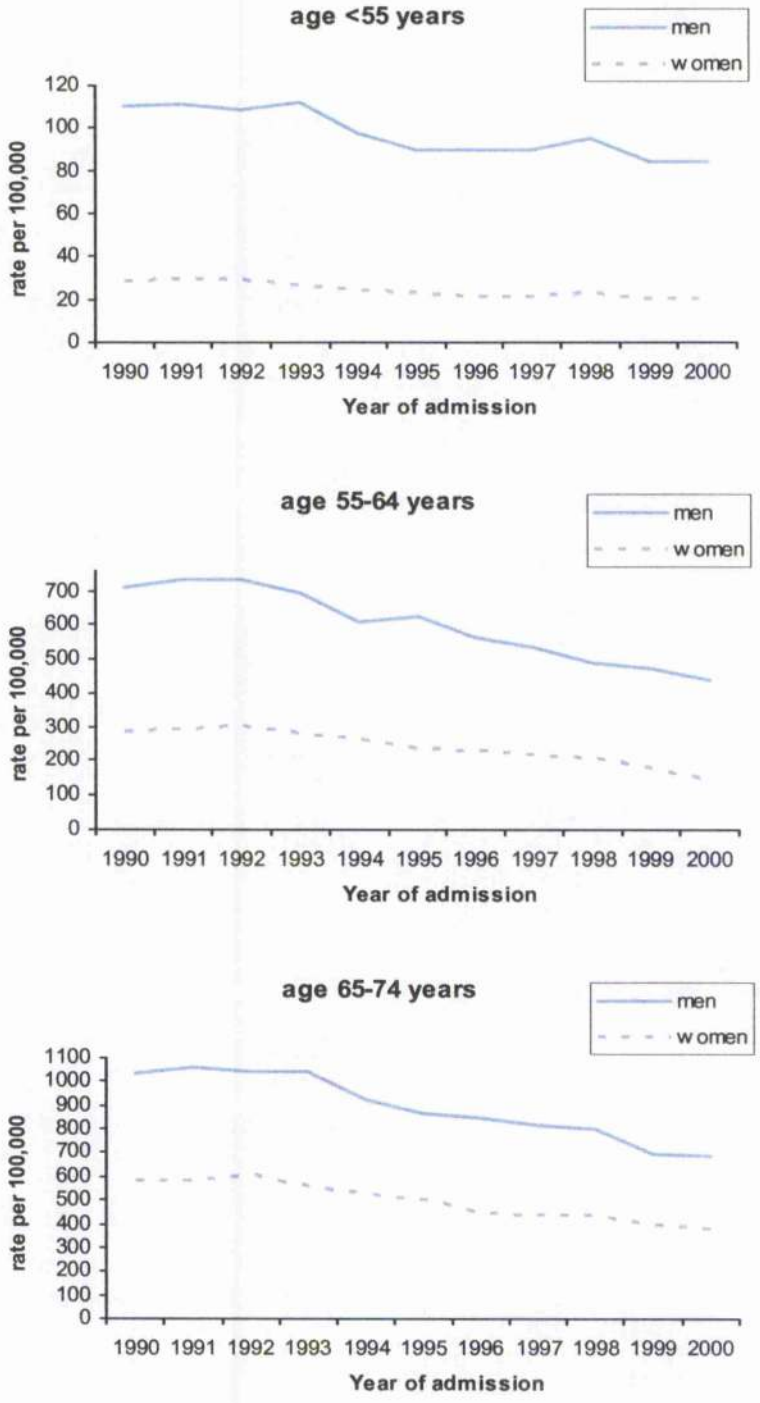
Table 36 Annual number of cases and population rates per 100,000 for men and women aged 75-84 years admitted to hospital following a first AMI

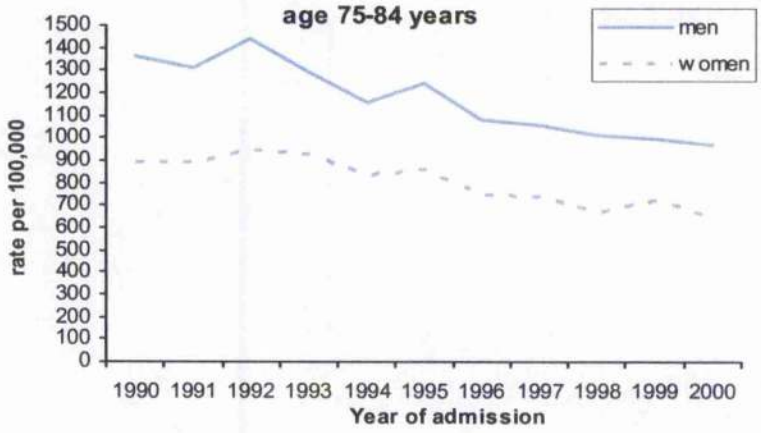
	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	1242	1511	1359	894
1991	1202	1489	1316	888
1992	1304	1556	1441	941
1993	1144	1487	1296	923
1994	997	1306	1155	830
1995	1118	1384	1241	859
1996	1005	1216	1084	744
1997	1002	1212	1053	733
1998	974	1104	1009	666
1999	981	1193	998	718
2000	971	1080	970	649
Crude % change	-22	-29	-29	-27
Average annual change (95% CI)	¯ 32 (¯ 46- ¨ 18)	¯ 49 (¨ 62- ¯ 35)	¯ 46 (¯ 59- ¯ 33)	¯ 29 (¯ 39- ¯ 19)

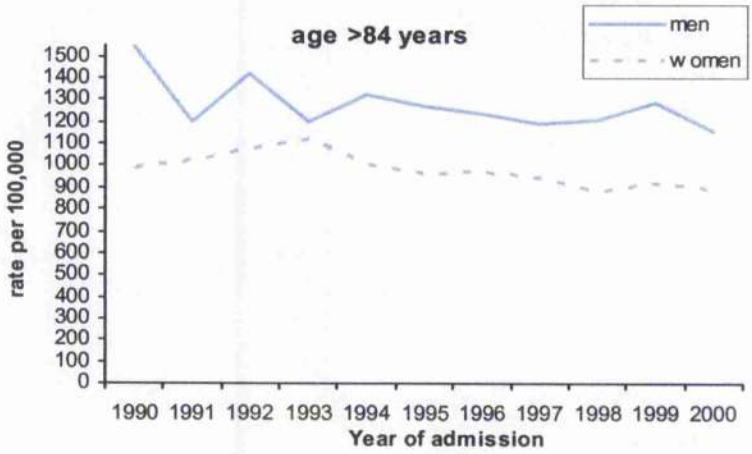
Table 37 Annual number of cases and population rates per 100,000 for men and women aged >84 years admitted to hospital following a first AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	234	514	1538	986
1991	192	556	1201	1024
1992	238	597	1422	1071
1993	209	640	1199	1117
1994	239	586	1323	1000
1995	241	578	1267	956
1996	242	594	1230	967
1997	243	585	1192	939
1998	257	558	1203	880
1999	283	589	1286	918
2000	262	580	1157	892
Crude % change	+12	+13	-25	-10
Average annual change (95% CI)	+6 (+2-+9)	+2 (¯5-+9)	¯21 (¯42-¯0.4)	¯17 (¯28-¯6)

Figure 11 Age and sex specific population rates for admission to hospital following a first AMI




age 75-84 years
men
women
rate per 100,000
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000
Year of admission


age >84 years
men
women
rate per 100,000
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000
Year of admission

7.1.2 Length of stay and bed days occupied following admission to hospital with a first AMI 1990-2000

Length of stay in days in men and women

Length of stay declined steadily in men and women between 1990 and 2000. In 1990 the mean length of stay was 11.8 days in men and 20.7 days in women. This difference was highly significant. By 2000 the mean length of stay had declined to 8.9 days in men and 11.8 days in women. Again these changes were highly significant. Median length of stay differed substantially from mean and was therefore a more appropriate summary measure. The median length of stay was 8 days in men and women in 1990 and declined to 6 days in men and 7 days in women by 2000. The interquartile range was greater in women than in men in each year suggesting that the distribution of length of stay was more widely spread.

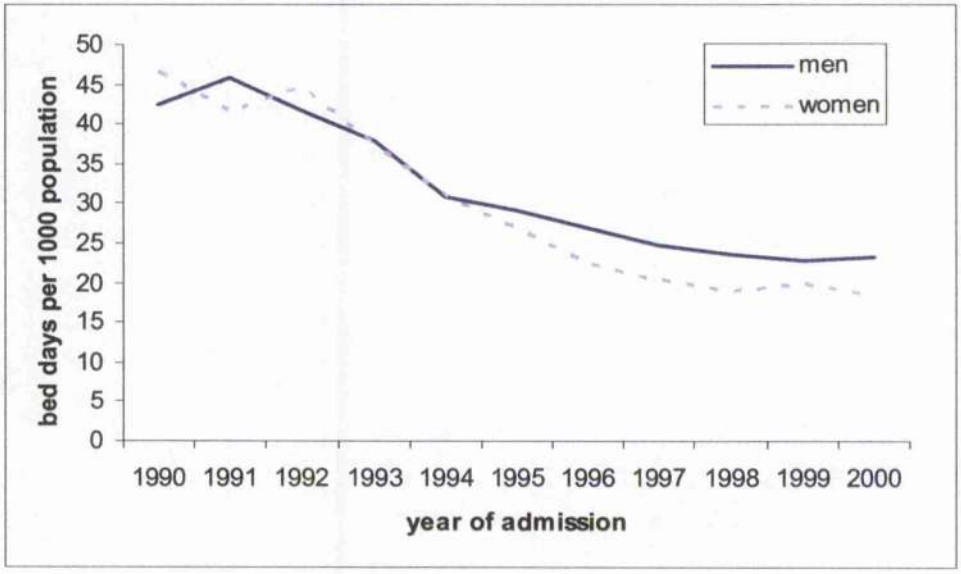
Table 38 Length of stay in men and women following a first AMI 1990-2000

	Men			Women		
year of admission	**Mean**	**Median**	**IQ range**	**Mean**	**Median**	**IQ range**
1990	11.8	8	6-10	20.7	8	6-13
1991	12.6	7	6-10	18.3	8	6-12
1992	11.3	7	6-9	18.8	8	6-12
1993	10.6	7	6-9	16.6	8	5-12
1994	9.7	7	5-9	14.9	8	6-12
1995	9.3	7	5-9	13.3	7	5-12
1996	9.1	7	5-9	12.1	7	5-12
1997	8.6	6	5-8	11.3	7	5-11
1998	8.3	6	5-8	10.8	7	5-11
1999	8.6	6	5-8	11.8	7	5-11
2000	8.9	6	5-8	11.8	7	5-11

Bed days in men and women

Figure 12 shows the bed days per 1000 population occupied by men and women following a first AMI between 1990 and 2000. Bed days declined substantially in men and in women. In men the number of bed days occupied per 1000 head of population fell from 42.5 in 1990 to 23.2 in 2000, a decline of 46%. The fall was even greater in women in whom the bed days declined from 46.6 in 1990 and 18.5 in 2000, a fall of 60%. Since 1995, the occupied bed days per 1000 population has been consistently greater in men than in women.

Figure 12 Bed days occupied by men and women following a first AMI 1990-2000



Total occupied bed days in men and women hospitalised with a first AMI between 1990 and 2000 are shown in Table 39. The total number of occupied bed days has declined substantially in men and women during the study period. In 1990, occupied bed days were similar in men and women, the lower numbers of admissions in women being offset against a longer length of stay. By 2000 the number of occupied bed days more than halved in men and women and women accounted for 46% of all bed days.

Table 39 Total occupied days in men and women hospitalised with first AMI 1990-2000

Year of admission	Men (%)	Women (%)	Total (%)
1990	43121 (49.9)	43254 (50.1)	86375 (100)
1991	38080 (49.4)	39073 (50.6)	77153 (100)
1992	37931 (51.4)	35825 (48.6)	73756 (100)
1993	32964 (50.6)	32220 (49.4)	65184 (100)
1994	2797 (49.0)	29127 (51.0)	31924 (100)
1995	27979 (51.4)	26402 (48.6)	54381 (100)
1996	23620 (52.8)	21157 (47.2)	44777 (100)
1997	21226 (52.5)	19228 (47.5)	40454 (100)
1998	19923 (53.2)	17500 (46.8)	37423 (100)
1999	18952 (51.3)	17975 (48.7)	36927 (100)
2000	18401 (53.6)	15923 (46.4)	34324 (100)

7.1.3In-hospital revascularisation rates in men and women following a first AMI 1990-2000

Table 40 shows the number and proportion of men and women with a first AMI undergoing a revascularisation procedure during their inpatient stay. The numbers and proportions are relatively small, but increased substantially over time in men and women (

Figure 13). In 1990, only two men and four women underwent a revascularisation procedure during their inpatient stay. By 2000 this had increased to 208 men and 71 women. The proportion of men and women undergoing a coronary artery bypass graft operation was similar in men and women whilst a higher proportion of men than women had a percutaneous angioplasty procedure. The proportion of individuals undergoing a revascularisation procedure varied with age and younger men and women were more likely to undergo in-hospital revascularisation than older men and women (Table 41). This trend was highly significant in men and in women, $p<0.001$.

Table 40 Numbers and rates of men and women with a first AMI undergoing revascularisation during their index hospital admission 1990-2000

	Men			Women		
	Revasc	**CABG**	**PTCA**	**Revasc**	**CABG**	**PTCA**
1990	2 (0%)	1 (0%)	1 (0%)	4 (0.1%)	3 (0.1%)	1 (0%)
1991	17 (0.3%)	7 (0.1%)	10 (0.1%)	3 (0.1%)	1 (0%)	2 (0%)
1992	16 (0.2%)	5 (0.1%)	11 (0.2%)	7 (0.1%)	1 (0%)	6 (0.1%)
1993	26 (0.4%)	10 (0.2%)	16 (0.2%)	16 (0.3%)	3 (0.1%)	13 (0.3%)
1994	25 (0.4%)	7 (0.1%)	19 (0.3%)	25 (0.6%)	7 (0.2%)	18 (0.4%)
1995	44 (0.8%)	8 (0.1%)	37 (0.6%)	33 (0.8%)	9 (0.2%)	25 (0.6%)
1996	63 (1.1%)	14 (0.3%)	50 (0.9%)	38 (1.0%)	8 (0.2%)	30 (0.8%)
1997	94 (1.8%)	17 (0.3%)	79 (1.5%)	44 (1.2%)	7 (0.2%)	37 (1.0%)
1998	127 (2.4%)	15 (0.3%)	112 (2.1%)	64 (1.8%)	8 (0.2%0	56 (1.5%)
1999	154 (3.1%)	10 (0.2%)	145 (2.9%)	76 (2.2%)	5 (0.1%)	71 (2.0%)
2000	208 (4.3%)	12 (0.2%)	198 (4.1%)	71 (2.2%)	6 (0.2%)	66 (2.0%)
Total	776 (0.1%)	106 (0.2%)	678 (1.0%)	381 (0.8%)	58 (0.1%)	325 (0.7%)

Figure 13 Proportion of men and women undergoing a revascularisation procedure during admission following a first AMI 1990-2000

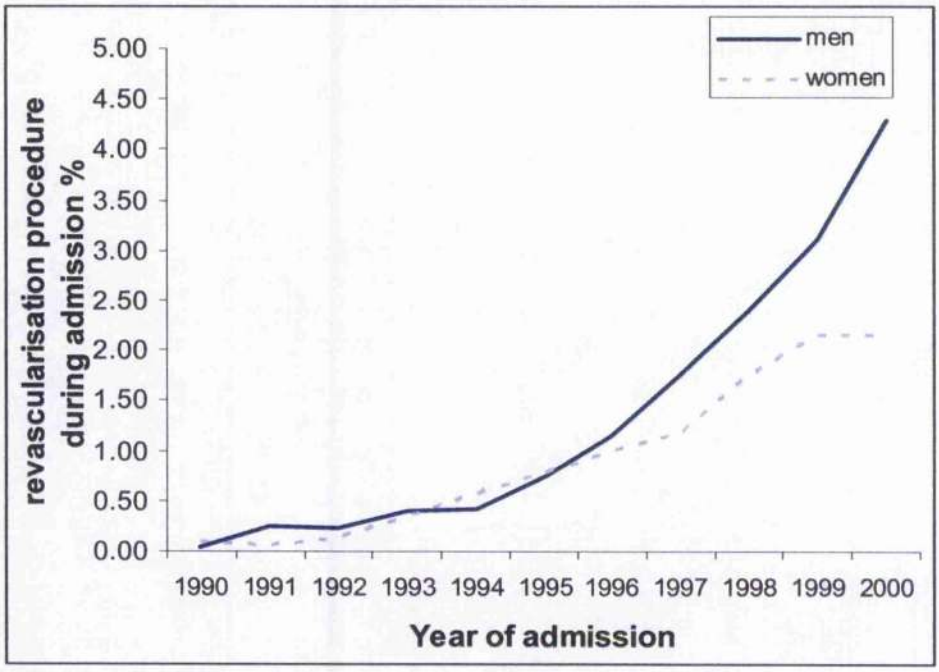


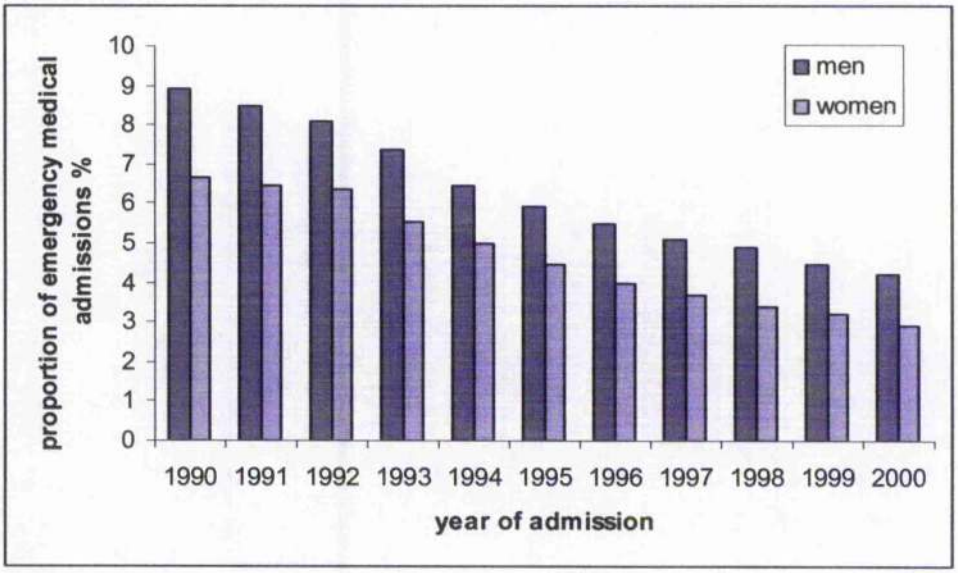
Table 41 Proportion of men and women in different age groups undergoing a revascularisation procedure during admission following a first AMI

Age group	Men	Women
< 55 years	264 (1.9%)	77 (2.1%)
55-64 years	241 (1.4%)	111 (1.5%)
56-74 years	227 (1.2%)	139 (1.0%)
75-84 years	39 (0.3%)	51 (0.4%)
>84 years	5 (0.2%)	3 (0.05%)

7.1.4First AMI as a proportion of all emergency medical admissions

In 1990 hospitalisations for first AMI accounted for 9% of all emergency medical admissions in men and 7% of all emergency medical admissions in women. By 2000 these figures had fallen to 4% and 3% in men and women respectively. First AMI accounted for a higher proportion of medical admissions in men than in women and this sex difference remained relatively stable between 1990 and 2000 (Figure 14).

Figure 14 Barchart showing admissions for first AMI as a proportion of all emergency medical admissions in men and women 1990-2000



7.2 Discussion regarding burden of disease for first AMI

7.2.1 Population discharge rates in men and women 1990-2000

In Scotland between 1990 and 2000, the population discharge rate for first AMI fell by 28% in men, from 361 to 260 per 100,000 and by 30% in women, from 225 to 157 per 100,000. The fall in hospitalisation rates for AMI is in keeping with numerous reports from many countries. [48;50-54;57;58;189-191] In the Worcester Heart Attack Study, the age adjusted incidence of first AMI declined by 26% in men (from 323 per 100,000 in 1975 to 240 per 100,000 in 1988) and by 22% in women (from 176 per 100,000 in 1975 to 137 per 1000,000 in 1988).[56] Similar declines were also seen in the Stockholm Study in which age adjusted incidence of first AMI fell by 18% in men and by 13% in women.[63] In the Minnesota Heart Survey there were more modest declines in the incidence of first AMI in men and women between 1985 and 1990.[55] Age adjusted incidence fell by 5% in men and 4% in women during the study period. Not all studies have reported sex specific analyses. Those that have reported sex specific findings have not been consistent in their findings. A number of studies have reported more modest changes in incidence in women than in men. For example NHANES 1, the Rochester Epidemiology Project and the OXMIS Study all reported an increasing incidence of AMI in women and a decreasing incidence of AMI in men over time.[54;59;60] In contrast to this and other studies, the ARIC Study reported an increasing incidence of AMI in men and women, although the findings were statistically non-significant.[62] The reasons for the conflicting findings regarding trends in AMI incidence, especially in women are not clear. Trends have varied across different populations and across different study types and consequently there is no obvious geographical or methodological explanation. Definition of AMI varies between studies and one observation is that those studies that have employed a narrower definition of AMI, such as the MONICA studies, are more likely to have reported a decline in incidence than those studies that have used a broader definition, such as ARIC, possibly including probable as well as definite AMI.

7.2.2 Population discharge rates in men and women and different age groups 1990-2000

Overall changes masked substantial variation within subgroups and this study has found that there are important differences in temporal trends in AMI incidence between men and

women in different age groups. Greatest relative changes were seen in men and women aged 55-64 years. In this age group men demonstrated a 38% decline and women a 49% decline in incidence rates between 1990 and 2000. Falls were more modest in the very elderly. In individuals aged greater than 84 years, men experienced a 25% decline in incidence compared to a 10% decline in women. Few studies have reported age and sex specific trends in AMI incidence. The Worcester Heart Attack Study, the OXMIS Study and the Rochester Epidemiology Project all examined age and sex specific trends in incidence of AMI, and found conflicting results.[54;56;59] In the Worcester Heart Attack Study, the greatest declines were seen in the very elderly in whom incidence rates declined by approximately 55% between 1975 and 1988.[56] The overall decline also disguised increasing incidence in women aged 65-74 years in whom incidence rates increased by 15%. The Rochester Epidemiology Project also reported differing secular trends in AMI incidence according to age and sex. They also reported increasing incidence in women aged 60 years and greater but declining rates in men of all ages. The reasons for the observed disparities between studies are not clear. There would appear to be consistent evidence for declining AMI incidence in men in all age groups, but conflicting evidence regarding secular trends in women. It is likely that differences in methodology including definition of AMI may account for some of the variation in findings. It is apparent that those population-based studies that have analysed routine data sets, such as the Swedish National AMI Register and the Ontario Myocardial, Infarction Database, have been more consistent in their findings than studies involving more select populations and specific diagnostic criteria.

7.2.3Length of stay and bed days in men and women

In this study the average length of stay in men and women hospitalised with AMI declined significantly between 1990 and 2000. Median length of stay declined from eight days in men and women in 1990, to six days in men and seven days in women in 2000. Total bed days also declined dramatically in both sexes, presumably a reflection of declining incidence and shorter lengths of stay. In 1990-1991, overall bed usage was slightly greater in women than in men, despite the fact that they accounted for only 41.1% of all admissions. This was a reflection of the longer average length of stay seen in women than in men. This is likely to be due to the older average age of women hospitalised with a first AMI and also because of the higher prevalence of comorbid disease seen in women compared to men. By 2000 however, total bed usage had declined by 57% in men and by 63% in women so that overall bed usage was greater in men than in women (18401 bed

days in men versus 15923 in women). Women still accounted for only 41.4% of all admissions so presumably reduction in length of stay has had a greater impact in women than in men. There are few existing data on the health service burden of AMI with which to compare these findings. The National Hospital Discharge Survey found that median length of stay declined by 38% between 1998 and 1997, from eight days to five days. [53] This is similar to the results of this study though sex specific results were not reported. In the Minnesota Heart Survey the median length of stay for individuals hospitalised with AMI between 1985 and 1990 decreased from 8.5 days to 6.2 days in men and from 8.9 days to 6.9 days among women. This study however excluded individuals over the age of 74 years. This would bias the average length of stay analyses as length of stay increases with age. The burden placed on the hospital sector by AMI has fallen substantially because of declining incidence and a reduction in length of stay in both men and women.

7.2.4 In-hospital revascularisation rates in men and women

In contrast to the falling incidence and length of stay, there has been a dramatic increase in the proportion of men and women hospitalised with a first AMI who underwent a revascularisation procedure during their inpatient stay. In 1990 less than 0.1% of individuals underwent a revascularisation procedure during their admission. By 2000 this had increased to 4.3% of men and 2.2% of women. The in-hospital intervention rate declined with increasing age in men and women. In 2000, the individuals who underwent revascularisation during their hospital stay were much more likely to have a percutaneous angioplasty procedure than a coronary artery bypass graft operation. In 2000, percutaneous angioplasty was carried out in 2.0% of women and 4.1% of men whereas coronary artery bypass grafting was carried out in only 0.2% of women and 0.2% of men. Again there are very few population-based data with which to compare these findings. The intervention rates are much lower than those reported by any other study. This is in part likely to reflect selection bias in existing surveys and studies which tend to include a high proportion of teaching hospitals with on-site revascularisaton facilities.[192;193] In the EURO Heart Survey, percutaneous angioplasty was carried out in 40.4% of individuals, and coronary artery bypass grafting in 3.4% of individuals diagnosed with ST-elevation AMI.[192] The relatively low levels of intervention are likely to be more representative of population based rates and also to reflect differing clinical practice. It also seems likely that the low intervention rates are in part due to deficiencies in coding in the routine data set analysed in the current study. The majority of revascularisation interventions are carried out in teaching hospitals and patients are transferred from district general hospitals

to these facilities. It is possible that the data extract used in the current study has not included all revascularisation procedures that are carried out in a hospital that is different from the admission hospital.

7.2.5Proportion of all emergency medical admissions

In 1990, first AMI accounted for 9% of all emergency medical admissions in men and for 7% of all emergency medical admissions in women. By 2000 these figures had declined to 4% and 3% respectively. There are no other studies with which to compare these data.

7.2.6Summary

The burden placed on the health service in Scotland by individuals hospitalised with first AMI has declined between 1990 and 2000. This has arisen as a result of declining incidence and length of stay. There has however been a substantial increase in coronary revascularisation procedures which will offset some of the benefits gained as a result of changing incidence and length of stay. It is also important to remember that these individuals represent first AMIs only and are only a proportion of individuals hospitalised with an AMI diagnosis. In addition, whilst AMI hospitalisation rates are declining, there has been a substantial rise increase in the number of hospital admissions for suspected acute coronary syndrome over the past decade. This has been accounted for by a striking increase in admissions with angina and chest pain, which have more than doubled during this period.[194] The overall pattern of suspected acute coronary syndrome has therefore changed with rapidly rising numbers of admissions with chest pain.

8 SURVIVAL FOLLOWING ADMISSION TO HOSPITAL WITH A FIRST AMI

8.1 Results of unadjusted survival analyses

This section describes the unadjusted case fatality of men and women hospitalised in Scotland with a first AMI. Case fatality is described at 30 days, six months, one year, two year and five years in men and women. Analyses in men and women have been stratified into different age groups, socioeconomic categories, years of admission and according to the presence of particular comorbid diagnoses. The aim is to provide actual mortality data and to gain further insight into survival differences that may exist between men and women that may be explored further in multivariate analyses.

8.1.1 Unadjusted case fatality from life tables

The overall unadjusted case fatality rates were higher in women than in men at all of the time periods examined (Table 42). In men the overall case fatality rates at 30 days, six months, one year, two years and five years were 16.3%, 20.7%, 23.5%, 28.0% and 39.0% respectively. In women the equivalent rates were 25.6%, 31.9%, 35.3%, 40.6% and 52.8%. These sex differences were all statistically significant. Prognosis following a first AMI was therefore relatively poor, especially in women, with almost one half of all women dead within 5 years of admission.

Table 42 Unadjusted case fatality rates in men and women following admission to hospital with a first AMI

	Case fatality %	
	Men	**Women**
30 days	16.3	25.6
Six months	20.7	31.9
One year	23.5	35.3
Two years	28.0	40.6
Five years	39.0	52.8

8.1.1.1 Age

30 day and six months case fatality

The effect of age on case fatality was powerful in men and in women. 30 day case fatality was 3.7% in men and 5.9% in women aged less than 55 years. It increased to 42.6% in men and 44.7% in women aged greater than 84 years (Table 43). By six months case fatality had risen to 4.8% in men and 7.0% in women aged <55 years (Table 44). Case fatality was higher in women than in men of all ages at 30 days and six months.

One, two and five years case fatality

By one year case fatality increased to 23.5% in men and 35.3% in women. Again case fatality was higher in women than in men in all age groups (Table 45). By two years the difference in case fatality between men and women was less apparent in the older age groups but remained a similar magnitude in the younger age groups (Table 46). At five years there was an interaction between age and sex so that the effect of sex could not be simply described and depended upon age (Table 47). Young women continued to have a higher case fatality than young men but in men aged 65 to 74 years and 75-84 years, case fatality was greater in men than in women. In men aged 75-84 years, case fatality was 70% compared to 68.4% in women.

8.1.1.2 Socioeconomic deprivation

30 day and six months case fatality

Socio-economic deprivation appeared to have a minimal effect on short-term case fatality. There was a reverse socioeconomic gradient, especially in women so that case fatality was higher in the least deprived groups and lower in the most deprived groups. This gradient was not as apparent in men. Case fatality was higher in all groups in women than in men at 30 days and at six months.

One, two and five years case fatality

Socio-economic deprivation had a similar effect in the longer term. Again, there was a reverse socioeconomic gradient in women but not in men, in whom the effect of socioeconomic deprivation was less consistent. For example, five year case fatality in women decreased from 54.8% in the least deprived group to 51% in the most deprived

group. In men, case fatality was similar in the different deprivation categories and there was no evidence of any significant differences or of trends.

8.1.1.3 Comorbidity

30 day and six months case fatality

At 30 days and six months the effect of prior and concurrent diagnoses had a marked effect on case fatality. The presence of one or more diagnoses increased six month case fatality from 13.4% to 30% in men and from 25.5% to 37.9% in women. The greatest effects were seen with renal failure, cancer, cerebrovascular disease, peripheral vascular disease and heart failure. For example, case fatality was 56.1% in men and 63.6% in women with a coding for renal failure, compared to an overall rate of 20.7% in men and 31.9% in women. Cancer was associated with a six month case fatality rate of 46.3% in men and 47.1% in women. Case fatality was generally higher in women, although this effect varied in its magnitude. Hypertension had a small effect on case fatality which increased to 20.7% in men and 28.7% in women at six months. None of the comorbidies coded appeared to have a protective effect and to reduce case fatality.

One, two and five years case fatality

Similar patterns to those seen at 30 days and six months were seen at one, two and five years. Cancer, renal failure, heart failure and cerebrovascular and peripheral vascular disease again carried the worst prognosis. 87.2% of women and 82.2% of men with renal failure and 75.3% of women and 74.2% of men with cancer were dead within five years. The presence of any coded comorbidity approximately doubled case fatality at five years in men. Five year case fatality was 54.6% with any comorbidity compared to 26.5% with none. The effect was not quite as marked in women; 63.1% compared to 41.5%. Again, hypertension, diabetes and coronary heart disease appeared to have the least effect on case fatality, especially in men. For example, men with a previous admission for coronary heart disease had a five year case fatality of 52% compared to 61.3% in women.

8.1.1.4 Trends in unadjusted case fatality in men and women

30 day and six months case fatality

In men, 30 day case fatality fell from 18.1% in 1990 to 14.6% in 2000, a decline of 19%. In women, case fatality declined by 8%, falling from 27.2% in 1990 to 25.1% in 2000

(Table 48). Smaller declines were also seen at six months, and again the fall was greater in men than in women, 9% compared to 6%.

One, two and five years case fatality

At one year case fatality in men declined from 25.3% in 1990 to 21.9% in 2000, a decline of 13% (**Error! Reference source not found.**). In women one year case fatality fell by 6%, from 37% to 34.8%. At two years however, case fatality fell by approximately 7% in men and women. Five years case fatality fell by 9% in men, from 41.8% to 38.2% and by 5% in women, from 54.2% to 51.7% (Table 49).

Table 43 Unadjusted 30 day case fatality rates in men and women following admission to hospital with a first AMI

	30 day case fatality	
	MEN	**WOMEN**
Overall	16.3	25.6
Age group		
<55	3.7	5.9
55-64	8.9	11.6
65-74	18.7	20.8
75-84	31.4	33.8
>84	42.6	44.7
Deprivation quintile		
1-least deprived	16.4	26.8
2	13.8	27.1
3	16.6	26.4
4	16.2	25.4
5-most deprived	15.4	23.2
Comorbidity		
Any comorbidity	22.8	29.3
No comorbidity	11.1	21.7
Diabetes	20.5	27.8
Cancer	34.2	36.0
Respiratory disease	27.3	32.5
Cerebrovascular disease	31.6	38.4
Peripheral vascular disease	28.5	32.7
Atrial fibrillation	20.6	27.8
Hypertension	15.0	22.3
Renal failure	44.2	52.0
Heart failure	27.7	33.2
Coronary heart disease	22.6	27.4

Table 44 Unadjusted six month case fatality rates in men and women following admission to hospital with a first AMI

	Six month case fatality	
	MEN	**WOMEN**
Overall	20.7	31.9
Age group		
<55	4.8	7.0
55-64	11.4	14.0
65-74	24.1	25.5
75-84	39.6	42.1
>84	54.1	57.3
Deprivation quintile		
1-least deprived	20.5	33.7
2	22.0	33.9
3	21.0	32.9
4	20.8	31.5
5-most deprived	20.3	29.1
Comorbidity		
Any comorbidity	30.0	37.9
No comorbidity	13.4	25.5
Diabetes	27.9	36.1
Cancer	46.3	47.1
Respiratory disease	35.8	41.4
Cerebrovascular disease	42.1	49.9
Peripheral vascular disease	38.1	43.0
Atrial fibrillation	30.2	40.0
Hypertension	20.7	28.7
Renal failure	56.1	63.6
Heart failure	37.5	44.7
Coronary heart disease	28.9	35.4

Table 45 Unadjusted one year case fatality rates in men and women following admission to hospital with a first AMI

	One year case fatality	
	MEN	**WOMEN**
Overall	23.5	35.3
Age group		
<55	5.7	8.2
55-64	13.1	15.6
65-74	27.2	28.5
75-84	44.7	46.7
>84	60.3	62.4
Deprivation quintile		
1-least deprived	23.4	37.0
2	24.5	37.5
3	23.9	36.5
4	23.7	34.8
5-most deprived	23.3	32.6
Comorbidity		
Any comorbidity	34.2	42.7
No comorbidity	15.0	27.5
Diabetes	32.5	41.1
Cancer	52.2	53.0
Respiratory disease	40.8	46.6
Cerebrovascular disease	47.4	55.3
Peripheral vascular disease	43.4	48.2
Atrial fibrillation	36.0	46.2
Hypertension	24.2	32.7
Renal failure	61.1	68.4
Heart failure	43.0	50.8
Coronary heart disease	33.3	40.2

Table 46 Unadjusted two years case fatality rates in men and women following admission to hospital with a first AMI

	Two year case fatality	
	MEN	**WOMEN**
Overall	28.0	40.6
Age group		
<55	7.2	10.3
55-64	16.2	18.7
65-74	32.4	33.3
75-84	52.6	53.4
>84	68.7	69.8
Deprivation quintile		
1-least deprived	27.9	42.4
2	28.8	42.6
3	28.4	41.3
4	28.4	40.5
5-most deprived	28.1	38.0
Comorbidity		
Any comorbidity	40.6	49.3
No comorbidity	17.9	31.4
Diabetes	38.8	49.0
Cancer	60.2	60.8
Respiratory disease	48.1	54.1
Cerebrovascular disease	55.5	62.1
Peripheral vascular disease	51.2	55.4
Atrial fibrillation	43.8	54.4
Hypertension	29.3	38.8
Renal failure	69.4	76.1
Heart failure	51.0	58.4
Coronary heart disease	38.9	47.3

Table 47 Unadjusted five years case fatality rates in men and women following admission to hospital with a first AMI

	Five year case fatality	
	MEN	**WOMEN**
Overall	39.0	52.8
Age group		
<55	11.5	14.8
55-64	25.1	27.0
65-74	45.5	45.1
75-84	70.0	68.4
>84	85.8	86.0
Deprivation quintile		
1-least deprived	38.3	54.8
2	40.1	54.2
3	39.7	53.4
4	39.6	53.2
5-most deprived	39.9	51.0
Comorbidity		
Any comorbidity	54.6	63.1
No comorbidity	26.5	41.5
Diabetes	53.2	63.5
Cancer	74.2	75.3
Respiratory disease	62.9	68.6
Cerebrovascular disease	69.9	74.1
Peripheral vascular disease	65.3	68.6
Atrial fibrillation	60.9	70.9
Hypertension	42.8	51.8
Renal failure	82.2	87.2
Heart failure	66.9	73.1
Coronary heart disease	52.0	61.3

Table 48 Trends in unadjusted 30 day and six months case fatality rates in men and women following admission to hospital with a first AMI

	30 day case fatality %		Six months case fatality %	
	MEN	**WOMEN**	**MEN**	**WOMEN**
1990	18.1	27.2	21.5	33.5
1991	17.3	26.2	22.6	32.9
1992	17.0	26.4	21.9	32.2
1993	16.7	26.8	21.1	33.2
1994	16.0	24.7	20.9	31.1
1995	15.9	24.7	20.1	31.1
1996	15.9	24.7	19.9	31.2
1997	15.5	25.4	19.9	31.3
1998	14.8	23.9	19.3	30.2
1999	15.8	25.5	20.3	32.1
2000	14.6	25.1	19.5	31.5
% change	19%	8%	9%	6%

vbwomen following admission to hospital with a first AMI 1990-2000

	One year case fatality %		Two years case fatality %	
	MEN	**WOMEN**	**MEN**	**WOMEN**
1990	25.3	37.0	29.2	42.6
1991	24.4	36.4	29.9	42.2
1992	25.0	36.1	29.8	41.4
1993	23.8	36.7	28.2	42.2
1994	23.5	34.4	28.1	39.6
1995	22.8	34.2	27.0	39.6
1996	23.0	34.3	27.3	38.9
1997	22.6	34.5	26.9	41.5
1998	21.9	33.7	26.2	38.7
1999	22.9	35.2	27.1	39.6
2000	21.9	34.8	-	-
% change	13%	6%	7%	7%

Table 49 Trends in unadjusted five year case fatality rates in men and women following admission to hospital with a first AMI 1990-2000

	Five years case fatality %	
	MEN	**WOMEN**
1990	41.8	54.2
1991	40.2	54.5
1992	40.8	52.6
1993	40.0	54.1
1994	38.8	52.4
1995	37.2	52.0
1996	38.2	51.7
% change	9%	5%

8.1.2 Kaplan-Meier Survival Curves and median survival time

8.1.2.1 Overall

The Kaplan Meier survival curve for men and women showed a progressive decline in cumulative survival in both men and women (Figure 15). Survival was consistently higher in men and this difference was statistically significant ($p<0.001$). The results of the log rank tests are shown in Table 52. Median survival times for men and women are shown in Table 50 and Table 51. The median survival of men admitted to hospital with a first AMI was 8.8 years in men compared to 4.3 years in women.

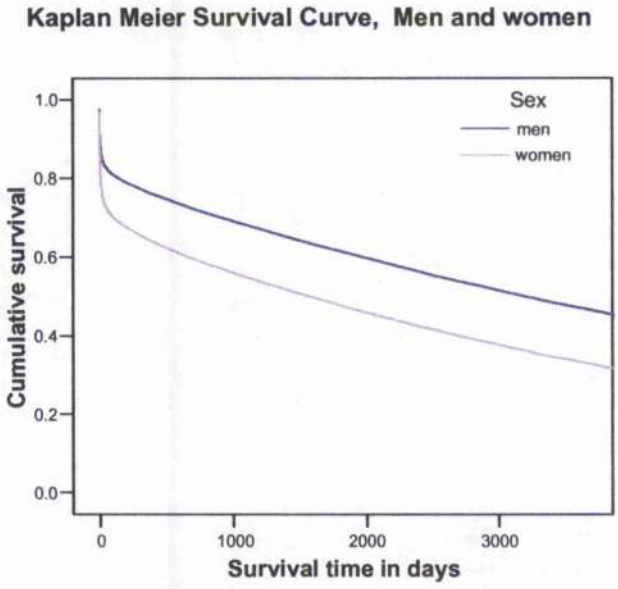
8.1.2.2 Age

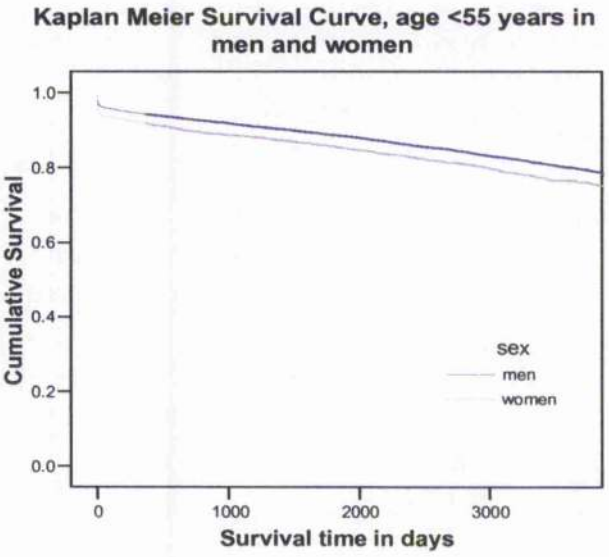
Figure 15 shows the Kaplan Meier survival curves for men and women in different age groups. As demonstrated in the life table, age had a powerful effect on prognosis. Median survival was greater than 10 years in both men and women aged <65 years, but decreased to 0.3 years in men and 0.2 years in women aged >84 years. Prognosis was better for men than for women, especially in the younger age groups. In individuals aged 65 and over, women appeared to have a worse prognosis than men in the short term, but a better prognosis than men in the longer term. Overall therefore, the survival curves were only significantly different in men and women aged less than 65 years. The effect of sex on prognosis seemed to change as survival time increased.

8.1.2.3 Socio-economic deprivation

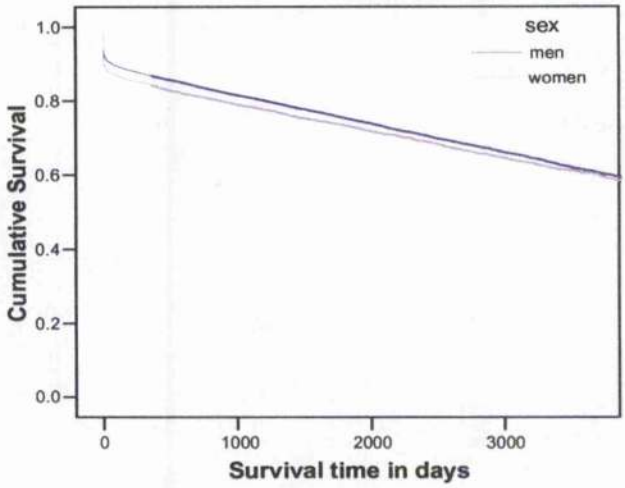
Figure 16 shows Kaplan Meier survival curves in men and women within deprivation categories. The effect of sex on survival was similar in each of the deprivation categories. Survival was significantly worse in women in all groups ($p<0.001$). In men, median survival was significantly longer in the least deprived category (9.5 years) when compared to other deprivation groups (8.2 years in most deprived group). There was little variation in median survival in the other categories. In women, median survival was significantly longer in the most deprived category (4.8 years) when compared to other deprivation categories.

Figure 15 Survival by sex for all ages and by age group for first AMI

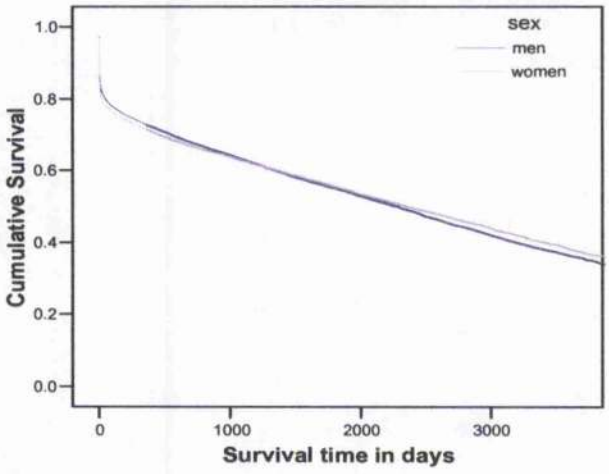




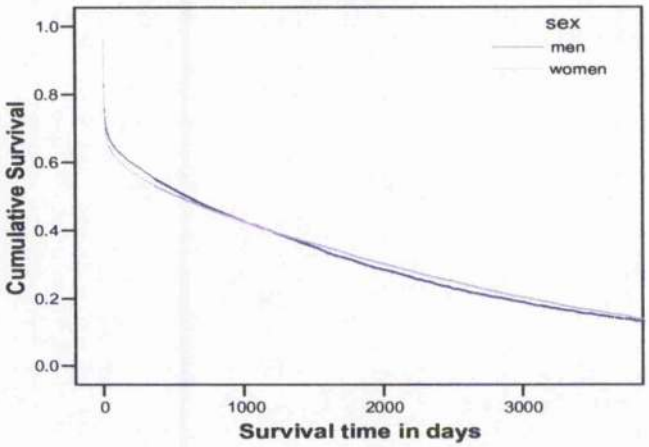
Kaplan Meier Survival Curve, age 55-64 years in men and women



Kaplan Meier Survival Curve, age 65-74 years in men and women



Kaplan Meier Survival Curve, age 75-84 years in men and women



Kaplan Meier Survival Curve, age >84 years in men and women

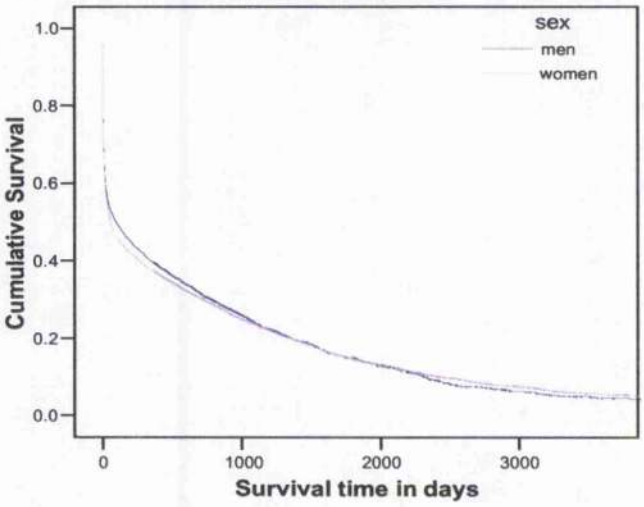
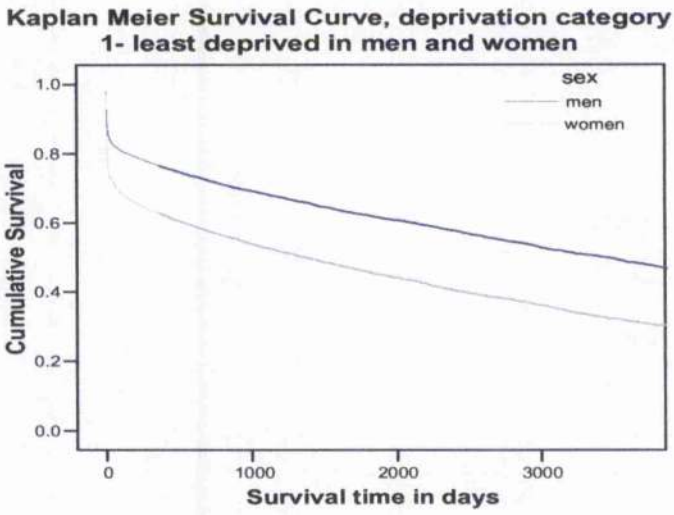
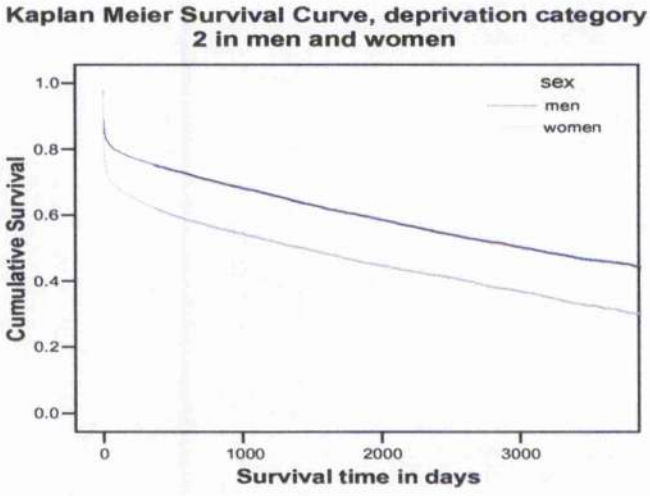
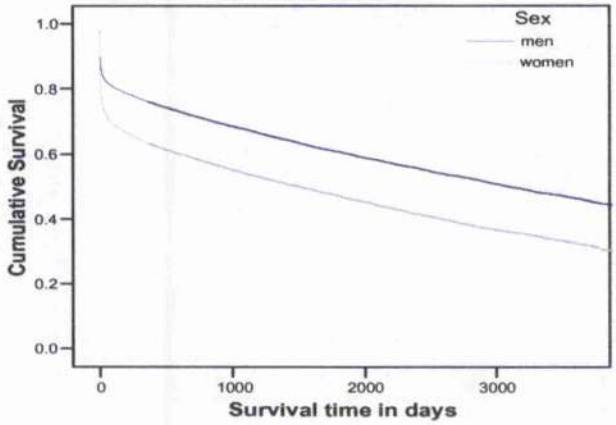


Figure 16 Survival by sex within deprivation categories

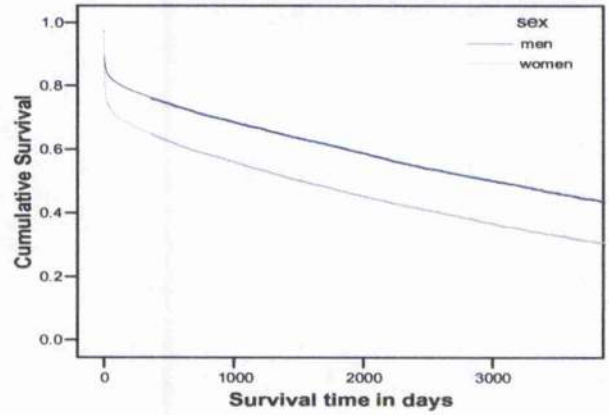




Kaplan Meier Survival Curve, deprivation category 3 in men and women



Kaplan Meier Survival Curve, deprivation category 4 in men and women



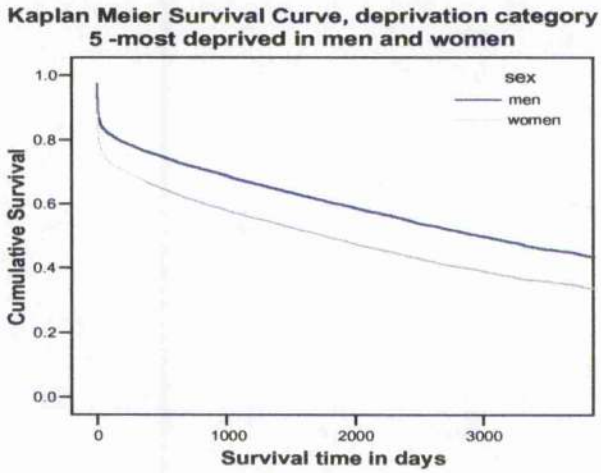

Kaplan Meier Survival Curve, deprivation category
5 -most deprived in men and women
sex
men
women
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
1000
2000
3000
Survival time in days

Table 50 Median survival time in years in men and women following a first AMI

	Median survival in years (95% CI)	
	MEN	**WOMEN**
Overall	8.8 (8.6-9.0)	4.3 (4.2-4.5)
Age group		
<55	>10	>10
55-64	>10	>10
65-74	6.2 (6.0-6.4)	6.4 (6.2-6.7)
75-84	1.6 (1.5-1.8)	1.4 (1.3-1.6)
>84	0.3 (0.2-0.4)	0.2 (0.1-0.2)
Deprivation quintile		
1-least deprived	9.5 (9.0-10.0)	3.8 (3.4-4.1)
2	8.3 (8.0-8.7)	4.0 (3.7-4.3)
3	8.5 (8.2-8.9)	4.1 (3.8-4.4)
4	8.3 (8.0-8.7)	4.2 (4.0-4.5)
5-most deprived	8.2 (7.8-8.5)	4.8 (4.6-5.1)
Comorbidity		
Any comorbidity	3.9 (3.7-4.0)	2.1 (2.0-2.2)
No comorbidity	>10	7.8 (7.5-8.0)
Diabetes	4.2 (3.9-4.6)	2.2 (1.9-2.4)
Cancer	0.8 (0.6-0.9)	0.7 (0.6-0.9)
Respiratory disease	2.3 (2.1-2.5)	1.4 (1.2-1.6)
Cerebrovascular disease	1.3 (1.1-1.5)	0.5 (0.4-0.6)
Peripheral vascular disease	1.8 (1.6-2.0)	1.2 (0.9-1.4)
Atrial fibrillation	2.8 (2.6-3.1)	1.4 (1.2-1.6)
Hypertension	7.1 (6.6-7.5)	4.5 (4.1-4.9)
Renal failure	0.2 (0.1-0.3)	0.1 (0.0-0.1)
Heart failure	1.9 (1.7-2.0)	0.9 (0.8-1.0)
Coronary heart disease	4.5 (4.1-4.9)	2.5 (2.1-2.8)S

Table 51 Trends in median survival time in years in men and women following a first AMI

	Median survival in years (95% CI)	
	MEN	**WOMEN**
1990	7.7 (7.3-8.2)	3.8 (3.4-4.2)
1991	8.5 (8.1-8.9)	3.8 (3.4-4.2)
1992	8.1 (7.7-8.5)	4.3 (3.9-4.7)
1993	>8	3.9 (3.5-4.3)
1994	>7	4.5 (4.1-4.9)
1995	>6	4.6
1996	>5	>5
1997	>4	>4
1998	>3	>3
1999	>2	>2
2000	>1	>1

Table 52 Results of log rank tests from Kaplan Meier Survival comparing men and women

	Log rank test, p-value
Sex	P<0.0001
Age group	
<55	P<0.0001
55-64	P=0.0022
65-74	**P=0.3666 NS**
75-84	**P=0.6990 NS**
>84	**P=0.4148 NS**
Deprivation quintile	
1-least deprived	P<0.0001
2	P<0.0001
3	P<0.0001
4	P<0.0001
5-most deprived	P<0.0001
Comorbidity	
Any comorbidity	P<0.0001
No comorbidity	P<0.0001
Diabetes	P<0.0001
Cancer	**P=0.36 NS**
Respiratory disease	P<0.0001
Cerebrovascular disease	P<0.0001
Peripheral vascular disease	P=0.0002
Atrial fibrillation	P<0.0001
Hypertension	P<0.0001
Renal failure	P<0.0001
Heart failure	P<0.0001
Coronary heart disease	P<0.0001

Continued over…

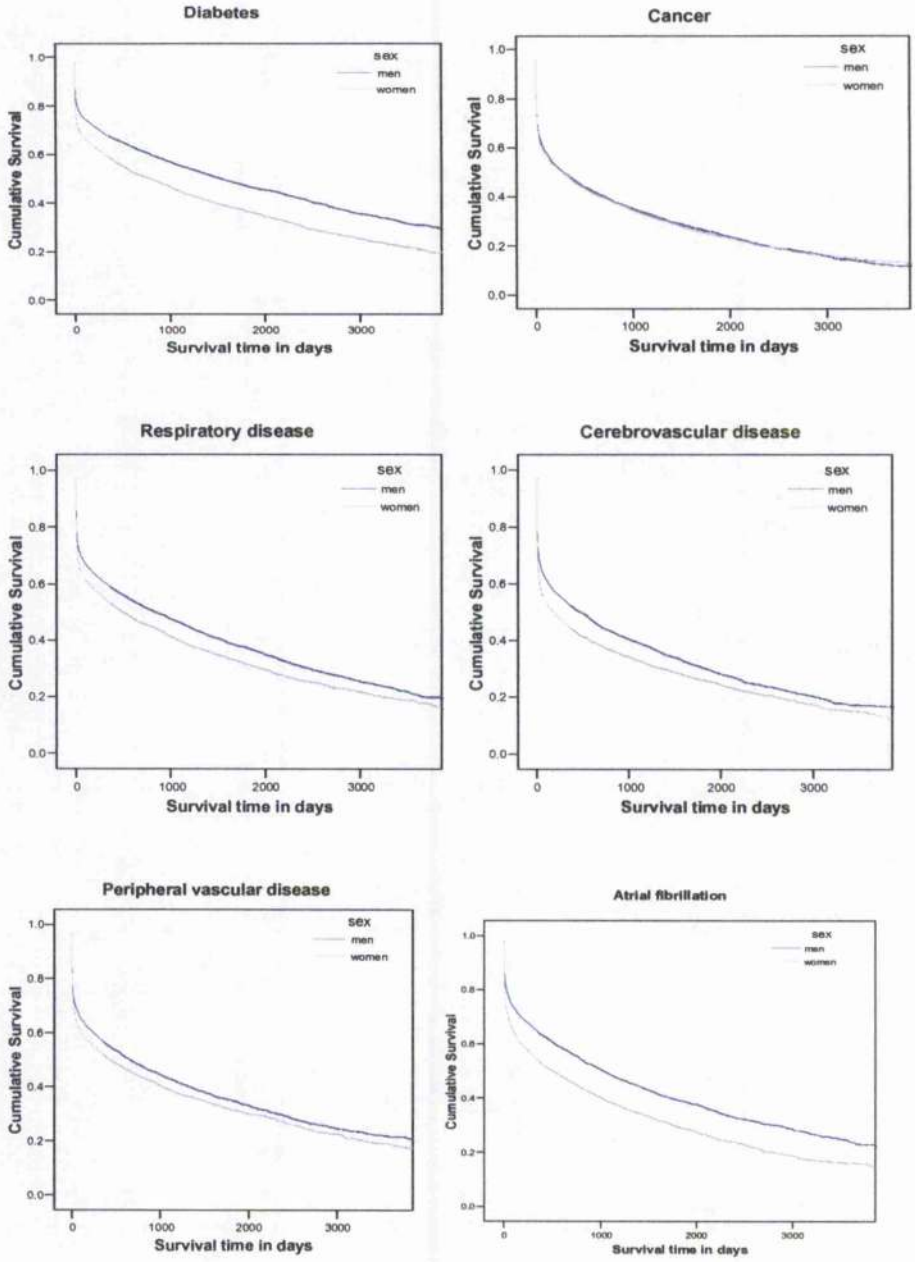
Table 53 ***continued***

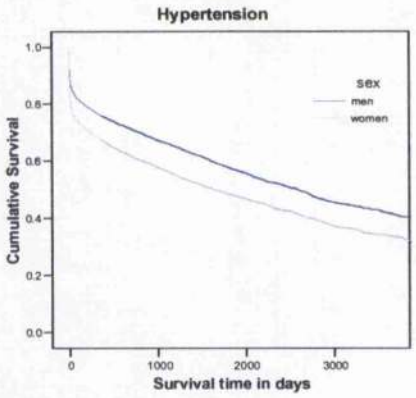
	Log rank test, p-value
1990	P<0.0001
1991	P<0.0001
1992	P<0.0001
1993	P<0.0001
1994	P<0.0001
1995	P<0.0001
1996	P<0.0001
1997	P<0.0001
1998	P<0.0001
1999	P<0.0001
2000	P<0.0001

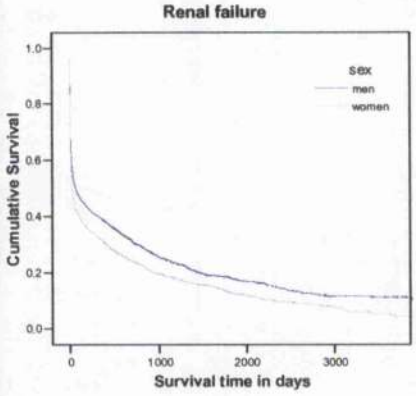
8.1.2.4 Comorbidity

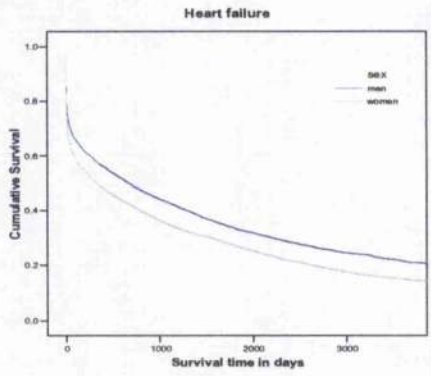
The presence of any comorbid diagnosis substantially reduced median survival in men and women following a first AMI (Table 50). Median survival was >10 years in men and 7.8 years in women who had no comorbid diagnosis but only 3.9 years in men and 2.1 years in women who had one or more comorbid diagnoses. Each of the comorbid diagnoses appeared to substantially reduce median survival. As seen in the life table analyses, the strongest effects were with renal failure, cancer, heart failure, cerebrovascular and peripheral vascular disease. Median survival was longer in men than in women with these comorbid diagnoses. Survival with all of these diagnoses except cancer was significantly different between men and women. Hypertension and coronary heart disease again had a lesser effect on median survival, especially in men.

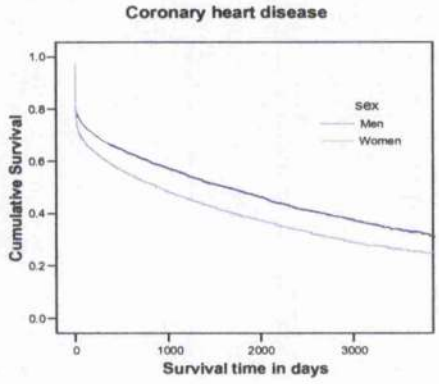
Figure 17 Kaplan Meier Survival Curves by sex within comorbid diagnoses




Hypertension
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
1000
2000
3000
Survival time in days
sex
men
women


Renal failure
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
1000
2000
3000
Survival time in days
sex
men
women


Heart failure
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
1000
2000
3000
Survival time in days
sex
men
women


Coronary heart disease
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
1000
2000
3000
Survival time in days
sex
Men
Women

8.2 Results of adjusted survival analyses

The aim of this section is to determine the independent effect of sex on the risk of short and longer term case fatality in individuals hospitalised with a first AMI after adjusting for the effects of other prognostic variables. The analyses also aim to examine the independent effects of the baseline characteristics including age, comorbid diagnoses socioeconomic deprivation and year of hospitalisation on the risk of death in men and women.

8.2.1 Logistic regression at 30 days in men and women following a first AMI

8.2.1.1 Overall

Table 53 shows the effect of other factors on sex as a predictor of prognosis at 30 days following a first AMI. The model started with sex and added other variables, in order of decreasing significance. Without adjusting for any factors, women's odds of death at 30 days were 77% greater than for men. Accounting for age differences between men and women removed much of this sex difference so that women's odds of death were 16% greater than that of men. There was a significant interaction between age and sex so that the effect of sex on short term survival could not be simply described and varied according to age ($p<0.0001$). Addition of other variables into the model slightly increased the sex difference in the odds of dying at 30 days. After all the variables had been included in the model, men had a survival advantage of 20% in the odds of death at 30 days. Again, after adjusting for other factors, there was a significant interaction between age and sex ($p=0.005$).

Table 54 shows the logistic regression models carried out in men and women separately. Age was the most powerful predictor of outcome at 30 days and appeared to have a stronger effect in men than in women. Men aged 85 and over had a fifteen fold increase in the risk of death when compared to men aged < 55 years (odds ratio 15.31, 95%CI 13.57-17.29). In women the equivalent odds ratio was 12.13 (95% CI 10.44-14.08). Socioeconomic deprivation appeared to have a more marked effect on the odds of death in men than in women. In men the most deprived deprivation category had a 9% increased risk of death relative to the least deprived category. In general, the effect of comorbid

conditions was greater in men than in women. For example a diagnosis of heart failure carried a 48% increase in the odds of death in men compared to a 15% increase in women. Previous coronary heart disease increased the odds of death in men but not in women. A number of diagnoses had a protective effect on survival, and these effects were of a similar magnitude in men and women. Atrial fibrillation and hypertension both decreased the odds of death at 30 days. Atrial fibrillation was associated with a 24% reduction in the odds of death in men and in women. The adjusted odds of death at 30 days decreased in men and women between 1990 and 2000 (Table 55). In men the odds of death fell by 38% and in women by 24%. These changes were all significant.

Table 53 Effect on sex of stepwise addition of other significant variables in logistic regression at 30 days

Step	Variable in model	Odds ratio (95%CI)	
		MEN	WOMEN
Enter	Sex	1.00	1.77 (1.71-1.82)
1	+ age group	1.00	1.16 (1.12-1.90)
2	+ renal failure	1.00	1.17 (1.13-1.20)
3	+ cerebrovascular disease	1.00	1.17 (1.30-1.20)
4	+ cancer	1.00	1.18 (1.14-1.22)
5	+ year of admission	1.00	1.18 (1.14-1.22)
6	+ heart failure	1.00	1.18 (1.14-1.22)
7	+ hypertension	1.00	1.19 (1.15-1.23)
8	+ respiratory disease	1.00	1.19 (1.15-1.23)
9	+ atrial fibrillation	1.00	1.19 (1.15-1.23)
10	+ peripheral vascular disease	1.00	1.20 (1.16-1.23)
11	+ diabetes	1.00	1.20 (1.16-1.24)
12	+ coronary heart disease	1.00	1.20 (1.16-1.24)
13	+ deprivation quintile	1.00	1.20 (1.16-1.24)

Table 54 Adjusted odds of death at 30 days in men and women admitted to hospital following a first AMI

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.20 (1.12-1.23)
Age group		
<55	1.00	1.00
55-64	2.33 (2.10-2.58)	2.01 (1.72-2.35)
65-74	5.07 (4.60-5.58)	3.96 (3.42-4.58)
75-84	9.47 (8.58-10.46)	7.60 (6.58-8.79)
>84	15.31 (13.57 -17.29)	12.13 (10.44-14.08)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.12 (1.04-1.20)	1.09 (1.01-1.17)
3	1.09 (1.01-1.17)	1.10 (1.02-1.18)
4	1.08 (1.00-1.16)	1.08 (1.00-1.16)
5-most deprived	1.09 (1.02-1.18)	1.04 (0.96-1.11)
Comorbidity		
Diabetes	1.17 (1.08-1.26)	1.17 (1.09-1.27)
Cancer	1.63 (1.51-1.77)	1.45 (1.33-1.58)
Respiratory disease	1.29 (1.21-1.39)	1.23 (1.14-1.32)
Cerebrovascular disease	1.67 (1.55-1.81)	1.61 (1.49-1.74)
Peripheral vascular disease	1.30 (1.20-1.40)	1.21 (1.11-1.31)
Atrial fibrillation	0.76 (0.70-0.83)	0.76 (0.70-0.82)
Hypertension	0.74 (0.68-0.81)	0.76 (0.70-0.81)
Renal failure	2.63 (2.35-2.93)	2.74 (2.45-3.06)
Heart failure	1.48 (1.39-1.56)	1.15 (1.09-1.22)
Coronary heart disease	1.26 (1.16-1.37)	1.02 (0.93-1.11)

Table 55 Trends in adjusted odds of death at 30 days in men and women admitted to hospital following a first AMI

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	**1.00**
1991	0.94 (0.86-1.04)	0.96 (0.87-1.06)
1992	0.90 (0.82-0.99)	0.94 (0.86-1.04)
1993	0.90 (0.81-0.99)	0.94 (0.85-1.03)
1994	0.82 (0.74-0.90)	0.85 (0.76-0.94)
1995	0.78 (0.70-0.86)	0.80 (0.72-0.89)
1996	0.77 (0.69-0.85)	0.79 (0.71-0.88)
1997	0.73 (0.66-0.81)	0.82 (0.74-0.91)
1998	0.68 (0.61-0.76)	0.77 (0.69-0.86)
1999	0.70 (0.63-0.78)	0.79 (0.71-0.88)
2000	0.62 (0.56-0.69)	0.76 (0.68-0.85)

8.2.1.2 Logistic regression at 30 days following a first AMI age <65 years

Sex had a stronger effect on prognosis at 30 days in individuals aged <65 years (Table 56). Women had a 29% increase in the odds of death after adjusting for other factors. Socioeconomic deprivation also appeared to have a stronger effect in this younger age group. Men in the most deprived category had a 33% increase in the odds of death when compared to the least deprived category. A similar effect was seen in women with a 30% increase in the odds of death. The presence of comorbid conditions also had a more marked effect on 30 day survival in this younger age group. For example a diagnosis of diabetes increased the odds of death by 39% in men and by 65% in women. Men with renal failure were more than four times likely to die at 30 days (odds ratio in men 4.5, 95%CI 3.47-5.84). Atrial fibrillation and hypertension continued to have a protective effect. Odds of dying at 30 days fell by 59% in men and 47% in women between 1990 and 2000 in this younger age group (Table 57). These falls were therefore greater than those seen in the overall analyses.

8.2.1.3 Logistic regression at 30 days following a first AMI age 65-74 years

Sex remained a significant predictor of outcome but had a lesser effect on outcome. Women had a 13% increase in the odds of death at 30 days when compared to men of a similar age (Table 58). Socio-economic deprivation continued to have a significant effect, but only in men. This effect was smaller in magnitude than that seen in individuals aged <65 years. For example, men in the most deprived deprivation category had a 20% increase in the odds of death relative to men in the most affluent deprivation category. The effect of comorbid diagnoses differed according to the nature of the diagnosis and sex. A number of conditions had a lesser effect on the odds of death in this age group than in the younger age group. This included peripheral vascular disease, cerebrovascular disease, heart failure and coronary heart disease. Diabetes was no longer a significant predictor of outcome in men or women. A previous diagnosis of coronary heart disease, excluding AMI, significantly increased the odds of death in men by 28% but not in women. Hypertension and atrial fibrillation continued to have a protective effect and to lower the odds of death in men and women at 30 days. Between 1990 and 2000 the odds of death at 30 days declined by 27% in men and by 35% in women (Table 59). These declines were significant and were smaller than those observed in younger men and women.

8.2.1.4 Logistic regression at 30 days following a first AMI age >74 years

Sex remained a significant predictor of outcome at 30 days with women carrying a 12% excess risk of death. Socio-economic deprivation no longer had a significant effect on outcome in men or in women in this older age group. In general the presence of comorbid conditions had a lesser effect on the odds of death in this older age group than in the two younger groups. For example, heart failure increased the odds of death by 45% in men aged 65-74 years and by 23% in men aged >74 years. Heart failure no longer had a significant effect on outcome in women in this age group. Hypertension and atrial fibrillation continued to have a protective effect and to lower the odds of death at 30 days in men and women.

Table 56 Adjusted odds of death at 30 days in men and women aged < 65 years admitted to hospital following a first AMI 1990-2000

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.29 (1.19-1.4)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.23 (1.04-1.46)	1.26 (0.97-1.63)
3	1.20 (1.01-1.42)	1.17 (0.91-1.51)
4	1.30 (1.11-1.54)	1.34 (1.05-1.71)
5-most deprived	1.33 (1.13-1.56)	1.30 (1.02-1.64)
Comorbidity		
Diabetes	1.39 (1.19-1.63)	1.65 (1.37-1.98)
Cancer	1.74 (1.41-2.15)	1.88 (1.46-2.42)
Respiratory disease	1.51 (1.28-1.79)	1.13 (0.90-1.41)
Cerebrovascular disease	1.94 (1.63-2.32)	2.27 (1.79-2.89)
Peripheral vascular disease	1.47 (1.21-1.79)	1.17 (0.90-1.53)
Atrial fibrillation	0.86 (0.66-1.11)	0.85 (0.57-1.27)
Hypertension	0.67 (0.56-0.80)	0.83 (0.67-1.01)
Renal failure	4.50 (3.47-5.84)	5.15 (3.66-7.23)
Heart failure	2.29 (2.01-2.61)	1.64 (1.35-1.97)
Coronary heart disease	1.58 (1.35-1.85)	1.17 (0.92-1.49)

Table 57 Trends in adjusted odds of death at 30 days in men and women aged <65 years admitted to hospital following a first AMI

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.83 (0.69-1.00)	0.89 (0.68-1.16)
1992	0.74 (0.61-0.90)	0.84 (0.64-1.09)
1993	0.79 (0.65-0.96)	0.88 (0.67-1.15)
1994	0.73 (0.60-0.89)	0.73 (0.55-0.97)
1995	0.67 (0.54-0.82)	0.59 (0.43-0.79)
1996	0.67 (0.54-0.82)	0.60 (0.44-0.82)
1997	0.62 (0.50-0.77)	0.62 (0.45-0.83)
1998	0.60 (0.48-0.75)	0.70 (0.52-0.94)
1999	0.55 (0.43-0.69)	0.61 (0.44-0.84)
2000	0.41 (0.32-0.53)	0.53 (0.37-0.76)

Table 58 Adjusted odds of death at 30 days in men and women aged 65-74 years admitted to hospital following a first AMI 1990-2000

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.13 (1.07-1.20)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.22 (1.08)	1.04 (0.90-1.21)
3	1.22 (1.08-1.38)	1.10 (0.95-1.28)
4	1.14 (1.01-1.29)	1.18 (1.02-1.36)
5-most deprived	1.20 (1.06-1.37)	1.04 (0.90-1.20)
Comorbidity		
Diabetes	1.08 (0.96-1.23)	1.10 (0.96-1.26)
Cancer	1.85 (1.62-2.11)	1.58 (1.34-1.86)
Respiratory disease	1.22 (1.09-.36)	1.26 (1.10-1.44)
Cerebrovascular disease	1.69 (1.50-1.91)	1.85 (1.60-2.15)
Peripheral vascular disease	1.31 (1.16-1.49)	1.19 (1.01-1.41)
Atrial fibrillation	0.76 (0.65-0.88)	0.76 (0.63-0.91)
Hypertension	0.76 (0.67-0.86)	0.73 (0.64-0.84)
Renal failure	2.51 (2.08-3.02)	3.01 (2.42-3.74)
Heart failure	1.45 (1.31-1.59)	1.36 (1.22-1.52)
Coronary heart disease	1.28 (1.13-1.46)	0.95 (0.80-1.12)

Table 59 Trends in adjusted odds of death at 30 days in men and women aged 65-74 years admitted to hospital following a first AMI

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.98 (0.83-1.15)	0.95 (0.79-1.14)
1992	1.01 (0.86-1.19)	0.96 (0.80-1.15)
1993	0.92 (0.78-1.08)	0.92 (0.77-1.11)
1994	0.85 (0.72-1.01)	0.76 (0.63-0.92)
1995	0.83 (0.70-0.99)	0.76 (0.63-0.92)
1996	0.85 (0.71-1.01)	0.74 (0.63-0.92)
1997	0.85 (0.71-1.01)	0.92 (0.76-1.12)
1998	0.74 (0.61-0.88)	0.71 (0.57-0.86)
1999	0.71 (0.58-0.85)	0.67 (0.54-0.82)
2000	0.73 (0.61-0.88)	0.65 (0.52-0.81)

Table 60 Adjusted odds of death at 30 days in men and women aged >74 years admitted to hospital following a first AMI 1990-2000

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.12 (1.07-1.18)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.03 (0.93-1.15)	1.10 (1.01-1.21)
3	0.98 (0.88-1.10)	1.11(1.01-1.21)
4	0.99 (0.88-1.10)	1.02 (0.93-1.12)
5-most deprived	0.93 (0.83-1.05)	1.03 (0.94-1.13)
Comorbidity		
Diabetes	1.05 (0.93-1.20)	1.10 (1.00-1.23)
Cancer	1.45 (1.29-1.62)	1.31 (1.17-1.46)
Respiratory disease	1.23 (1.12-1.36)	1.20 (1.10-1.32)
Cerebrovascular disease	1.45 (1.29-1.62)	1.42 (1.29-1.57)
Peripheral vascular disease	1.16 (1.04-1.29)	1.19 (1.07-1.33)
Atrial fibrillation	0.73 (0.65-0.83)	0.75 (0.68-0.82)
Hypertension	0.77 (0.67-0.88)	0.75 (0.68-0.82)
Renal failure	2.15 (1.85-2.51)	2.29 (2.00-2.62)
Heart failure	1.23 (1.13-1.33)	1.02 (0.95-1.09)
Coronary heart disease	1.03 (0.90-1.17)	1.01 (0.90-1.13)

Table 61 Trends in adjusted odds of death at 30 days in men and women aged >74 years admitted to hospital following a first AMI

	Odds ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.99 (0.85-1.16)	0.98 (0.86-1.12)
1992	0.90 (0.77-1.05)	0.95 (0.84-1.08)
1993	0.93 (0.80-1.09)	0.95 (0.83-1.08)
1994	0.82 (0.70-0.97)	0.90 (0.79-1.03)
1995	0.79 (0.67-0.93)	0.86 (0.76-0.98)
1996	0.76 (0.64-0.89)	0.85 (0.75-0.98)
1997	0.70 (0.59-0.83)	0.83 (0.72-0.95)
1998	0.69 (0.58-0.82)	0.82 (0.72-0.95)
1999	0.79 (0.67-0.93)	0.88 (0.77-1.01)
2000	0.66 (0.56-0.78)	0.85 (0.74-0.98)

8.2.2 Cox's Proportional Hazards Regression in men and women at one year excluding 30 days

8.2.2.1 Overall

When no other variables were included in the model, sex was a significant predictor of outcome at one year following a first AMI ($p<0.0001$). The unadjusted hazard of death was 1.54 in women relative to men. Adjusting for age alone accounted for all of this sex difference and sex was no longer a significant independent predictor of outcome. Addition of other variables into the model had little effect on the hazard of death and did not therefore appear to account for initial sex differences. In the final model, the risk of death was similar in men and women. The adjusted hazard of death was 1.02 (0.97-1.06) so that there was no significant difference in survival between the sexes. All other variables remained significant and were included in the final model. An age sex interaction term was included in the model and was found to be significant, $p=0.04$.

Table 62 shows the Cox Proportional Hazard regression models carried out in men and women separately. As at 30 days, age had a powerful effect on prognosis so that the hazard of death was 11.6 times greater in men aged >84 when compared to men age <55 years. A similar effect was seen in women. Socioeconomic deprivation was an independent predictor of outcome in men but not in women. Men in the most deprived category had a 28% increase in the hazard of death than men in the least deprived category. The presence of comorbid conditions increased the hazard of death in men and women though the magnitude of effect varied according to the diagnosis and by sex. Cancer, heart failure, renal failure and cerebrovascular disease had the greatest effect. For example, the hazard of death was 93% greater in men and 84% greater in women who had a diagnosis of heart failure. Hypertension and previous coronary heart disease did not have a significant effect on prognosis. None of the comorbid conditions had a protective effect. Between 1990 and 2000 the adjusted hazard of death at one year fell by 33% in men and by 31% in men. This difference was not significant, $p=0.813$.

Table 62 Hazard ratios for death at one year excluding 30 days in men and women admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.02 (0.97-1.06)
Age group		
<55	1.00	1.00
55-64	1.98 (1.72-2.28)	1.73 (1.36-2.21)
65-74	4.01 (3.52-4.56)	3.51 (2.81-4.40)
75-84	6.91 (6.07-7.88)	6.85 (5.49-8.54)
>84	11.61 (9.97-13.52)	11.82 (9.44-14.80)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.08 (0.98-1.19)	1.12 (1.01-1.23)
3	1.11 (1.01-1.22)	1.08 (0.98-1.19)
4	1.15 (1.04-1.26)	1.03 (0.93-1.13)
5-most deprived	1.28 (1.17-1.41)	1.08 (0.98-1.19)
Comorbidity		
Diabetes	1.48 (1.35-1.61)	1.38 (1.26-1.51)
Cancer	1.85 (1.69-2.03)	1.74 (1.58-1.92)
Respiratory disease	1.34 (1.24-1.45)	1.30 (1.19-1.42)
Cerebrovascular disease	1.70 (1.55-1.85)	1.81 (1.65-1.98)
Peripheral vascular disease	1.57 (1.44-1.71)	1.51 (1.37-1.67)
Atrial fibrillation	1.29 (1.18-1.42)	1.30 (1.19-1.42)
Hypertension	0.98 (0.89-1.08)	0.88 (0.80-0.96)
Renal failure	1.92 (1.69-2.18)	1.67 (1.46-1.91)
Heart failure	1.93 (1.81-2.07)	1.84 (1.73-1.97)
Coronary heart disease	1.10 (1.00-1.21)	1.09 (0.98-1.21)

Table 63 Trends in hazard ratio for death at one year excluding 30 days in men and women admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.98 (0.86-1.11)	1.02 (0.89-1.16)
1992	1.04 (0.92-1.18)	0.91 (0.80-1.04)
1993	0.89 (0.78-1.02)	0.94 (0.82-1.07)
1994	0.91 (0.80-1.04)	0.86 (0.75-0.99)
1995	0.80 (0.70-0.92)	0.79 (0.69-0.91)
1996	0.77 (0.67-0.88)	0.78 (0.68-0.89)
1997	0.74 (0.65-0.85)	0.73 (0.63-0.84)
1998	0.74 (0.64-0.84)	0.77 (0.67-0.89)
1999	0.71 (0.62-0.82)	0.72 (0.62-0.83)
2000	0.67 (0.59-0.78)	0.69 (0.59-0.80)

8.2.2.2 Cox's Proportional Hazards Regression at one year following a first AMI age <65 years excluding 30 days

Survival was similar in men and women aged less than 65 years and sex was not an independent predictor of prognosis at one year in this age group (Table 64). The adjusted hazard of death in women relative to men was 0.92 (0.81-1.03). Socioeconomic deprivation was a significant predictor of outcome in men but not in women, p=0.013. Men in the most deprived category had a 44% increase in the hazard of death relative to men in the least deprived category. The effect of some of the comorbid diagnoses on prognosis appeared greater in this age group than in the overall cohort. For example, cancer was associated with 2.71 times the risk of death in the under 65 year old men compared to an increased risk of 85% in the whole cohort. Peripheral vascular disease and heart failure were also associated with substantial increases in the risk of death in men and in women. Between 1990 and 2000 the adjusted hazard of death fell by 44% in men and by 51% in women (Table 65). This sex difference was not significant, p=0.301.

8.2.2.3 Cox's Proportional Hazards Regression at one year following a first AMI age 65-74 years excluding 30 days

Sex was a significant predictor of one year survival in this age group (Table 66). The hazard of death was 8% lower in women relative to men. Socioeconomic deprivation remained a significant predictor of death in men but not in women. Men in the most deprived category had a 23% in the risk of death when compared to men in the least deprived category. Comorbid diagnoses had a similar effect to that seen in the younger age group, although the magnitude of these effects varied slightly. Heart failure, renal failure and cancer had the strongest impact on prognosis, especially in men. For example, heart failure was associated with more than twice the risk of death (hazard ratio 2.06 in men and 2.35 in women). Between 1990 and 2000 the risk of death fell by 42% in men and by 45% in women (Table 63). This difference reached statistical significance, p=0.04.

8.2.2.4 Cox's Proportional Hazards Regression at one year following a first AMI age >74 years excluding 30 days

As in the younger age group, sex was not a significant predictor of outcome at one year excluding 30 days in men and women following a first AMI, p=0.47. Unlike in the two younger age groups, socioeconomic deprivation was a significant predictor of outcome in men and in women, although the effect was not as great in magnitude as that seen in younger men (Table 68). For example, men in the most deprived category had a 29%

increased risk of death and women a 15% increased risk of death when compared to men and women in the least deprived categories. Comorbid diagnoses continued to have a significant effect on prognosis, though the magnitude of these effects was generally less than that seen in younger age groups. For example, heart failure was associated with a 60% in the risk of death in women aged >74 years compared to an excess risk of 2.45 times in women aged <65 years. Hypertension appeared to have a protective effect in women but not in men. Hypertension was associated with an 12% reduction in the hazard of death in women.

Table 64 Hazard ratios for death at one year excluding 30 days in men and women aged < 65 years admitted to hospital following a first AMI 1990-2000

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.92 (0.81-1.03)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.20 (0.96-1.52)	0.56 (0.36-0.85)
3	1.19 (0.95-1.50)	1.05 (0.73-1.49)
4	1.32 (1.06-1.65)	0.89 (0.62-1.26)
5-most deprived	1.44 (1.16-1.78)	0.96 (0.69-1.34)
Comorbidity		
Diabetes	1.44 (1.19-1.75)	2.40 (1.88-3.07)
Cancer	2.71 (2.16-3.40)	2.21 (1.59-3.06)
Respiratory disease	1.37 (1.11-1.68)	1.11 (0.82-1.52)
Cerebrovascular disease	1.84 (1.47-2.30)	2.34 (1.69-3.25)
Peripheral vascular disease	2.00 (1.61-2.50)	2.10 (1.52-2.89)
Atrial fibrillation	1.37 (1.05-1.79)	1.56 (1.01-2.40)
Hypertension	1.02 (0.84-1.24)	0.90 (0.68-1.20)
Renal failure	1.59 (1.09-2.32)	2.65 (1.67-4.22)
Heart failure	2.66 (2.27-3.13)	2.45 (1.90-3.15)
Coronary heart disease	1.17 (0.95-1.45)	1.18 (0.85-1.65)

Table 65 Trends in hazard ratios of death at one year excluding 30 days in men and women aged <65 years admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.92 (0.70-1.21)	1.10 (0.75-1.62)
1992	0.97 (0.75-1.27)	0.86 (0.57-1.28)
1993	0.91 (0.69-1.19)	0.70 (0.45-1.08)
1994	0.82 (0.62-1.09)	0.57 (0.36-0.89)
1995	0.77 (0.57-1.02)	0.71 (0.46-1.10)
1996	0.75 (0.56-1.01)	0.59 (0.37-0.93)
1997	0.79 (0.59-1.06)	0.36 (0.21-0.63)
1998	0.82 (0.62-1.10)	0.65 (0.40-1.03)
1999	0.90 (0.67-1.19)	0.69 (0.43-1.10)
2000	0.56 (0.40-0.78)	0.49 (0.28-0.85)

Table 66 Adjusted hazard ratios for death at one year excluding 30 days in men and women aged 65-74 years admitted to hospital following a first AMI 1990-2000

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.92 (0.85-0.99)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.00 (0.85-1.19)	1.12 (0.90-1.38)
3	1.05 (0.89-1.23)	1.01 (0.82-1.25)
4	1.12 (0.96-1.32)	1.11 (0.90-1.36)
5-most deprived	1.23 (1.05-1.44)	1.02 (0.84-1.26)
Comorbidity		
Diabetes	1.54 (1.34-1.77)	1.47 (1.24-1.74)
Cancer	2.15 (1.85-2.49)	1.72 (1.41-2.10)
Respiratory disease	1.29 (1.12-1.48)	1.53 (1.28-1.82)
Cerebrovascular disease	1.72 (1.49-1.98)	1.48 (1.21-1.80)
Peripheral vascular disease	1.47 (1.27-1.70)	1.93 (1.58-2.34)
Atrial fibrillation	1.48 (1.28-1.72)	1.53 (1.27-1.86)
Hypertension	0.98 (0.84-1.14)	0.94 (0.79-1.12)
Renal failure	2.08 (1.68-2.57)	1.64 (1.23-2.20)
Heart failure	2.06 (1.84-2.31)	2.35 (2.05-2.69)
Coronary heart disease	1.03 (0.88-1.22)	1.16 (0.94-1.43)

Table 67 Trends in adjusted hazard ratios for death at one year excluding 30 days in men and women aged 65-74 years admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.92 (0.74-1.13)	0.93 (0.72-1.21)
1992	0.99 (0.81-1.21)	0.80 (0.62-1.03)
1993	0.86 (0.70-1.06)	0.81 (0.62-1.03)
1994	0.91 (0.74-1.12)	0.79 (0.61-1.02)
1995	0.68 (0.54-0.86)	0.68 (0.52-0.90)
1996	0.74 (0.59-0.92)	0.57 (0.42-0.76)
1997	0.56 (0.44-0.71)	0.67 (0.50-0.89)
1998	0.63 (0.50-0.80)	0.72 (0.54-0.94)
1999	0.55 (0.43-0.71)	0.54 (0.40-0.74)
2000	0.58 (0.45-0.74)	0.55 (0.41-0.75)

Table 68 Adjusted hazard ratios for death at one year excluding 30 days in men and women aged >74 years admitted to hospital following a first AMI 1990-2000

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.04 (0.96-1.08)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.13 (0.98-1.30)	1.21 (1.08-1.35)
3	1.17 (1.02-1.34)	1.11 (0.99-1.25)
4	1.13 (0.98-1.31)	1.04 (0.93-1.17)
5-most deprived	1.29 (1.12-1.48)	1.15 (1.02-1.29)
Comorbidity		
Diabetes	1.41 (1.23-1.62)	1.22 (1.08-1.37)
Cancer	1.52 (1.33-1.72	1.71 (1.51-1.92)
Respiratory disease	1.35 (1.20-1.51)	1.21 (1.09-1.35)
Cerebrovascular disease	1.55 (1.37-1.76)	1.88 (1.69-2.09)
Peripheral vascular disease	1.48 (1.31-1.67)	1.31 (1.16-1.49)
Atrial fibrillation	1.13 (1.00-1.29)	1.22 (1.20-1.35)
Hypertension	0.97 (0.83-1.13)	0.88 (0.78-0.98)
Renal failure	1.82 (1.53-2.17)	1.56 (1.33-1.83)
Heart failure	1.62 (1.48-1.79)	1.60 (1.48-1.73)
Coronary heart disease	1.06 (0.93-1.25)	1.05 (0.93-1.20)

Table 69 Trends in adjusted hazard ratios for death at one year excluding 30 days in men and women aged >74 years admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	1.08 (0.88-1.30)	1.01 (0.86-1.19)
1992	1.13 (1.02-1.34)	0.97 (0.83-1.14)
1993	0.90 (0.98-1.31)	1.01 (0.86-1.19)
1994	0.93 (0.75-1.14)	0.92 (0.78-1.09)
1995	0.92 (0.75-1.13)	0.83 (0.70-0.98)
1996	0.82 (0.66-1.01)	0.88 (0.74-1.04)
1997	0.88 (0.72-1.09)	0.79 (0.67-0.94)
1998	0.80 (0.65-0.99)	0.81 (0.68-0.97)
1999	0.76 (0.61-0.94)	0.80 (0.67-0.95)
2000	0.83 (0.671.02)	0.75 (0.63-0.90)

8.2.3 Cox's Proportional Hazards in men and women at five years excluding 30 days

8.2.3.1 Overall

Before adjusting for any other prognostic factors, women had an increased risk of death at five years (hazard ratio 1.42). Accounting for the age differences between men and women revealed women to be at a survival advantage and their risk of death was 6% less than that of men (hazard ratio 0.94). Addition of other variables into the model had a marginal effect on this hazard ratio, and women continued to have a better prognosis than men after adjusting for other prognostic factors. All the variables were retained in the final model.

Table 70 shows the result of the Cox Proportional Hazard regression models carried out in men and women separately. Age had a similar effect in men and women and again was the most powerful predictor of outcome. Socioeconomic deprivation had a highly significant effect on outcome, and the magnitude of this effect seemed to be slightly greater in men than in women. Men in the most deprived category had a 27% increase in the hazard of death at five years than men in the least deprived category. The presence of comorbid diagnoses had a similar effect in men and women, more so than at any other time periods. Renal failure had the most powerful effect and increased the hazard of death by 2.13 times in men and by 73% in women. Hypertension was the only diagnosis which did not have a significant effect on outcome in men or women. No comorbid diagnoses had a protective effect. Between 1990 and 1996, the five year hazard of death declined by 27% in men and 23% in women (Table 71). This sex difference was not significant, p=0.10.

Table 70 Hazard ratios for death at five years excluding 30 days in men and women admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.94 (0.91-0.96)
Age group		
<55	1.00	1.00
55-64	2.04 (1.87-2.22)	1.75 (1.52-2.03)
65-74	3.97 (3.67-4.30)	3.19 (2.79-3.66)
75-84	7.21 (6.64-7.83)	6.16 (5.38-7.05)
>84	11.38 (10.22-12.66)	10.98 (9.54-12.63)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.06 (0.99-1.13)	1.06 (0.98-1.13)
3	1.10 (1.03-1.18)	1.03 (0.96-1.11)
4	1.14 (1.07-1.22)	1.07 (1.00-1.15)
5-most deprived	1.26 (1.18-1.34)	1.27 (1.09-1.25)
Comorbidity		
Diabetes	1.52 (1.42-1.63)	1.54 (1.44-1.65)
Cancer	1.68 (1.56-1.82)	1.68 (1.55-1.83)
Respiratory disease	1.38 (1.29-1.46)	1.39 (1.30-1.49)
Cerebrovascular disease	1.67 (1.56-1.79)	1.67 (1.54-1.80)
Peripheral vascular disease	1.44 (1.35-1.54)	1.44 (1.33-1.56)
Atrial fibrillation	1.33 (1.24-1.43)	1.24 (1.16-1.34)
Hypertension	1.02 (0.95-1.10)	1.00 (0.93-1.07)
Renal failure	2.13 (1.90-2.39)	1.73 (1.53-1.96)
Heart failure	1.90 (1.81-2.00)	1.73 (1.64-1.82)
Coronary heart disease	1.11(1.03-1.20)	1.17 (1.08-1.27)

Table 71 Trends in hazard ratio for death at five years excluding 30 days in men and women admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.94 (0.88-1.01)	1.02 (0.94-1.10)
1992	0.94 (0.88-1.01)	0.88 (0.81-0.95)
1993	0.89 (0.83-0.96)	0.92 (0.85-0.99)
1994	0.85 (0.78-0.91)	0.89 (0.82-0.96)
1995	0.74 (0.69-0.80)	0.81 (0.75-0.88)
1996	0.73 (0.68-0.79)	0.77 (0.71-0.84)

8.2.3.2 Cox's Proportional Hazards Regression at five years following a first AMI age <65 years excluding 30 days

Sex remained a significant independent predictor of outcome at five years in individuals aged less than 65 years, p=0.04. Hazard of death was 7% lower in women relative to men (Table 72). The effect of socioeconomic deprivation was greater in men than in women. For example, in men the hazard of death was 70% greater in the most deprived category than in the least deprived category. In women, the hazard of death was 24% greater in the most deprived category than in the least deprived category. The magnitude of the effect in men was also significantly greater than that seen in the whole cohort at five years. As seen in shorter term survival, the presence of comorbid conditions had a marked impact on prognosis at five years in this younger age group. Men and women with renal failure, cancer and heart failure all had more than twice the increased risk of death at five years. All of the diagnoses carried an adverse effect, although hypertension was not a significant predictor of outcome in men or women in this age group. The risk of death fell by 40% in men and 44% in women between 1990 and 1996 (Table 73). This sex difference was not significant.

8.2.3.3 Cox's Proportional Hazards Regression at five years following a first AMI age 65-74 years excluding 30 days

Hazard of death at five years was 14% lower in women than in men in this age group (Table 74). This sex effect was highly significant, p<0.001. The effect of socioeconomic deprivation was significant and was similar in magnitude in men and women. Both men and women in the most deprived category had a 32% increase in the hazard of death relative to individuals in the least deprived category. The presence of comorbid diagnoses had an adverse effect on outcome which was similar in men and women. Heart failure and renal failure again carried the worst prognosis. Neither hypertension nor previous coronary heart disease were independent predictors of outcome in men. Previous coronary heart disease did however have a significant effect on survival in women, whose hazard of death at five years was increased by 19% when they were coded with this diagnosis. Between 1990 and 1996 the decline in the risk of death at five years was similar in men and women, (hazard ratio 0.74 in men and 0.75 in women) (Table 75).

8.2.3.4 Cox's Proportional Hazards Regression at five years following a first AMI age >74 years excluding 30 days

In this age group, as in the two younger age groups, sex remained a significant predictor of outcome at five years and the hazard of death was 8% lower in women than in men (Table 76). Socioeconomic deprivation did not have a significant effect on prognosis in men or women in this age group. All comorbid diagnoses except hypertension had a significant and adverse effect on prognosis at five years. The magnitude of these effects varied and in general was not as great as that observed in the younger age groups. For example, cancer increased the hazard of death by 47% in men and by 58% in women in this age group, compared to an increased risk of more than two fold in the younger age groups. The decline in the risk of death between 1990 and 1996 was 13% in men and 20% in women, which again was less than that observed in younger age groups (Table 77). This sex difference was not significant.

Table 72 Hazard ratios for death at five years excluding 30 days in men and women aged < 65 years admitted to hospital following a first AMI 1990-2000

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.93 (0.86-0.99)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.28 (1.10-1.48)	0.92 (0.72-1.18)
3	1.34 (1.16-1.55)	1.11 (0.88-1.40)
4	1.46 (1.27-1.68)	1.15 (0.92-1.44)
5-most deprived	1.70 (1.49-1.94)	1.24 (1.00-1.53)
Comorbidity		
Diabetes	1.68 (1.48-1.90)	2.33 (1.99-2.73)
Cancer	2.05 (1.73-2.43)	2.11 (1.69-2.64)
Respiratory disease	1.44 (1.25-1.65)	1.41 (1.16-1.72)
Cerebrovascular disease	1.82 (1.57-2.12)	1.97 (1.56-2.49)
Peripheral vascular disease	1.62 (1.39-1.89)	1.69 (1.36-2.11)
Atrial fibrillation	1.35 (1.12-1.63)	1.39 (1.02-1.89)
Hypertension	1.07 (0.93-1.22)	0.92 (0.76-1.11)
Renal failure	2.73 (2.14-3.49)	2.95 (2.08-4.18)
Heart failure	2.40 (2.15-2.67)	2.14 (1.81-2.53)
Coronary heart disease	1.17 (1.02-1.35)	1.08 (0.87-1.07)

Table 73 Trends in hazard ratios of death at five years excluding 30 days in men and women aged <65 years admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.89 (0.78-1.01)	0.98 (0.80-1.21)
1992	0.87 (0.77-1.00)	0.86 (0.69-1.06)
1993	0.82 (0.71-0.93)	0.81 (0.65-1.01)
1994	0.67 (0.58-0.77)	0.70 (0.56-0.88)
1995	0.64 (0.55-0.74)	0.75 (0.60-0.94)
1996	0.60 (0.51-0.69)	0.56 (0.44-0.72)

Table 74 Adjusted hazard ratios for death at five years excluding 30 days in men and women aged 65-74 years admitted to hospital following a first AMI 1990-2000

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.86 (0.81-0.90)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.09 (0.97-1.21)	1.18 (1.01-1.37)
3	1.15 (1.03-1.28)	1.17 (1.01-1.35)
4	1.16 (1.04-1.29)	1.24 (1.07-1.44)
5-most deprived	1.32 (1.18-1.47)	1.32 (1.14-1.52)
Comorbidity		
Diabetes	1.45 (1.30-1.62)	1.71 (1.52-1.93)
Cancer	1.81 (1.60-2.04)	1.79 (1.54-2.08)
Respiratory disease	1.41 (1.27-1.55)	1.61 (1.42-1.83)
Cerebrovascular disease	1.76 (1.58-1.97)	1.28 (1.10-1.49)
Peripheral vascular disease	1.37 (1.23-1.53)	1.75 (1.50-2.03)
Atrial fibrillation	1.55 (1.39-1.73)	1.56 (1.35-1.81)
Hypertension	0.97 (0.86-1.08)	1.08 (0.95-1.23)
Renal failure	2.20 (1.82-2.67)	2.25 (1.80-2.82)
Heart failure	2.08 (1.92-2.25)	1.88 (1.70-2.08)
Coronary heart disease	0.99 (0.88-1.12)	1.19 (1.03-1.11)

Table 75 Trends in adjusted hazard ratios for death at five years excluding 30 days in men and women aged 65-74 years admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.91 (0.81-1.03)	1.07 (0.92-1.24)
1992	0.93 (0.82-1.04)	0.92 (0.79-1.07)
1993	0.90 (0.80-1.01)	0.88 (0.75-1.02)
1994	0.83 (0.73-0.93)	0.85 (0.73-0.99)
1995	0.71 (0.62-0.81)	0.77 (0.66-0.90)
1996	0.74 (0.65-0.84)	0.75 (0.63-0.88)

Table 76 Adjusted hazard ratios for death at five years excluding 30 days in men and women aged >74 years admitted to hospital following a first AMI 1990-2000

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.92 (0.88-0.96)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.91 (0.89-1.09)	1.07 (0.98-1.16)
3	1.00 (0.90-1.11)	0.99 (0.91-1.09)
4	1.03 (0.93-1.15)	1.04 (0.95-1.14)
5-most deprived	1.01 (0.91-1.12)	1.14 (1.04-1.25)
Comorbidity		
Diabetes	1.46 (1.30-1.64)	1.30 (1.18-1.43)
Cancer	1.47 (1.32-1.64)	1.58 (1.42-1.76)
Respiratory disease	1.30 (1.18-1.43)	1.26 (1.15-1.38)
Cerebrovascular disease	1.45 (1.30-1.62)	1.77 (1.61-1.95)
Peripheral vascular disease	1.38 (1.24-1.53)	1.27 (1.14-1.41)
Atrial fibrillation	1.12 (1.00-1.24)	1.14 (1.05-1.25)
Hypertension	1.05 (0.92-1.19)	0.98 (0.88-1.08)
Renal failure	1.71 (1.42-2.06)	1.42 (1.21-1.67)
Heart failure	1.54 (1.43-1.66)	1.58 (1.49-1.68)
Coronary heart disease	1.12 (0.99-1.27)	1.17 (1.06-1.08)

Table 77 Trends in adjusted hazard ratios for death at five years excluding 30 days in men and women aged >74 years admitted to hospital following a first AMI

	Hazard ratio (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	1.03 (0.91-1.16)	0.99 (0.90-1.10)
1992	1.00 (0.89-1.13)	0.86 (0.78-0.96)
1993	0.93 (0.82-1.06)	0.94 (0.84-1.04)
1994	1.00 (0.89-1.13)	0.91 (0.82-1.02)
1995	0.84 (0.74-0.95)	0.82 (0.73-0.91)
1996	0.87 (0.77-0.98)	0.80 (0.72-0.90)

8.3 Discussion regarding unadjusted and adjusted survival in men and women following a first AMI

The prognosis of men and women hospitalised with a first AMI in Scotland is much worse than indicated by clinical trials. One fifth of the patients in this study died within one month of admission and almost one half died by five years. Unadjusted short and longer survival was considerably better in men than in women. Median survival was 8.8 years in men and only 4.3 years in women. Short and longer term survival has improved in men and women between 1990 and 2000, though the degree of improvement varied according to age and sex. There are many factors affecting prognosis following AMI and most of the baseline characteristics examined in this study were strong independent predictors of outcome, although their relationship with outcome varied according to age and sex and the follow-up period examined.

8.3.1Sex

Short term unadjusted case fatality

In this study overall 30 day case fatality was 16.3% in men and 25.6% in women. These figures are higher than those reported by most other population-based studies. There is however considerable variation in 30 day case fatality rates reported by different studies. For example in the Rochester Epidemiology Project, 28 day case fatality in 1994 was 7% in men and 15% in women hospitalised with a first AMI.[54] The Worcester Heart Attack Study also examined survival in men and women hospitalised with a first AMI between 1975 and 1988 and reported 30 day case fatality rates of 12.7% in men and 21.7% in women.[56] In the Ontario Myocardial Infarction database, 30 day case fatality in 1996 was 11.6% in men and 19.1% in women.[106] The Ontario database is similar to the one analysed in the current study. 30 day case fatality rates in men and women in the current study are more consistent with reports from other British studies. For example, in-patient case fatality in 1995 in the Yorkshire AMI Study was 19% in men and 30% in women and in 1992 in the Nottingham Heart Attack Register in-patient case fatality was 21.7% overall.[85;107] Neither of these studies were restricted to first AMI and the average age of individuals was greater in the Yorkshire AMI Study which may account for the higher case fatality rates. The reason for the differences in 30 day case fatality between countries is not clear, although in general the average age of individuals is greater in the British studies than in the American studies. Numerous studies have reported a more favourable short

term prognosis in men following hospitalisation with AMI.[56;78;85;107;113;170;195;196] Whilst the literature is consistent in reporting higher unadjusted short term case fatality rates in women than in men, the magnitude of these differences varies considerably between studies.

In this study one year case fatality was 23.5% in men and 35.3% in women. This is again higher than the rates reported by most other studies, though again there are few population based data available with which to make useful comparisons. In the Göteborg Study, one year case fatality was 25% in men and 36% in women.[79]

Age adjusted case fatality

Much of the sex difference seen in short term survival following AMI is thought to be explained by differences in the baseline characteristics between men and women. Age is thought to be the most important prognostic factor in survival. Controlling for age through age adjusted or age stratified analyses should therefore reduce these sex differences. In this study controlling for age through age stratification did reduce sex differences in survival. It did not however remove them, and women of all ages continued to have a higher case fatality than men. The sex difference in case fatality was greater in younger individuals than in older individuals. The finding that controlling for age reduces sex differences in survival is consistent with a number of other studies, although the age categories used did vary and hinder comparison between studies.[56;115;197;198] Controlling for age completely removed sex differences in survival in a number of studies.[56;111;115;199] The literature is therefore divided into those studies that have found a residual excess risk of death in women compared to men after adjusting for age differences, and those that have not. In the current study there was an excess risk of death at 30 days of 16% in women compared to men after adjusting for age differences. This figure is consistent with a number of other studies which have carried out similar analyses.[83;112;200] For example in the National Registry of Myocardial Infarction 2 Study the age adjusted odds of death were 1.18 in women relative to men.[78] In a number of studies it is not possible to discern from the methodology whether age adjusted case fatality differs significantly between men and women.[54;55]

Multivariate adjusted case fatality

In the current study adjusting for age and other variables including socio-economic differences as well as comorbid diagnoses did not remove the excess risk of death seen in women at 30 days following an AMI. Women remained at a 20% increased risk of death

at 30 days when compared to men. Inclusion of the additional prognostic variables slightly increased the excess risk in women. This would therefore suggest that the distribution of these variables did not account for much if any of the excess risk seen in women after adjusting for age differences between men and women. The results of other studies that have controlled for factors other than age are conflicting. The comparison of results is difficult because factors that were controlled for varied across studies and very few studies controlled for comorbid diseases other than previous coronary heart disease and coronary heart disease risk factors. The results from the current study are in agreement with a number of other studies including ISIS-3, the National Hospital Discharge Survey and the MITI Registry.[53;83;113] In the National Hospital Discharge Survey the risk of in-hospital death was 13% greater in women than in men.[53] In the current study, at one year and excluding 30 days, sex was no longer a significant predictor of outcome and all of the differences in case fatality seen at one year could be explained by differences in the age distribution of men and women.

Age sex interaction

Many of these studies have not examined the effect of sex on survival in any detail and have often failed to consider the varying effects of sex according to age. This may disguise differences in survival rates and lead to inaccurate assessment of risk. In this study age stratified analyses revealed important survival differences between men and women. Sex differences in short term survival were much greater in younger age groups and decreased with increasing age. Unadjusted 30 day case fatality in women aged less than 55 years was almost 60% greater than in men (5.9% versus 3.7%). By 65 years this excess risk in women had fallen to around 11%. At 30 days, there was an age sex interaction in the unadjusted analyses which was highly significant in a logistic regression model. When the study population was divided into three subgroups on the basis of age, sex continued to be a significant predictor of 30 day survival in all three groups. The effect of sex on survival did vary and was greatest in the youngest age group. In individuals aged less than 65 years, women had a 29% excess risk of death compared to men but by age greater than 74 years this excess risk had decreased to 12%. The age sex interaction remained significant after adjusting for differences in the distribution of baseline characteristics. These findings are in keeping with a number of other studies that have also reported age sex interactions in short term survival following AMI.[78;111;114] Almost all of these studies have reported similar findings, namely an excess risk of death in younger women compared to men and decreasing sex differences in survival with increasing age. In the National Registry of Myocardial Infarction 2 Study, case fatality rates were twice as

high in women as in men in those aged less than 50 years.[78] The sex difference was no longer apparent by 74 years.

The fact that women are older at the time of their first AMI seems to account for much of the sex difference that exists in short term case fatality rates following hospitalisation with AMI. In the current study, adjusting for age reduced much of the excess risk seen in women but did not remove it completely. Controlling for other baseline characteristics had a marginal effect on the effect of sex on survival. The presence of an age sex interaction in short term survival following AMI suggests that the excess mortality risk in women seen in women following hospitalisation with AMI is greater in younger women. Various mechanisms have been put forward to explain the apparent excess short term risk in women following AMI.[78;198] These include sex based differences in pathophysiology including different plaque types, clotting mechanisms and coaguability. Possible explanations for the higher risk of death seen in younger women may include a lower rate of use of established treatments for AMI in women than in men, and sex based differences in these treatments have been reported.[201-203] It is also possible that differences in short term survival may be due to differences in baseline characteristics between men and women that have not been adjusted for. This is especially true of non-cardiac diagnoses which are rarely included in description of baseline characteristics. This study does not include deaths following AMI that occur in individuals who do not survive to reach hospital. It has been suggested that women are more likely to survive to reach hospital and that including these deaths in the analysis of short term case fatality may remove or reduce any sex differences in survival observed following hospitalisation.[204] There is some evidence that women are more likely to survive an out of hospital cardiac arrest which would support these findings.[205]

Longer term unadjusted case fatality

In the current study 28% of men and 40.6% of women were dead at two years following their first AMI. By five years case fatality had increased to 39% in men and 52.8% in women. Overall unadjusted longer term case fatality was therefore higher in women than in men. The literature is not consistent in its description of longer term case fatality in men and women following AMI. The findings from the current study are in broad agreement with a number of other studies. For example, in the Worcester Heart Attack Study two year case fatality was 19.6% in men and 28.9% in women.[56] Two year case fatality in the current study was 28% in men and 40.6% in women. In the Alberta Health and Wellness database, five year case fatality was 26.8% in men and 38.8% in women.[80] Five year case

fatality in the current study was 39% in men and 52.8% in women. The mean age of individuals in these studies was less than in the current study that did not exclude older individuals. A number of other studies that have included the very elderly have reported similar unadjusted case fatality rates in men or women.[121;198]

Age adjusted case fatality

At two years, age stratified case fatality in this study was still higher in women than in men in all age groups. As for short term case fatality, the greatest sex differences were seen in the younger age groups. By five years however case fatality was very similar in men and women within age groups. At five years, adjusting for age after removing the deaths that occurred within the first 30 days accounted for all of the excess risk seen in women in the crude analyses and the risk of death in women was less than that seen in men. There are few studies with which to compare these data. Most studies that have examined longer term case fatality in AMI in men and women have reported either a similar case fatality in men and women[114;121] or a trend towards a lower case fatality in women.[86]

Multivariate adjusted case fatality

In the current study after adjusting for age and other baseline variables, the risk of death at five years after excluding deaths in the first 30 days, was greater in men than in women. The risk of death was 6% less in women than in men. This female survival advantage was present in all age groups. There are a number of studies with which to compare these data, although useful comparison in hindered by variation in the follow-up periods that have been examined. In addition, the studies have controlled for different baseline characteristics when modelling survival and few have taken into account non-cardiac morbidity. The results of the current study are in broad agreement with most other studies that have examined adjusted longer term survival following AMI. In general improved survival in women was observed particularly when the length of follow-up was greater than one year. In the Worcester Heart Attack Study and the Perth Coronary Register, men had significantly poorer long term survival than women after adjusting for age and other factors.[56] In a number of other studies including TRACE, the MITI Registry, the Danish Verapamil Infarction Trial and the Yorkshire AMI Study, there was a trend towards better long term survival in women than in men although this trend was not statistically significant.[85;86;113;114]

The reasons for the better longer term survival following AMI in women compared to men are not clear. The lower long term case fatality in women does not appear to be due to

their excess short term case fatality, which is not large enough to be responsible for such a bias.[206] It is possible that the better long term survival in women reflects the overall survival advantage of women in the general population. The effects of the infarct are greatest on short term case fatality. For those individuals who survive this period, it maybe that woman then have a better survival than men as occurs in the general population. Competing causes of death are also important. Causes of death in individuals in the current study have not been examined and it maybe that such an analysis would provide further evidence for this theory.

8.3.2 Age

Short term case fatality

Age was the most powerful predictor of survival in men and women. The effect of age on survival was consistent with other studies, although comparison with other studies is limited by use of different age categories and the tendency for studies to look at the effect of age on survival in men and women together. In the current study 30 day case fatality rose from 3.7% in men aged less than 55 years to 42.6% in men aged greater than 84 years. The equivalent figures in women were 5.9% and 44.7% respectively. In the Swedish National Register case fatality rose from 6% in men aged 30-49 years to 43% in men aged 85-89 years. In women the equivalent figures were 10% and 40% respectively. In the multivariate analyses age had a powerful effect and in women approximately doubled the risk of death for each additional decade. The effect of age on 30 day case fatality in the multivariate analyses was similar in men and women. There are no data with which to compare these findings.

Longer term case fatality

There are even less data available describing longer term case fatality in men and women of different ages. In the current study two year case fatality rose from 7.2% in men aged less than 55 years to 68.7% in men aged greater than 84 years. The equivalent figures in women were 10.3% and 69.8%. In the Worcester Heart Attack Study two year case fatality increased from 6.0% in men aged less than 50 years to 51.3% in men aged greater than 79 years.[120] In women the equivalent figures were 8.9% and 46% respectively. Age continued to have a powerful effect in the multivariate analyses with each additional decade resulting in a doubling in the risk of death at five years.

8.3.3Socioeconomic deprivation

There is a limited literature describing the relationship between socioeconomic deprivation and survival following first AMI in men and in women. The situation is complicated further by a lack of consistency regarding the definition and measurement of socioeconomic deprivation. There are therefore few studies with which to compare the results of this study.

Short term case fatality

Unadjusted 30 day case fatality decreased as the level of socioeconomic deprivation increased. This can be at least partly explained by the younger age of men and women in more deprived groups compared to those in less deprived groups. The difference in the distribution of age across deprivation categories means that it is difficult to draw any conclusions from unadjusted analyses. In the multivariate analyses, socioeconomic deprivation had a more powerful effect on the risk of death at 30 days in men than in women, although overall it was a significant independent predictor of outcome in both sexes. In men the most deprived deprivation category had a 9% increased risk of death relative to the least deprived category. The results from the current study are in-keeping with the FINMONICA MI Register Study who found that the adjusted risk of death in low income men compared to high income men was 2.01 for deaths occurring between 2 and 27 days post-AMI in individuals aged 35-64 years.[207] As with the current study the effect of socioeconomic deprivation was greatest in men and the adjusted risk in low income women compared to high income women was 1.25. When multivariate modelling was carried out within age groups, socioeconomic deprivation had the greatest effect in younger men and women. In individuals aged less than 65 years, men in the most deprived category had a 33% increase in the risk of death compared to those in the least deprived category. The magnitude of effect was similar in women. The effect of socioeconomic deprivation on short term survival declined with increasing age and it was no longer a significant independent predictor of outcome in women aged 65 years and above or in men aged 75 years and over. There are no other studies with which to compare these data though the FINMONICA MI Study only included individuals aged 35-64 years. It is not clear why socioeconomic deprivation should adversely affect short term prognosis following AMI, especially in younger age groups and in men. A possible contributing factor could be varying access to medical care and the quality of this care. There is some evidence that socioeconomic status may affect access to specialised cardiac services,[122;208] though studies that have examined this have not been consistent in their findings. If this

effect was predominately caused by lack of access to specialised cardiac services then you might expect the effect to be greater in women and the elderly who have been shown to have reduced access to these services.

Longer term case fatality

Longer term case fatality was again higher in individuals in the least deprived categories compared to those in the most deprived categories, who were on average younger in age. At five years and excluding 30 days, socioeconomic deprivation had a powerful effect on prognosis in men and women. As for short term survival, the magnitude of this effect was greater in men than in women. Men in the most deprived category had a 27% increased risk of death compared to those in the least deprived category. There are few studies with which to compare these data. It is unclear why socioeconomic deprivation should exert a greater effect on longer term prognosis than on short term prognosis following AMI, and why this effect should be greater in men than in women. Again it could be due to competing risks and a reflection of the survival advantage of women in the general population. It has been suggested that the longer term effects of socioeconomic deprivation may arise as a result of less efficient secondary prevention in these individuals.[174;207;209] It is however difficult to know how much of the effect is due to the greater longevity of individuals in less deprived categories compared to those in more deprived groups. This might also partly explain the greater effect in men than in women. The effect of socioeconomic deprivation on five year survival was much greater in younger age groups than in the older age groups. Men aged less than 65 years in the most deprived category had a 70% increased risk of death at five years compared to those in the least deprived category. The magnitude of effect was greater in men than in women. As for short term survival, socioeconomic deprivation was not an independent predictor of outcome in the elderly.

8.3.4 Comorbid diagnoses

8.3.4.1 Diabetes

Short term case fatality

In this study 30 day case fatality following a first AMI in men and women with a diagnosis of diabetes was approximately twice that of individuals with no comorbid diagnoses. After adjusting for the effect of other variables, men and women with diabetes had a 17% increase in the risk of death at 30 days compared to those without a diagnosis of diabetes.

The effect was greatest in the younger age groups, especially in women. For example, women aged less than 65 years with diabetes had a 65% increased risk of death compared to those with no diagnosis of diabetes. Diabetes was not however a significant independent predictor of short term survival in men or women over the age of 65 years. A number of other studies have found that diabetes has a greater adverse effect in women than in men on short term case fatality following AMI.[125;126;129] The reasons for this are not clear though it is thought that the presence of diabetes in women may negate the protective effect of oestrogen, and that women with diabetes may have more comorbid conditions and coronary artery disease risk factors than men.[81;125] These studies have not however shown that this effect is greater in younger individuals. In this study diabetes had a greater effect on one year survival following a first AMI after adjusting for other factors than on 30 day survival. Again this was more marked in younger age groups and in women. Women aged less than 65 years with a diagnosis of diabetes were 2.4 times more likely to die by one year than those who did not have a diabetes diagnosis.

Longer term case fatality

Unadjusted case fatality in men and women with a diagnosis of diabetes remained elevated in the longer term compared to those individuals with no comorbid diagnoses. The five years case fatality rate was 53.2% in men and 63.5% in women hospitalised with a first AMI who had a diagnosis of diabetes. In the multivariate analyses diabetes remained a significant independent predictor of five year survival after adjusting for other variables. The effect of diabetes on survival was again greater in younger age groups, especially in women although diabetes remained a significant and powerful predictor of five year survival in all age groups. These findings are consistent with reports from other studies.[128;132;133] Overall the risk of death at five years was increased by 52% in men and by 54% in women coded with diabetes compared to those with no diabetes coding.

8.3.4.2 Heart failure

Short term case fatality

In this study in the unadjusted analyses almost one third of men and women hospitalised with a first AMI who had a diagnosis of heart failure were dead within 30 days of their first AMI. By one year this had risen to almost one half. In the multivariate analyses heart failure was a powerful predictor of short term survival after adjusting for the effects of other factors. The risk of death at 30 days was increased by 48% in men and by 15% in women with heart failure compared to those without a diagnosis of heart failure. The

effect of heart failure was greatest in younger age groups and in men. Men aged less than 65 years with a diagnosis of heart failure were 2.29 times were more likely to die at 30 days than men without heart failure. The equivalent risk in women was 64%. The effect of a heart failure diagnosis was even more marked on one year survival and was again greater in younger age groups but similar in men and women. There are few data with which to compare these findings. A number of studies have reported elevated short term case fatality in men in individuals hospitalised with AMI but not in men and women and in different age groups.[136;137] The increased case fatality in men hospitalised with AMI with a comorbid diagnosis of heart failure may relate to the higher rate of systolic dysfunction seen in men with heart failure and the fact that women who develop heart failure are more likely to have preserved left ventricular systolic function.[210;211]

Longer term case fatality

By five years two thirds of men and three quarters of women hospitalised with a first AMI who had a diagnosis of heart failure were dead. Median survival was less than two years in men and less than one year in women. Heart failure continued to have a significant adverse effect on longer term survival in the adjusted analyses. Overall men hospitalised with a first AMI who had a diagnosis of heart failure were 90% more likely to die than men without a diagnosis of heart failure. Again the risk was greatest in younger age groups.

8.3.4.3 Hypertension

Short term case fatality

In the unadjusted analyses hypertension had a small effect on short term survival in men and women hospitalised with a first AMI relative to other comorbid diagnoses. In the multivariate analyses hypertension was a significant independent predictor of outcome after adjusting for other variables. A diagnosis of hypertension reduced the risk of death at 30 days in men and women in different age groups. Overall the risk of death at 30 days was reduced by 26% in men and by 24% in women in individuals hospitalised with a first AMI who had a diagnosis of hypertension. The effect of hypertension on survival was similar in all age groups. Previous studies have not provided consistent results on the importance of hypertension on survival following an AMI. A number of other studies that have demonstrated that hypertension adversely affects case fatality after AMI.[142;212-216] A number of possible explanations have been put forward to explain this finding including increased coronary vascular resistance, decreased coronary reserve and muscle fibre

hyperplasia.[187] In addition, hypertension is causally related to heart failure which has a high mortality and it is possible that individuals with a diagnosis of hypertension are more likely also to have a diagnosis of heart failure. Some of the inconsistency in findings between studies may relate to the importance of a change in blood pressure that may arise as a result of an AMI.[212] A drop in blood pressure may reflect a badly damaged myocardium and be associated with a poor prognosis. It is possible that these individuals are not recorded as being hypertensive. Another possibility is that individuals in the current study who have a coding of hypertension are a biased sample of all individuals with the diagnosis and that they are likely to be receiving appropriate secondary prevention treatments which would improve their prognosis.

Longer term case fatality

As for short term survival, hypertension had a small effect on unadjusted longer term survival relative to other comorbid diagnoses. Median survival was reduced however in men and women with a diagnosis of hypertension. Median survival in men hospitalised with a first AMI was 7.1 years in those with a diagnosis of hypertension compared to over 10 years in those with no comorbid diagnoses. After adjusting for other factors in the multivariate analyses hypertension was not a significant independent predictor of longer term survival. It is not clear why hypertension should be associated with decreased case fatality in the short term but not in the longer term. A lack of association between hypertension and longer term survival following AMI has been reported previously.[217] It has been suggested that hypertension is important in the prognosis AMI but only in younger patients and not among older patients.[216] The effects of hypertension on longer term case fatality therefore may have been masked by the presence of an interaction between age and hypertension which were not fully accounted for in previous studies.[216] In the current study however, the effect of hypertension did not vary with age.

8.3.4.4 Chronic obstructive pulmonary disease

Short term case fatality

In the current study 27.3% of men and 32.5% of women hospitalised with a first AMI who had a comorbid diagnosis of respiratory disease were dead within 30 days. Overall the risk of death at 30 days was increased by 29% in men and by 23% in women after adjusting for other factors in the multivariate analyses. In individuals aged less than 65 years, respiratory disease was only a significant predictor of outcome in men and not in women. In other age groups however, respiratory disease was a significant independent predictor of

survival and its effect was similar in men and women. In the SPRINT Study unadjusted in-hospital case fatality was raised in individuals with COPD compared to those with no COPD (23.9% versus 17.2%).[101] Individuals with COPD were also more likely to have a diagnosis of heart failure and atrial fibrillation. After adjusting for other factors COPD was not a significant independent predictor of outcome. In the TRACE Study COPD was not a significant predictor of survival at 30 days in individuals hospitalised with AMI.[103] COPD is an important confounding factor for the diagnosis of heart failure. Both TRACE and SPRINT collected detailed clinical information so that individuals were more likely to be given an accurate diagnosis of COPD or heart failure. The apparently significant independent effect of COPD on survival may be partly explained by an under recording of heart failure so that it was inadequately controlled for in the multivariate analyses.

Longer term case fatality

Approximately half of all men and women hospitalised with a first AMI who had a comorbid diagnosis of respiratory disease were dead within two years of admission. Median survival was less than 2.5 years in men and 1.5 years in women. Respiratory disease had a more powerful effect on longer term than on short term survival and at five years the risk of death in individuals with a comorbid diagnosis of respiratory disease was increased by 38% in men and by 39% in women. The effect of this comorbid diagnosis on survival was again greater in younger age groups than in the elderly but was similar in men and women. In the SPRINT Study COPD was not a significant predictor of five year survival after adjusting for other factors in the multivariate analyses.[101] In the SPRINT Study, individuals with COPD were more likely to have a diagnosis of heart failure. In the TRACE Study COPD was found to be a significant independent predictor of outcome but only in those individuals without a diagnosis of heart failure.[103] Potential interactions between these two comorbid diagnoses have not been explored in the current study and further examination of this issue could provide more information as to the relative importance of these diagnoses and the relationship between them.

8.3.4.5 Atrial fibrillation

Short term case fatality

In the current study, unadjusted short term case fatality was increased in men and women hospitalised with a first AMI who had a diagnosis of atrial fibrillation. The prevalence of atrial fibrillation increases with age and individuals with a comorbid diagnosis of atrial fibrillation are on average older than individuals with no comorbid diagnosis of atrial

fibrillation. You would therefore expect these individuals to have an increased unadjusted case fatality and this finding is consistent with other studies.[96;97;218] After adjusting for other factors in the multivariate analyses, atrial fibrillation had a protective effect and 30 day case fatality was significantly lower in those individuals with a comorbid diagnosis of atrial fibrillation. Overall the risk of death at 30 days was reduced by 24% in men and women. The effect was only present in individuals aged 65 years and over and was similar in magnitude in men and women. By one year and after excluding 30 day deaths, case fatality was increased in individuals with a comorbid diagnosis of atrial fibrillation. The magnitude of this effect was much greater in younger and middle aged men and women so that the risk of death in individuals aged less than 65 years was increased by 37% in men and by 56% in women. These findings have not been reported previously, although the prognostic significance of atrial fibrillation complicating AMI is controversial. It is not clear why a diagnosis of atrial fibrillation might decrease short term case fatality, especially in older people, and increase longer term case fatality. Most studies have found that the presence of atrial fibrillation increases short term case fatality, however none of the studies have looked at the effect in different age groups. The Worcester Heart Attack Study found that atrial fibrillation was not a significant independent predictor of outcome after adjusting for other factors.[109] There is some evidence to suggest that the temporal relationship between AMI and atrial fibrillation is important when considering prognosis and that pre-existing atrial fibrillation is less likely to be associated with an adverse short term outcome than atrial fibrillation that develops as a complication of an AMI.[98;99;139] The current study does not differentiate between those individuals with pre-existing atrial fibrillation and those who develop atrial fibrillation subsequent to their AMI. Bias in coding towards those individuals with a pre-existing diagnosis of atrial fibrillation might contribute to the observed findings.

Longer term case fatality

Longer term case fatality rates were increased substantially in men and women hospitalised with a first AMI who had a comorbid diagnosis of atrial fibrillation. Five years case fatality in these individuals was 61% in men and 71% in women whilst median survival was only 2.8 years in men and 1.4 years in women. After adjusting for other factors in the multivariate analyses atrial fibrillation remained a significant predictor of outcome. The risk of death in individuals aged 65-74 years was increased by 55% in men and by 56% in women. As for short term case fatality, the effect of atrial fibrillation was greater in younger and middle aged groups. This finding is new and has not been reported previously. As with short term case fatality, controversial results have been reported in

patients surviving hospitalisation with respect to long term case fatality.[95;96;219] Atrial fibrillation may act as a marker for left ventricular dysfunction and a compromised myocardium which may explain the association with reduced longer term survival.

8.3.4.6 Renal impairment

Short term case fatality

In the current study renal failure more than doubled the risk of death at 30 days in the unadjusted analyses. Almost half of all men and women hospitalised with a first AMI who had a diagnosis of renal failure were dead within 30 days. Median survival was less than three months in men and less than two months in women. After adjusting for the effect of other factors, renal failure was a significant predictor of short term outcome and had the most powerful effect on survival of all comorbid diagnoses. The effect of renal failure was greatest in younger age groups so that men aged less than 65 years were 4.5 times more likely to die at 30 days and women 5.2 times more likely to die than individuals aged less than 65 years with no comorbid diagnosis of renal failure. The magnitude of effect decreased with increasing age but remained significant in all age groups and was similar in men and women. Impaired renal function has consistently been found to be independently associated with poor outcome following AMI, and the effect on prognosis seems to be dependent on the degree of renal impairement.[89;90;146;220] Several potential mechanisms have been suggested to explain the association between impaired renal function and survival following AMI.[145] These mechanisms include high levels of homocysteine and reduced nitric acid production which may result in accelerated atherosclerosis. There are no sex-specific data with which to compare the findings of this current study in which renal failure had a similar effect on survival in men and women. Sex has been included in some of the multivariate modelling and women with impaired renal function have been found to be at a decreased risk of death following AMI than men.[90;146] Interpretation of these findings is complicated by the fact that sex is incorporated into the estimation and definition of glomerular filtration rate, creatinine clearance and elevated creatinine levels. This may bias the results of any multivariate analyses that further adjust for the effects of sex. Prevalence of impaired renal function in individuals hospitalised with AMI varies according to the definition of renal impairment used and the study type and population involved. There is concern that the increasing prevalence of hypertension, obesity and diabetes among an ageing population will lead to a higher prevalence of renal failure.[220]

Longer term case fatality

Five year case fatality was 82.2% in men and 87.2% in women hospitalised with a first AMI who had a comorbid diagnosis of renal failure. At five years renal failure remained a significant predictor of outcome and the risk of death was increased 2.1 times in men and 1.7 times in women with a comorbid diagnosis of renal failure. As for short term case fatality the effect of renal failure was greatest in younger age groups and was similar in men and women. The long term survival of patients with renal failure who have been hospitalised with AMI is much worse than survival in patients without renal failure and patients with other comorbid diagnoses. As for short term case fatality there are few data with which to compare these findings. One study found a small long term survival advantage in women with renal failure hospitalised with AMI, however this was in patients on dialysis which represent a minority of patients with impaired renal function.[146] It seems clear that short and long term case fatality are significantly increased in men and women with impaired renal function but that the independent effect of sex on survival in this group of patients has not yet been established.

8.3.4.7 Other vascular diseases

Short term case fatality

In the current study approximately one third of men and women hospitalised with a first AMI who had a comorbid diagnosis of cerebrovascular disease or peripheral vascular disease died within 30 days of admission. Both diagnoses were significant independent predictors of short term survival though cerebrovascular disease had a more powerful effect on survival than peripheral vascular disease after adjusting for the effect of other factors. The risk of death at 30 days was increased by 67% in men and by 61% in women with a comorbid diagnosis of cerebrovascular disease and by 30% in men and 21% in women with a diagnosis of peripheral vascular disease. As with many of the other comorbid diagnoses, the effect of these diagnoses was greater in younger age groups than in older age groups. Peripheral vascular disease had a greater effect on short term survival in men than in women, especially in younger age groups. More extensive coronary artery disease may contribute to the excess mortality seen in these individuals. Individuals with peripheral vascular disease may also have increased mortality due to sequelae of their non-cardiac arterial disease including stroke.[221] There are few data with which to compare these findings and no sex-specific data. In the SPRINT Study, peripheral vascular disease increased the risk of in-hospital death by 37% in individuals hospitalised with AMI after adjusting for other factors.[105] In the SPRINT Study, patients with a diagnosis of peripheral

vascular disease were also more likely to have heart failure and atrial fibrillation and it is possible that interactions exist between these diagnoses that have not been explored in the current or any other studies.

Longer term case fatality

Approximately two thirds of men and women with a comorbid diagnosis of peripheral vascular disease or cerebrovascular disease were dead within five years of hospitalisation with their first AMI. Median survival was only six months in women and 16 months in men who had a diagnosis of cerebrovascular disease. After adjusting for the effect of other factors, both diagnoses remained significant independent predictors of outcome at five years and the effect of cerebrovascular disease on case fatality was consistently greater than that of peripheral vascular disease. The effect of these diagnoses on case fatality was similar in men and women and was again greater in younger than in older individuals. The only study to look at the significance of peripheral vascular disease as a prognostic indicator following AMI is the SPRINT Study.[105] In this study peripheral vascular disease was not found to be a significant independent predictor of five year survival following AMI after adjusting for other factors. Another study looked at the effect of peripheral vascular disease on long term mortality following coronary artery bypass surgery.[221] It found that individuals with peripheral vascular disease had substantially increased long term mortality compared to those individuals without peripheral vascular disease. The reason for this disparity is unclear, although in the SPRINT Study only a small number of individuals with peripheral vascular disease were followed up for five years which would have limited the power of the study to detect differences in survival.

8.3.4.8 Previous coronary heart disease and angina

Short term case fatality

In the current study unadjusted short term case fatality was increased in individuals with a previous diagnosis of coronary heart disease. 30 day case fatality was 22.6% in men and 27.4% in women with a previous diagnosis of coronary heart disease hospitalised with a first AMI. In the multivariate analyses, previous coronary heart disease was a significant predictor of 30 day outcome but only in men in whom the risk of death was increased by 26%. The effect of previous coronary heart disease was greater in younger age groups and was not a significant predictor of outcome in either men or women aged 75 years and over. There are few studies with which to compare these findings and none that describe the effect of previous angina on prognosis in men and women of different ages who are

hospitalised with a first AMI. As discussed previously, studies have reported conflicting results regarding the effect of previous angina on prognosis following AMI. The SPRINT Registry found that in-hospital case-fatality was significantly increased in individuals hospitalised with a first AMI who had a previous history of angina (16% versus 12%).[149] A Japanese Study analysed outcomes in 990 individuals hospitalised with AMI and reported better in-hospital and five year case fatality rates in patients aged less than 70 years with a previous history of angina.[222] There is evidence to suggest that the effect of previous angina on survival following AMI may depend upon the site of the infarct, the length of history of angina as well as the age of the individual.[151;152;154;155]

Longer term case fatality

Unadjusted five year case fatality in individuals hospitalised with a first AMI with a previous diagnosis of coronary heart disease was 52% in men and 61.3% in women in the current study. In the multivariate analyses previous coronary heart disease was a significant independent predictor of five year outcome in men and women, although the effect was modest when compared to other comorbid diagnoses. Men had an 11% increased risk of death at five years and women a 17% increased risk of death, though the risk varied with age. Previous coronary heart disease was only significant in men aged less than 65 years and in women aged greater than 65 years. In the Framingham Study, pre-existing angina increased the long term risk of coronary death but not of all cause mortality in men but not in women.[93] The multivariate adjusted risk of coronary death was increased by 49% in men. Pre-existing angina is usually indicative of severe double or triple vessel coronary artery disease and it therefore reasonable to suggest that these individuals have more extensive coronary artery disease.

8.3.5Temporal trends in case fatality in men and women following a first AMI

Short term case fatality

In the current study unadjusted 30 day case fatality in individuals hospitalised with a first AMI fell from 18.1% in men and 27.2% in women in 1990 to 14.6% in men and 25.1% in women in 2000. This represents a decline of 19% in men and 8% in women which occurred in the context of an increase in age in both sexes. One year case fatality fell by 13% in men and 6% in women over the same time period. In the multivariate analyses 30 day case fatality fell by 38% in men and by 24% in women. The magnitude of decline decreased with increasing age and was greatest in individuals aged less than 65 years.

Adjusted one year case fatality fell by 33% in men and by 31% in women and again the declines were greater in younger than in older individuals. The falls observed in the current study were greater than those reported from European MONICA centres including Glasgow.[1] However the MONICA Studies included individuals with all AMIs as oppose to first AMIs and were confined to younger patients. The sex difference in temporal trends in case fatality has been described previously and a number of studies including the Swedish MONICA Project, the Minnesota Heart Survey and the Ontario Study have reported significant reductions in short term case fatality in men but not in women.[55;82;106] No other studies have however described age and sex specific temporal trends. Possible explanations for this sex difference may include bias in treatment practices. It has been suggested that women are less likely to receive thrombolytic therapy which may be due to the fact that they are older and have more comorbid illness.[83;223] Women also tend to arrive at hospital later and have more atypical AMI presentations which would restrict their eligibility for acute therapy like thrombolysis.[224;225] Age related trends in case fatality following AMI occurring between 1975 and 1995 were examined in the Worcester Heart Attack Study who found encouraging declines in case fatality in all age groups but greater changes in younger age groups.[226] It is possible that differential receipt of therapies may in part explain age related differences in case fatality improvements over time. Older patients are less likely to be treated with effective therapies including beta blockers and thrombolysis.[227-230] The data from this current study are consistent with the suggestion that modern treatments are making an increasing population impact on survival following AMI.[231] The progressive improvements observed in short term case fatality may indicate the importance of immediate therapies for AMI such as ACE inhibitors, aspirin and thrombolysis.[232-234]

Longer term case fatality

The decline in unadjusted longer term case fatality that occurred in the current study was smaller than the decline that occurred in short term case fatality. Five year case fatality rates fell from 41.8% in men and 54.2% in women in 1990 to 38.2% in men and 51.7% in women. The declines observed in adjusted five year case fatality were similar in men and women (27% in men versus 23% in women). The magnitude of the declines was similar in men and women and the greatest declines in case fatality were seen in younger individuals. The substantial improvements in long term survival may be attributed to improvements in diet and smoking as well as secondary prevention therapies including aspirin and beta-blockers.[160;226;235;236] The similar trends in long term case fatality seen in men and women

may reflect the more equitable treatment once a diagnosis of coronary heart disease has been established.

8.3.6 Summary

In the current study, the prognosis of men and women hospitalised with a first AMI was much worse than indicated by clinical trials. One fifth of patients died within one month of admission and almost one half by five years. Unadjusted survival was substantially better in men than in women. Much but not all of the excess short term risk in women could be explained by the fact that women were older than men at the time of their first AMI. Women however remained at a 20% increased risk of death at 30 days even after adjusting for age and other factors. There was an age sex interaction in short term survival and the excess short term risk seen in women compared to men was greater in younger women. This finding is in keeping with a growing literature that reports similar observations. After excluding early deaths, adjusted longer term case fatality was slightly greater in men than in women. Age was the most powerful predictor of survival in men and women. Socioeconomic deprivation also had a powerful effect on survival, especially on longer term survival, in younger age groups and in men. Most comorbid diagnoses substantially increased the risk of death in the short and longer term. Heart failure, renal failure and cancer had the most powerful effects. Comorbid diagnoses tended to have a greater effect on longer term survival than on short term survival and in younger men and women than in older individuals. Atrial fibrillation and hypertension reduced the risk of death in the short term but not in the longer term. Between 1990 and 2000, the risk of death at 30 days fell by more than one third in men and a quarter in women. Declines were greater in younger age groups.

9 SECOND AMI: BASELINE CHARACTERISTICS

9.1 Results of descriptive analyses

This section describes the baseline characteristics of men and women who are admitted to hospital following a second acute myocardial infarction. Their first AMI took place up to ten years previously. The distribution of age and socio-economic status as well as the presence of comorbid conditions may differ in men and women. It is therefore important to have a clear understanding of these factors which may contribute to differences in survival between men and women.

9.1.1 Overall

Between January 1st 1990 and December 31st 2000, a total of 9,664 individuals aged 16 years and over, were admitted to Scottish hospitals following a second acute myocardial infarction. 3,849 were women. This comprised 39.8% of the cohort and was similar to the 41.4% of women hospitalised with a first AMI.

9.1.2 Age

Table 78 shows the distribution of age in men and women admitted to hospital following their second AMI. Mean age on admission to hospital was 74.2 years in women and 67.7 years in men. Women were on average six and a half years older than men at the time of second admission to hospital and 2.1 years older than at the time of their first admission to hospital. A two-sample t-test to compare the mean ages of men and women was highly significant, $p<0.001$. The age distribution of men and women differed significantly. 82.6% of women were aged greater than 64 years compared to 62.3% of men ($p<0.001$). This represented a substantial shift from the age distribution described in individuals hospitalised following a first AMI, especially in men. In those individuals, 75.8% of women were aged greater than 64 years compared to 52.4% of men. The distribution of age was relatively normal in men and women and can be summarised using a histogram as seen in Figure 18 and by the median, quartiles and extremes shown in **Table** 78. Age ranged from 24 to 96 years in men and from 29 to 104 years in women. The distribution of age was clustered around the median with 50% of women aged between 68 and 82 years and 50% of men aged between 60 and 76 years.

Table 78 Descriptive statistics for age of men and women following a second hospital admission for acute myocardial infarction

Number of cases (%)	Men	Women	Both
Age-group <55 years	790 (13.6%)	168 (4.4%)	958 (9.9%)
55-64 years	1398 (24.0%)	499 (13.0%)	1897 (19.6%)
65-74 years	1910 (32.8%)	1100 (28.6%)	3010 (31.1%)
75-84 years	1402 (24.1%)	1499 (38.9%)	2901 (30.0%)
>84 years	315 (5.4%)	583 (15.1%)	898 (9.3%)
Total	5815 (60.2%)	3849 (39.8%)	9664 (100%)

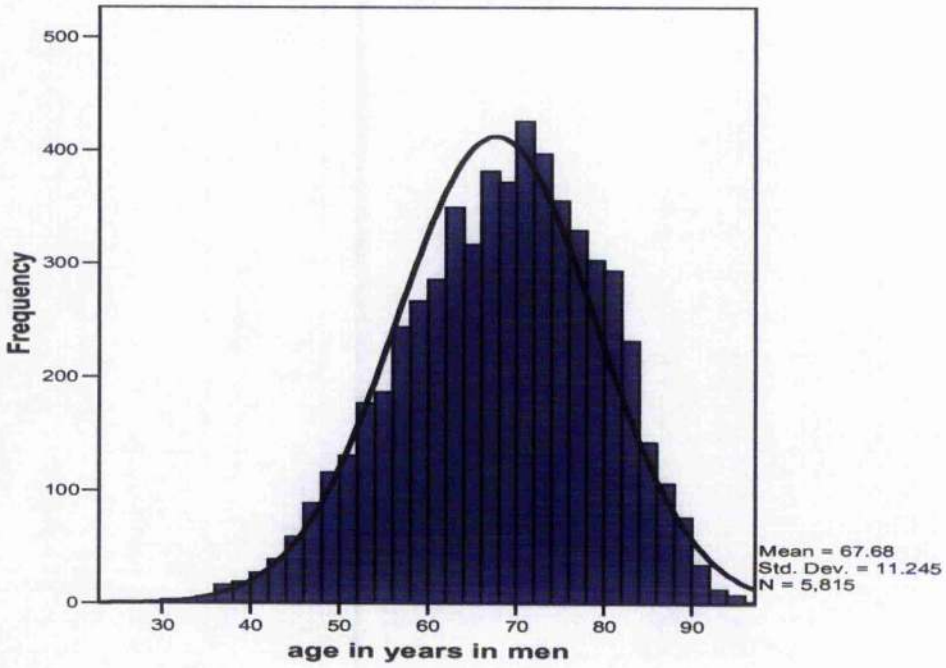
vi. Summary Statistics

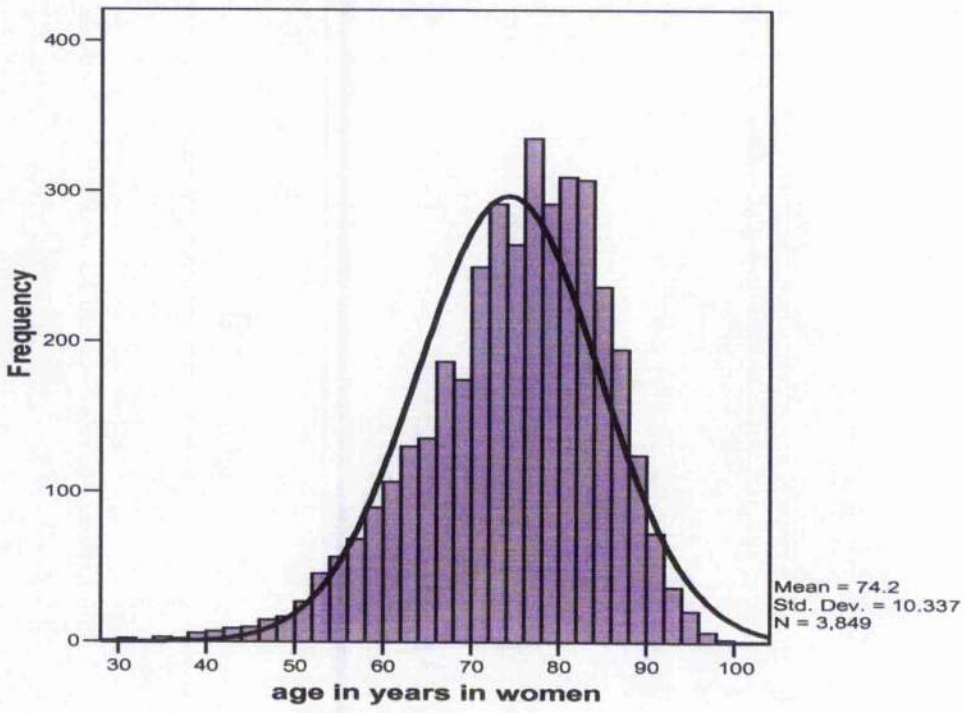
	Mean (95%CI)	MEDIAN	SD	MIN	MAX	RANGE	IQR
Men	67.7 (67.4-67.8)	68	11.2	24	96	72	16
Women	74.2 (73.9-74.5)	76	10.4	29	104	75	14

vii. Percentiles

	PERCENTILE						
	5	**10**	**25**	**50**	**75**	**90**	**95**
Men	48	52	60	68	76	82	85
Women	55	60	68	76	82	86	89

Figure 18 Histograms showing age distribution in men and women admitted to hospital with a second AMI





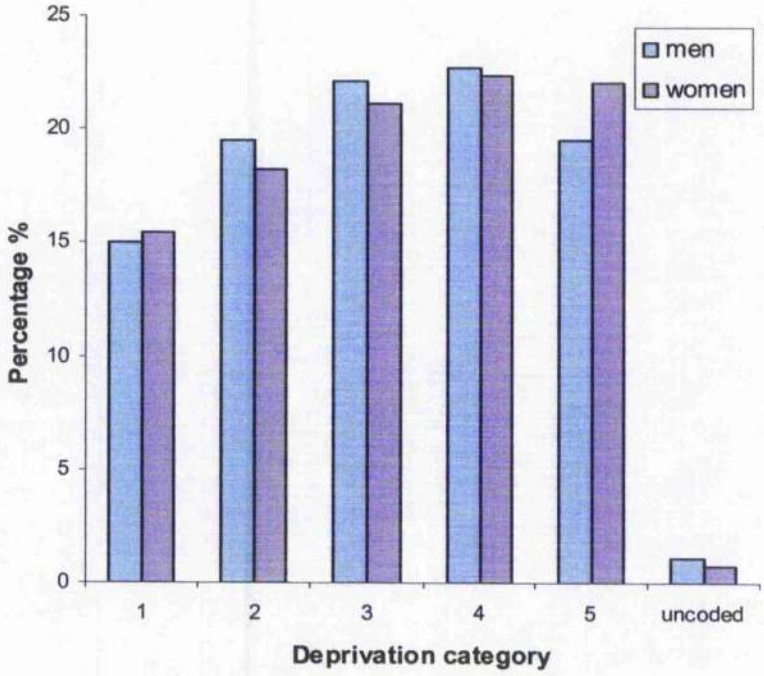
9.1.3Deprivation and sex

Overall 42.2% of men and 44.5% of women admitted to hospital with a second AMI came from the two most deprived deprivation categories. Table 79 and Figure 19 show the distribution of deprivation in men and women. As for individuals admitted to hospital with a first AMI, there was a socioeconomic gradient in men and women with the number of individuals admitted with a second AMI increasing across the deprivation categories from the least to the most deprived. A chi square test for trend was highly significant, $p<0.001$ after excluding the relatively small number of individuals not assigned to a deprivation category. The socio-economic gradient appeared to be slightly steeper in individuals admitted with a second AMI compared to individuals admitted with a first AMI. Only 15.2% of individuals with a second AMI were from the least deprived category compared to 16.4% of individuals with a first AMI ($P<0.001$).

Table 79 Distribution of deprivation in men and women with a second AMI

	Men	Women	All
Deprivation categories			
I- least deprived	876 (15.1%)	595 (15.5%)	1471 (15.2%)
II	1133 (19.5%)	702 (18.2%)	1835 (19.0%)
III	1289 (22.2%)	814 (21.1%)	2103 (21.8%)
IV	1320 (22.7%)	861 (22.4%)	2181 (22.6%)
V- most deprived	1135 (19.5%)	849 (22.1%)	1984 (20.5%)
Uncoded	62 (1.1%)	28 (0.7%)	90 (0.9%)

Figure 19 Distribution of deprivation in men and women hospitalised with a second AMI



9.1.4Deprivation and age

The distribution of age groups varied between deprivation categories. As shown in Table 80, the least deprived and more affluent individuals were older than the most deprived individuals. 78.1% of those in the least deprived category were aged 65 and over, compared to 65.3% of those in the most deprived category. There was a significant trend of decreasing age with increasing deprivation and this was statistically significant (Chi square test for trend $p<0.001$). The distribution of age within deprivation categories therefore displayed similar patterns in individuals admitted with a second AMI as for individuals admitted with a first AMI.

Table 80 Age distribution within deprivation quintiles in individuals with a second AMI

	Deprivation category					
Age group	**1-least deprived**	**2**	**3**	**4**	**5-most deprived**	**uncoded**
<55 years	103 (7.0%)	144 (7.8%)	208 (9.9%)	236 (10.8%)	256 (12.9%)	958 (9.9%)
55-64 years	218 (14.8%)	333 (18.1%)	418 (19.9%)	473 (21.7%)	432 (21.8%)	1897 (19.6%)
65-74 years	440 (29.9%)	570 (31.1%)	664 (31.6%)	727 (33.3%)	584 (29.4%)	3010 (31.1%)
75-84 years	505 (34.3%)	606 (33.0%)	622 (29.6%)	587 (26.9%)	560 (28.2%)	2901 (30.0%)
>84 years	205 (13.9%)	182 (9.9%)	191 (9.1%)	158 (7.2%)	152 (7.7%)	898 (9.3%)
Total	1471 (100%)	1835 (100%)	2103 (100%)	2181 (100%)	1984 (100%)	9664 (100%)

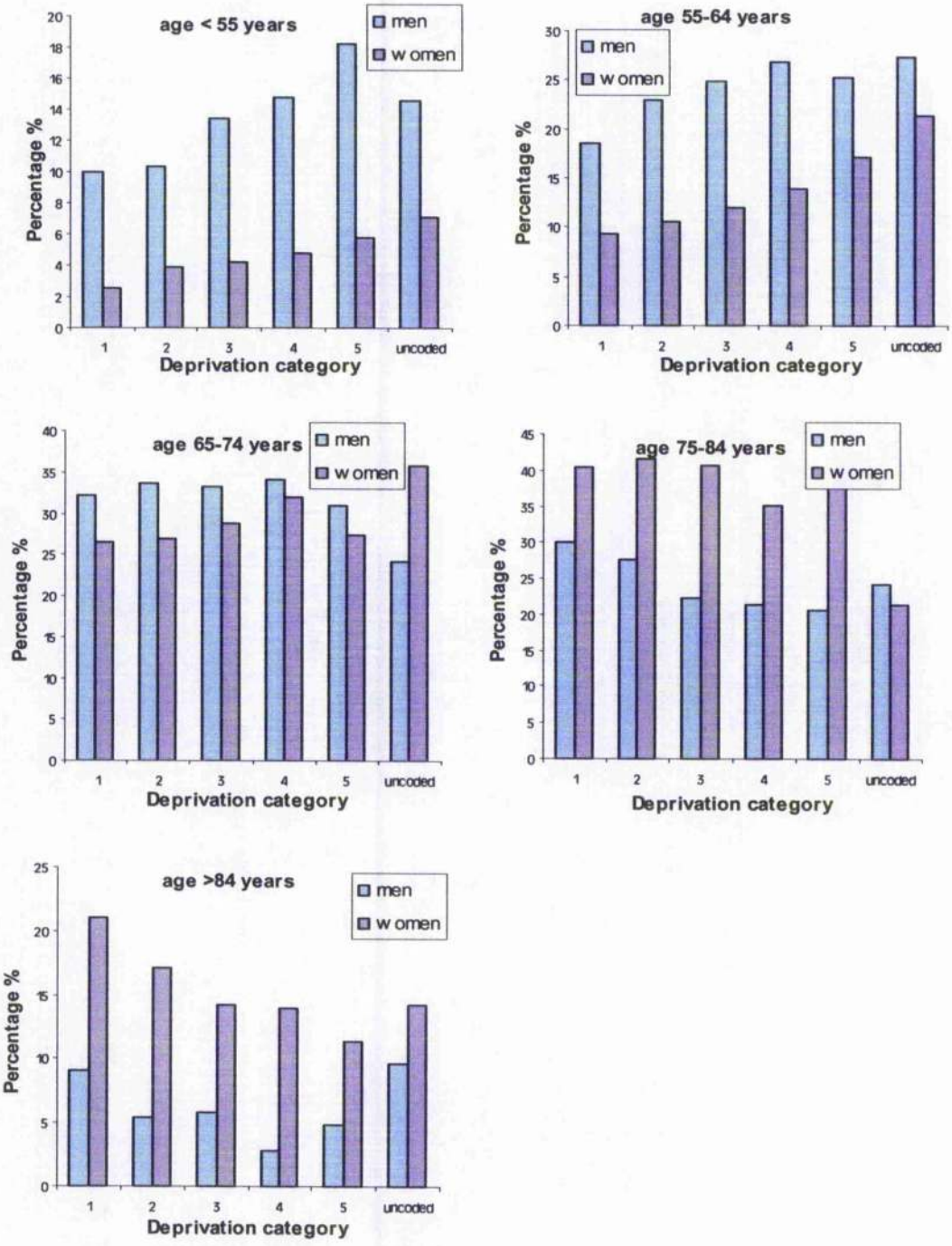
9.1.5Deprivation, age and sex

Table 81 shows the distribution of age by sex and deprivation category. There was a trend across deprivation categories so that more deprived men and women were younger than less deprived men and women. Women were on average older than men. The differences were significant. (Chi square test for trend $p<0.001$ in men and women). As for first AMI, the socio-economic gradient was greater in younger individuals aged <65 years. In the elderly, there was a reverse socioeconomic gradient so that elderly individuals were more likely to come from less deprived categories than from more deprived categories. Individuals aged 85 years and over accounted for only 11.4% of women in the most deprived category compared to 21% of women in the least deprived category. In men the figures were 4.8% and 9.1%. Figure 20 shows the distribution of deprivation categories by age group and by sex. The interaction between deprivation and sex seen in all patients was seen in all age groups but was more marked in younger age groups. The socio-economic gradient was stronger in women and in younger age groups.

Table 81 Age distribution by sex and deprivation category in individuals with a second AMI

		Deprivation category					
Men	**Age group**	**1-least deprived**	**2**	**3**	**4**	**5-most deprived**	**uncoded**
	<55 years	88 (10.0%)	117 (10.3%)	174 (13.5%)	195 (14.8%)	207 (18.2%)	9 (14.5%)
	55-64 years	162 (18.5%)	259 (22.9%)	321 (24.9%)	353 (26.7%)	286 (25.2%)	17 (27.4%)
	65-74 years	282 (32.2%)	381 (33.6%)	429 (33.3%)	451 (34.2%)	352 (31.0%)	15 (24.2%)
	75-84 years	264 (30.1%)	314 (27.7%)	290 (22.5%)	284 (21.5%)	235 (20.7%)	15 (24.2%)
	>84 years	80 (9.1%)	62 (5.5%)	75 (5.8%)	37 (2.8%)	55 (4.8%)	6 (9.7%)
Women	**Age group**						
	<55 years	15 (2.5%)	27 (3.8%)	34 (4.2%)	41 (4.8%)	49 (5.8%)	2 (7.1%)
	55-64 years	56 (9.4%)	74 (10.5%)	97 (11.9%)	120 (13.9%)	146 (17.2%)	6 (21.4%)
	65-74 years	158 (26.6%)	189 (26.9%)	235 (28.9%)	276 (32.1%)	232 (27.3%)	10 (35.7%)
	75-84 years	241 (40.5%)	292 (41.6%)	332 (40.8%)	303 (35.2%)	325 (38.3%)	6 (21.4%)
	>84 years	125 (21.0%)	120 (17.1%)	116 (14.3%)	121 (14.1%)	97 (11.4%)	4 (14.3%)

Figure 20 Distribution of deprivation categories by age group and sex



9.1.6Co-morbidity

71.3% of women and 65.5% of men admitted to hospital following their second AMI had either an admission in the five years prior to their AMI admission, or had a secondary diagnosis falling into one or more of the categories listed (Table 82). These figures were higher than for first AMI for which 51.5% of women and 44.3% of men had a recorded comorbidity. As for first AMI, heart failure was the most commonly recorded comorbidity and was more frequently coded in men than in women (37.1% versus 27%). Previous admission for coronary heart disease (excluding AMI), increased dramatically in men and women, rising from 7% to 24.7% in men and from 6.9% to 23.4% in women. A diagnosis of atrial fibrillation also increased substantially, especially in women in whom the prevalence rose from 7.4% to 12.5%. Coronary heart disease, cancer, cerebrovascular disease and peripheral vascular disease were more commonly recorded in men than in women. All other comorbid conditions were more commonly recorded in women than in men.

Table 82 Distribution and comparison of comorbid diagnoses by sex in individuals with a second AMI

Comorbidity	Men	Women	All
Any	3809 (65.5%)	2745 (71.3%)	6552 (67.8%)
Diabetes	672 (11.6%)	549 (14.3%)	1221 (12.6%)
Cancer	632 (10.9%)	397 (10.3%)	1029 (10.6%)
Respiratory	718 (12.3%)	516 (13.4%)	1234 (12.8%)
Cerebrovascular disease	673 (11.6%)	386 (10.0%)	1059 (11.0%)
Peripheral vascular disease	497 (8.5%)	283 (7.4%)	780 (8.1%)
Atrial fibrillation	516 (8.9%)	480 (12.5%)	996 (10.3%)
Hypertension	659 (11.3%)	574 (14.9%)	1233 (12.8%)
Renal failure	265 (4.6%)	197 (5.1%)	462 (4.8%)
Heart failure	1568 (27%)	1427 (37.1%)	2995 (31.0%)
Coronary heart disease	1435 (24.7%)	899 (23.4%)	2334 (24.2%)

9.1.7Comorbidity, age and sex

The prevalence of comorbid conditions varies substantially with age. In order to make more valid comparisons between men and women, each comorbid condition was then examined according to age group and sex. Figure 21 shows the distribution of age group by comorbid condition in men and in women and Table 83 shows the results of the chi square tests of association between age group and sex within each comorbid diagnosis.

Comorbid diagnoses that decreased in prevalence with increasing age

A previous admission for coronary heart disease was more common in younger individuals admitted to hospital following their second AMI. 34.5% of women and 29.5% of men aged <55 years had a previous admission for coronary heart disease (excluding AMI). These figures declined to 20.2% in women and 21.6% in men aged >84 years. The observed trends were significant in men and in women, p<0.001. These trends were in contrast to those seen in individuals admitted with a first AMI in whom coronary heart disease increased marginally with age. Diabetes decreased with increasing age, with the exception of men aged <55 years in whom prevalence was only 6.8% compared to the 15.9% seen in women of the same age. These trends were significant in women, but not in men (p=0.092 in men and 0.003 in women). Hypertension remained relatively stable with age but showed a marked reduction in the very elderly, especially in women. Again, hypertension was more common in women than in men except in the >84 year old age group.

Comorbid diagnoses that increased in prevalence with increasing age

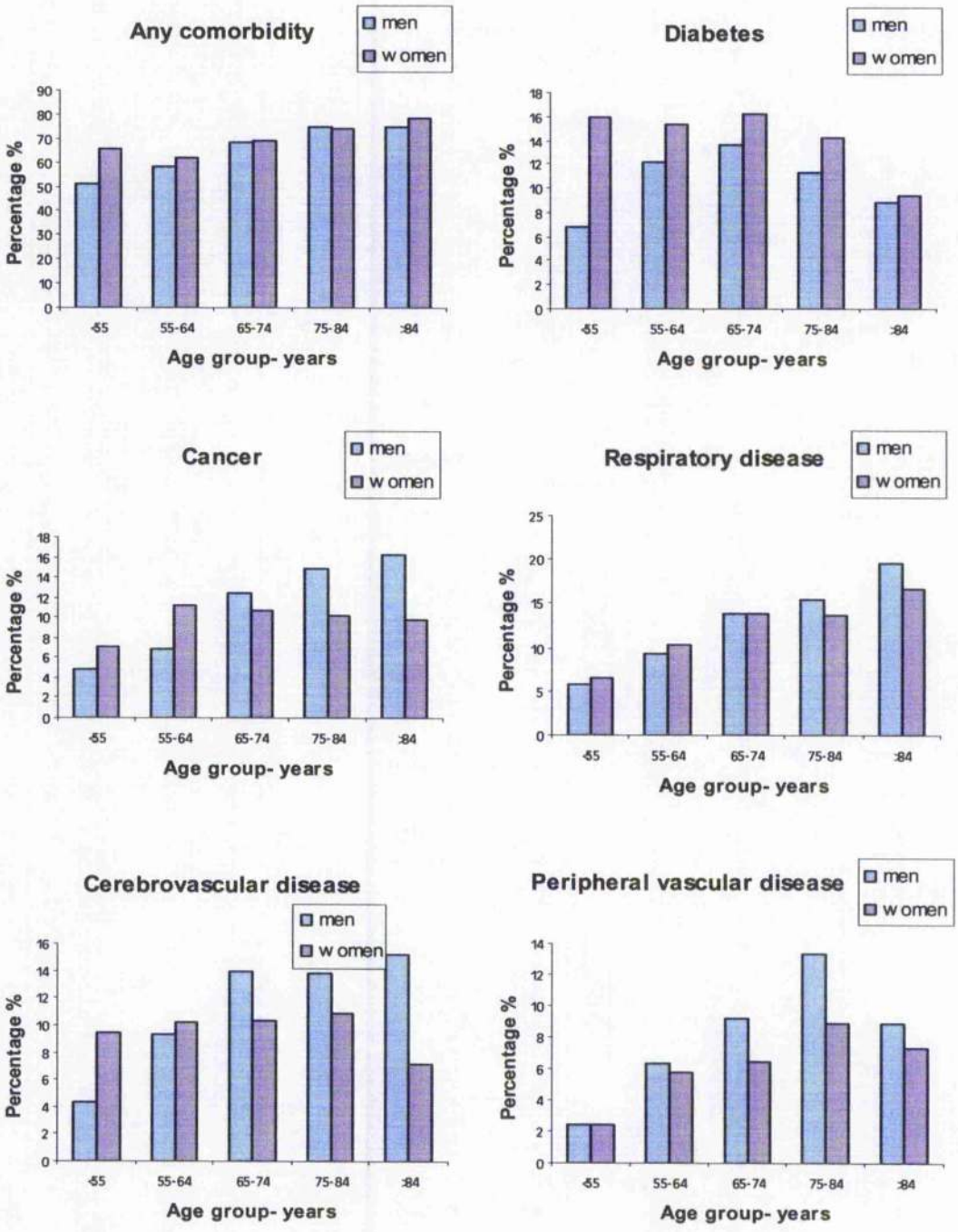
The prevalence of a previous or co-existing heart failure diagnosis increased significantly with age in men and in women, p<0.001. Heart failure was more commonly coded in women than in men in all age groups, although this female excess became more apparent in the elderly. 11.4% of men and 16.7% of women aged less than 55 years had a heart failure diagnosis coding compared to 39.7% of men and 53.2% of women aged 85 years and over. A similar pattern was seen in first AMI. The prevalence of atrial fibrillation increased substantially with age in men and in women and was slightly more common in women than in men. Only 2.4% of men and 3% of women aged <55 years had a diagnosis of atrial fibrillation. This rose to 17.8% of men and 20.9% of women aged >84 years. Peripheral vascular disease increased dramatically in prevalence with age in men but was less common in women in whom there was less of an age effect. There was no age sex

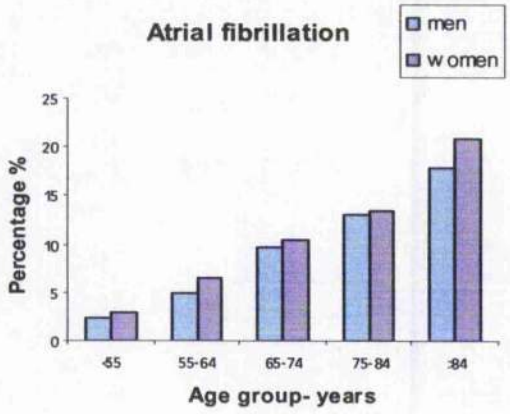
interaction as observed for first AMI. 8.9% of men aged greater than 84 years had a diagnosis of peripheral vascular disease compared to 7.3% of women.

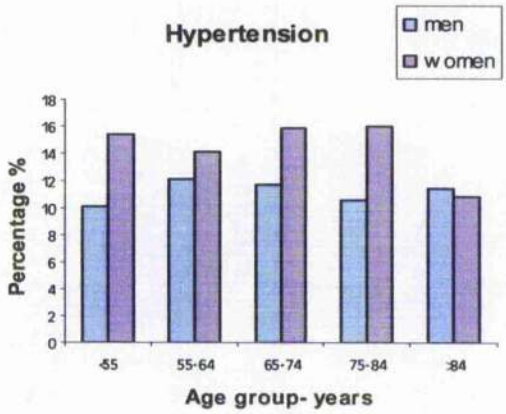
Comorbid diagnoses that displayed an interaction between age and sex

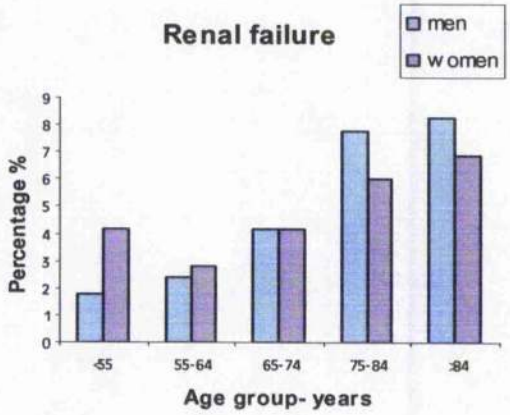
As for first AMI, a cancer diagnosis displayed an interaction between age and sex. Cancer was more commonly coded in younger women and less commonly coded in older women. For example, 7.1% of women aged less than 55 years were coded for cancer compared to 4.9% of men. However, 16.2% of men aged >84 years were coded for cancer compared to 9.9% of women. Respiratory disease showed a similar pattern and increased more with age in men than in women. 19.7% of men aged greater than 84 years had a respiratory diagnosis compared to 16.6% of women. Renal failure displayed a similar pattern although the differences between men and women were less marked in all age groups. This again was similar to patterns observed for first AMI. Cerebrovascular disease also displayed an age sex interaction and was more common in younger women and in older men. For example, 9.5% of women and 4.3% of men aged <55 years had a diagnosis of cerebrovascular disease compared to 7.2% of women and 15.2% of men aged >84 years.

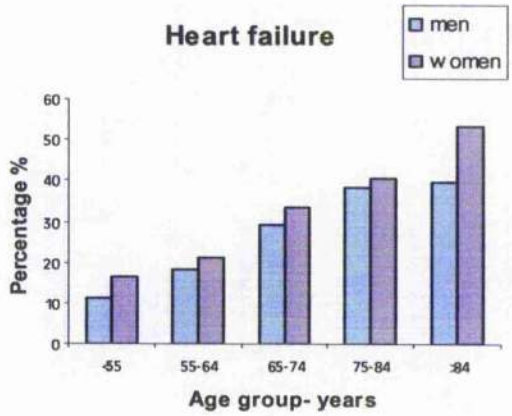
Figure 21 Distribution of comorbid diagnosis by age and sex




Atrial fibrillation
men
women
Percentage %
25
20
15
10
5
0
-55
55-64
65-74
75-84
:84
Age group- years


Hypertension
men
women
Percentage %
18
16
14
12
10
8
6
4
2
0
-55
55-64
65-74
75-84
:84
Age group- years


Renal failure
men
women
Percentage %
9
8
7
6
5
4
3
2
1
0
-55
55-64
65-74
75-84
:84
Age group- years


Heart failure
men
women
Percentage %
60
50
40
30
20
10
0
-55
55-64
65-74
75-84
:84
Age group- years

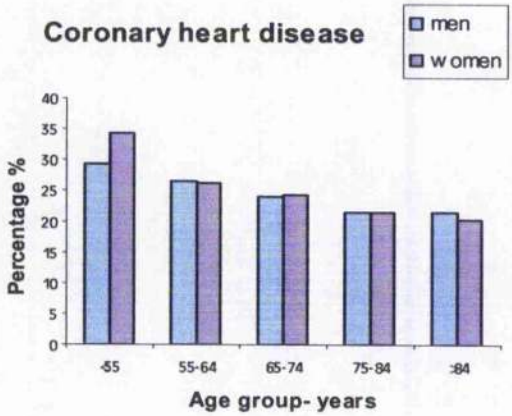

Coronary heart disease
men
women
Percentage %
40
35
30
25
20
15
10
5
0
-55
55-64
65-74
75-84
:84
Age group- years

Table 83 Tests of association between sex and age group within comorbid diagnoses in individuals with a second AMI

	CHI SQUARE TEST		CHI SQUARE TEST FOR TREND	
Comorbidity	**Men**	**Women**	**Men**	**Women**
Diabetes	P<0.001	P=0.004	**P=0.092**	P=0.003
Cancer	P<0.001	**P=0.631**	P<0.001	**P=0.990**
Respiratory disease	P<0.001	P=0.003	P<0.001	P<0.001
Cerebrovascular disease	P<0.001	**P=0.162**	P<0.001	**P=0.312**
Peripheral vascular disease	P<0.001	P=0.006	P<0.001	P=0.003
Atrial fibrillation	P<0.001	P<0.001	P<0.001	P<0.001
Hypertension	**P=0.527**	P=0.039	**P=0.917**	**P=0.192**
Renal failure	P<0.001	P=0.008	P<0.001	P=0.001
Heart failure	P<0.001	P<0.001	P<0.001	P<0.001
Coronary heart disease	P<0.001	P=0.001	P<0.001	P<0.001

9.1.8Comorbidity, deprivation and sex

The distribution of deprivation categories within each comorbid diagnosis was examined (Figure 22). Table 84 shows the results of the chi square tests of association between sex and deprivation within comorbid diagnoses. Individuals who had not been assigned to a deprivation category were excluded from these tests. Variation by deprivation category was not as marked as that observed between age groups, and there were minimal differences in the prevalence of comorbid diagnoses between deprivation categories. There appeared to be less variation between deprivation categories than observed for first AMI, and many of the associations seen previously were no longer evident.

The proportion of men and women with a comorbid diagnosis of cancer varied by deprivation category. There was a socio-economic gradient so that 9.4% of men and 8.9% of women in the least deprived category had a diagnosis of cancer, rising to 14.3% of men

and 13.3% of women in the most deprived category. This trend was significant in men and women (p=0.001 and 0.011 in men and women respectively).

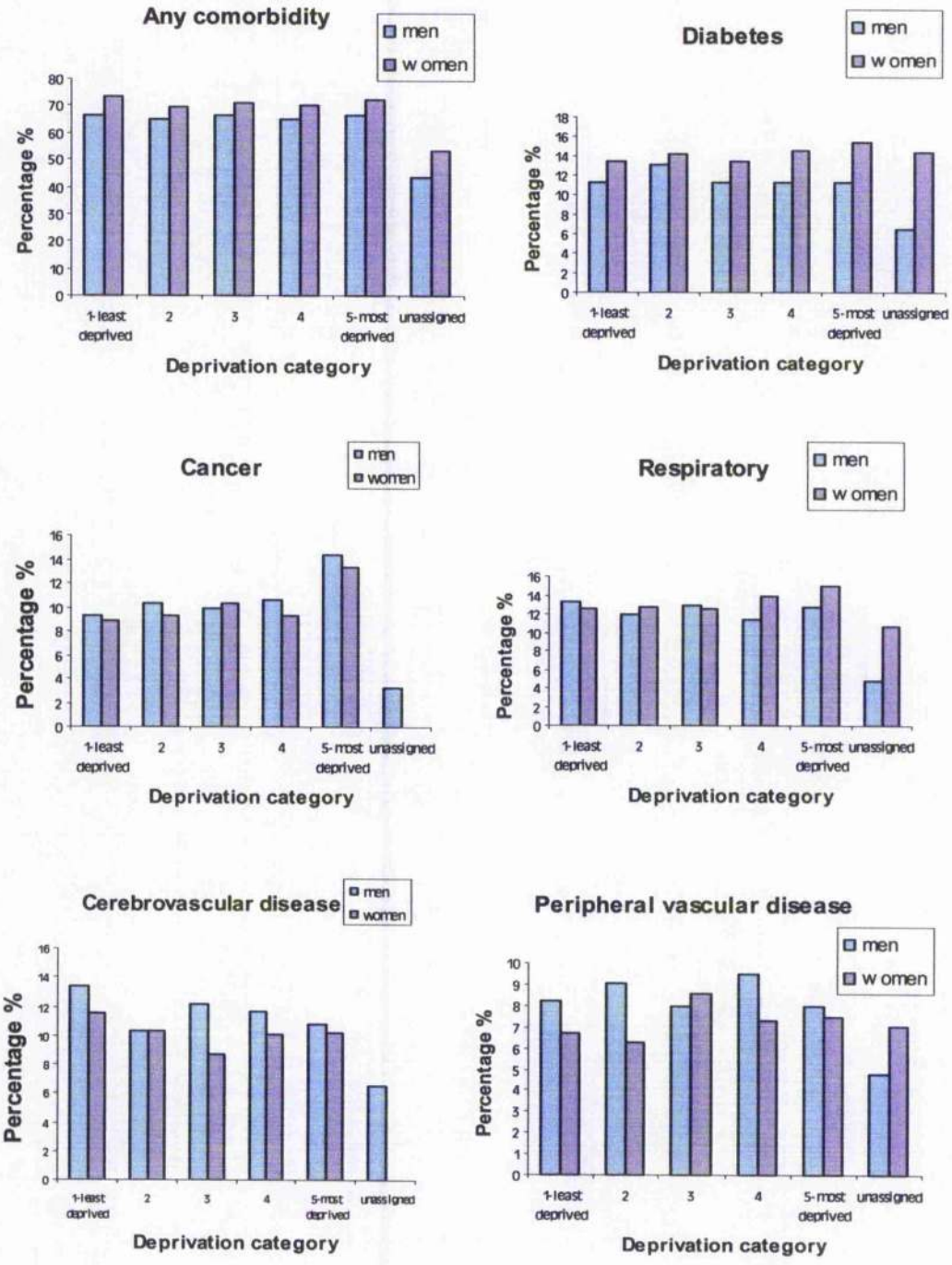
Atrial fibrillation did display significant variation across deprivation categories in men. The most deprived were less likely to have a diagnosis of atrial fibrillation than the least deprived. 10.8% of men in the least deprived category had a coding for atrial fibrillation compared to 6.7% in the most deprived category. This trend was significant, p=0.004.

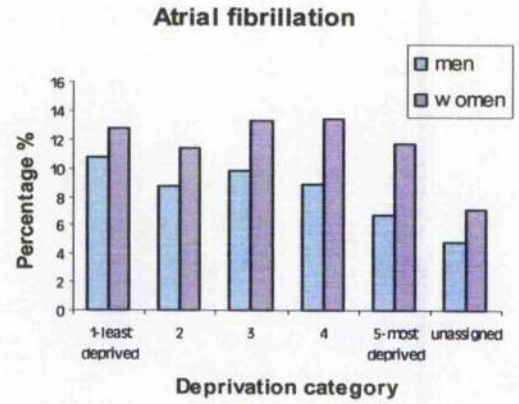
In women, renal failure was more commonly coded in more deprived categories than in least deprived categories. This trend was significant, p=0.015 and was not observed in men.

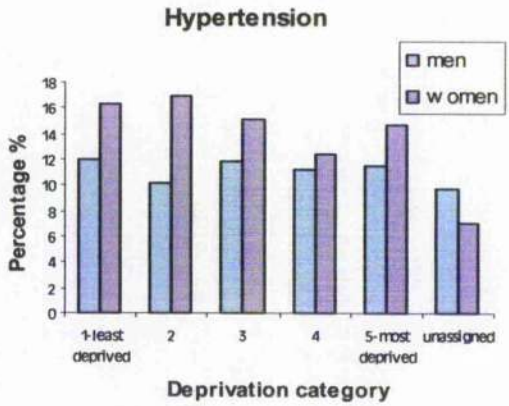
Finally, coronary heart disease displayed significant variation across deprivation categories, but only in men. The most deprived were more likely to have a coding for coronary heart disease. For example, 24.3% of men in the least deprived category were coded for coronary heart disease compared to 26.4% in the most deprived category. A similar pattern was seen in men and women following a first AMI.

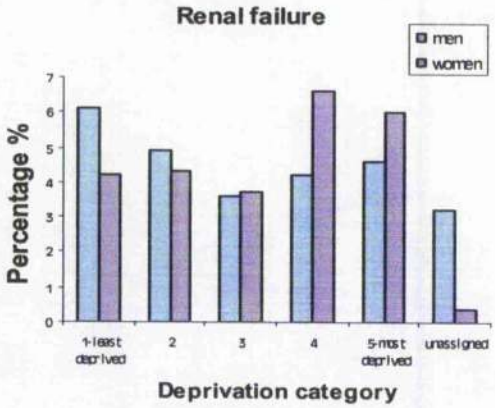
The prevalence of respiratory disease, cerebrovascular disease and diabetes did not vary by deprivation category, unlike in first AMI.

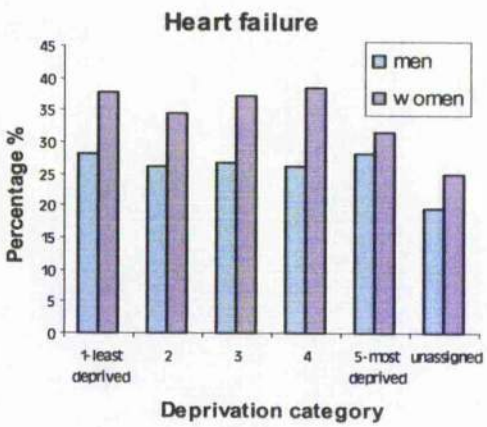
Figure 22 Distribution of deprivation categories by comorbid diagnosis and sex in individuals following a second AMI




Atrial fibrillation
men
w omen
Percentage %
0
2
4
6
8
10
12
14
16
1-least deprived
2
3
4
5-most deprived
unassigned
Deprivation category


Hypertension
men
w omen
Percentage %
0
2
4
6
8
10
12
14
16
18
1-least deprived
2
3
4
5-most deprived
unassigned
Deprivation category


Renal failure
men
women
Percentage %
0
1
2
3
4
5
6
7
1-least deprived
2
3
4
5-most deprived
unassigned
Deprivation category


Heart failure
men
w omen
Percentage %
0
5
10
15
20
25
30
35
40
45
1-least deprived
2
3
4
5-most deprived
unassigned
Deprivation category

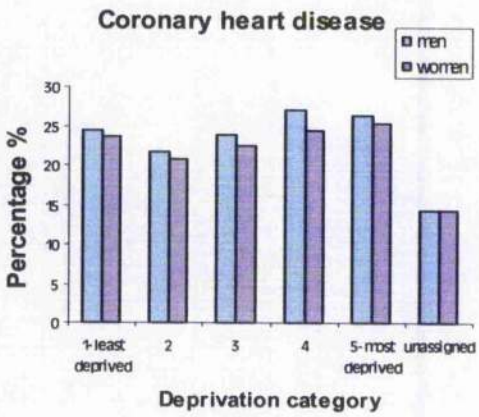

Coronary heart disease
men
women
Percentage %
0
5
10
15
20
25
30
1-least deprived
2
3
4
5-most deprived
unassigned
Deprivation category

Table 84 Tests of association between sex and deprivation within comorbid diagnoses in individuals with a second AMI

	CHI SQUARE TEST		CHI SQUARE TEST FOR TREND	
Comorbidity	**Men**	**Women**	**Men**	**Women**
Diabetes	***P=0.574***	***P=0.768***	***P=0.447***	***P=0.284***
Cancer	P=0.002	P=0.029	P=0.001	P=0.011
Respiratory disease	***P=0.651***	***P=0.532***	***P=0.580***	***P=0.117***
Cerebrovascular disease	***P=0.239***	***P=0.524***	***P=0.328***	***P=0.522***
Peripheral vascular disease	***P=0.578***	***P=0.484***	***P=0.985***	***P=0.419***
Atrial fibrillation	P=0.016	***P=0.666***	P=0.004	***P=0.931***
Hypertension	***P=0.716***	***P=0.114***	***P=0.853***	***P=0.066***
Renal failure	***P=0.090***	P=0.027	***P=0.108***	P=0.015
Heart failure	***P=0.666***	***P=0.605***	***P=0.889***	***P=0.494***
Coronary heart disease	P=0.027	***P=0.259***	P=0.014	P=0.121

9.1.9Time since first AMI

The median time since the first AMI was 2.3 years in men and 1.8 years in women (Table 85). This time was consistently greater in men than in women. Median time since first AMI varied by age group but did not demonstrate any clear trend. As with age, there was some variation according to socioeconomic deprivation but no obvious trend. Median time since first AMI appeared to increase in men and women between 1990 and 1996 / 1997, and then decrease. Overall however, the median time since previous AMI did increase from one year in men and women in 1990 to 2.5 years in men and 1.7 years in women in 2000.

Table 85 Median time since first AMI in men and women with second AMI

	MEDIAN TIME SINCE FIRST AMI (YEARS)	
	MEN	**WOMEN**
Overall	2.3	1.8
Age		
<55 years	2.0	1.9
55-64 years	2.4	2.3
65-74 years	2.4	2.1
75-84 years	2.2	1.9
84 years	2.0	1.9
Deprivation quintile		
1-least deprived	2.23	1.74
2	2.06	1.48
3	2.23	1.74
4	2.52	2.02
5-most deprived	2.19	1.72
Year of admission		
1990	1.0	1.0
1991	1.6	1.4
1992	2.0	1.3
1993	2.3	1.7
1994	2.8	1.8
1995	2.9	2.1
1996	2.9	3.2
1997	3.7	2.8
1998	3.4	2.8
1999	2.9	2.1
2000	2.5	1.7

9.2 Discussion of second AMI baseline characteristics

Whilst there is an extensive literature that describes the baseline characteristics in men and women hospitalised with first AMI, there are very few studies that have distinguished between first and recurrent AMI and no other studies that have specifically examined second AMI. Consequently there are no other studies with which to compare many of the findings reported from the current study. The findings from the description and analyses of first AMI in the current study were compared to the literature and it would therefore not be appropriate to repeat this process for second AMI. The findings from the current study relating to second AMI will therefore be discussed briefly and in context of the findings regarding first AMI and where appropriate any relevant literature.

9.2.1 Age and sex

Between 1990 and 2000, 9,664 individuals were hospitalised in Scotland with a second AMI. Women comprised 39.8% of the cohort and had a mean age of 74.2 years, which is just over two years older than at the time of their first AMI. Men were on average three years older at the time of admission with their second AMI than with their first AMI. This represents a substantial shift in age distribution, especially in men. Men and women hospitalised with a second AMI were on average older than individuals hospitalised with a first AMI. Nearly three quarters of individuals hospitalised with a second AMI were aged greater than 64 years. The age distribution of men and women presenting with a first and second AMI are therefore different. The majority of studies examining epidemiological aspects of AMI do not discern between first and subsequent AMI, although it would be useful to do so because of their differing characteristics which have considerable implications in terms of survival. The proportion of men and women in each cohort was similar for first and second AMI (41.4% women with first AMI versus 39.8% with second AMI). There are few studies with which to compare these data and no population based studies that have looked specifically at second AMI as oppose to recurrent AMI. The 60 Minutes Myocardial Infarction Project did describe the characteristics of patients with re-infarction compared to patients with a first infarction in 14,980 patients hospitalised in Germany between 1992 and 1994.[164] The mean age of patients admitted with re-infarction was 69 years which was four years older than individuals hospitalised with a first AMI. Women accounted for 28% of patients with a re-infarction and 33% of patients with a first infarction. Sex specific data were not reported.

9.2.2Socioeconomic characteristics

As for first AMI, there was a socio-economic gradient with a greater proportion of men and women who were hospitalised with a second AMI belonging to the most deprived categories compared to the least deprived categories. The socioeconomic gradient was stronger for second AMI than for first AMI, so that the association between hospitalisation with AMI and socioeconomic deprivation was slightly greater for second than for first AMI. Overall 42.2% of men and 44.5% of women hospitalised with a second AMI came from the two most deprived deprivation categories, compared to 41% of men and 43.2% of women with a first AMI. There is no literature with which to compare these findings. The implication is that men and women from deprived areas are more likely to be readmitted with a subsequent AMI. However it is not reasonable to draw this conclusion. Individuals hospitalised with a first and second AMI are two separate cohorts and also subsequent AMIs can only occur in survivors which introduces an immediate bias. The association between socioeconomic deprivation and recurrent AMI is interesting but is not something that can be examined in this study.

9.2.3Comorbid diagnoses

No previous studies have examined the distribution of comorbid diagnoses in individuals hospitalised with a second AMI. In the current study 65.5% of men and 71.3% of women hospitalised with a second AMI had one or more comorbid diagnoses. This is substantially higher than the proportions for first AMI which were 44.3% and 51.5% of men and women respectively. As for first AMI, heart failure was the most commonly recorded comorbidity. The prevalence of heart failure almost doubled from first to second AMI. Large relative increases were also seen with cancer, cerebrovascular disease, renal failure and coronary heart disease. Men and women hospitalised with a second AMI are on average two to three years older than individuals hospitalised with a first AMI and because there is a strong association between age and the prevalence of comorbid conditions, one would expect to see some increase in the prevalence of comorbid diagnoses. Overall there was a stronger association between age and prevalence of comorbid diagnoses with first AMI than with second AMI. The prevalence of one or more comorbid diagnoses more than doubled in men and increased by 70% in women hospitalised with a first AMI between the youngest and oldest age groups. In individuals hospitalised with a second AMI the prevalence of any comorbid diagnosis increased by 48% in men and by 19% in

women between the youngest and oldest age groups. In younger individuals hospitalised with a second AMI there was a striking excess of women compared to men who had comorbid diagnoses of diabetes, cerebrovascular disease and renal failure. This may reflect the fact that coronary heart disease is relatively infrequent in young women and that young women hospitalised with a second AMI are likely to have particularly adverse risk profiles and high levels of comorbid illness.

9.2.4 Median time since first AMI

The median interval between infarctions was greater in men than in women (2.3 and 1.8 years in men and women, respectively) but remained relatively consistent across different age groups. The median interval between infarctions in men increased from one year in 1990 to 3.7 years in 1997 and then decreased to 2.5 years in 2000 (P<0.001). The pattern was similar in women, rising from one year to 3.2 years in 1996 and then falling back to 1.7 years in 2000 (P<0.001). Second infarctions represented a decreasing proportion of all infarctions over the duration of the study. It is not clear why the median time since a previous AMI would decline over time and then increase in recent years. One possibility is that the improving short term survival seen following a first AMI has resulted in individuals surviving who might have previously died. Such individuals are likely to have severe disease and may then be at higher risk of subsequent events.

9.2.5 Summary

Patients with a second MI were older (3 years on average) and had more cardiovascular risk factors (e.g. diabetes and hypertension) than patients with a first AMI, presumably demonstrating the potential of these factors to increase the likelihood of a recurrent event. Patients with a second MI also had more cardiovascular co-morbidity, probably reflecting the consequences of greater cardiac injury. For example, these patients had more atrial fibrillation and a notable excess of heart failure. In addition, individuals with a second MI had more non-cardiovascular co-morbidity, presumably reflecting common aetiological factors (e.g. smoking in relation to COPD) and their older age.

10 Temporal trends in baseline characteristics of individuals admitted to hospital following a second AMI 1990-2000

Temporal trends in the distribution of prognostic factors may affect the prognosis of men and women following admission to hospital with a second AMI. It is therefore important to examine the distribution of these factors over time. Variation in the age and the presence of comorbid diagnoses may contribute to observed trends in survival and need to be taken into account when considering trends in survival.

10.1 Results

10.1.1 Age

As for first AMI, year of admission was categorised into three time periods, 1990-1992, 1993-1996 and 1997-2000. The age distribution of men and women admitted to hospital following a second AMI has undergone modest changes which are similar to those seen for first AMI. The proportion of younger individuals aged less than 75 years has declined in men and in women. In men the proportion of individuals aged less than 75 years fell from 72% in 1990-1992 to 65.3% in 1997-2000. A similar decline was seen in women in whom the proportion fell from 49.1% in 1990-1992 to 40.0% in 1997-2000. There has been a corresponding rise in the number of elderly men and women. In 1990-1992, 4.1% of men and 12% of women were aged over 84 years. By 1997-2000 these figures had risen to 8% and 21% respectively. These trends were all highly significant, $p<0.001$. The average age of men and women on admission has also increased. In men the median age increased from 68 to 70 years and in women from 75 to 77 years. These data are shown in Table 86. Figure 23 shows a scatterplot of mean age on admission in men against year of admission. A linear trend line has been fitted to the data. The sample correlation coefficient R^2 suggests that 70% of the variability in mean age can be explained by its relationship with year of admission and there is consequently a strong relationship between the two variables. As for first AMI, the strength of the relationship is greater in women in whom the R^2 is 83% (Figure 24).

Table 86 Temporal trends in age distribution of men and women

viii. Age group distribution

Number of cases (%)	MEN			WOMEN		
Year of admission	**1990-1992**	**1993-1996**	**1997-2000**	**1990-1992**	**1993-1996**	**1997-2000**
Age-group <55 years	275 (13.3%)	334 (24.0%)	181 (12.6%)	65 (4.6%)	65 (4.3%)	38 (4.1%)
55-64 years	533 (25.7%)	552 (24.0%)	313 (21.7%)	208 (14.7%)	193 (12.7%)	98 (10.7%)
65-74 years	685 (33.0%)	778 (33.8%)	447 (31.0%)	422 (29.8%)	447 (29.5%)	231 (25.2%)
75-84 years	495 (23.9%)	523 (22.7%)	384 (26.7%)	552 (39.0%)	589 (38.9%)	358 (39%)
>84 years	85 (4.1%)	115 (5.0%)	115 (8.0%)	170 (12.0%)	220 (14.5%)	193 (21.0%)
Total	2073	2302	1440	1417	1514	918

ix. Summary Statistics

	MEN			WOMEN		
Year of admission	**1990-1992**	**1993-1996**	**1997-2000**	**1990-1992**	**1993-1996**	**1997-2000**
Mean age (years)	67.3 (66.8-67.7)	67.4 (66.9-67.8)	68.8 (68.2-69.4)	73.3 (72.7-73.8)	74.2 (73.7-74.8)	75.6 (74.9-76.3)
Standard deviation	11.0	11.2	11.5	10.2	10.1	10.7
Median age (years)	68	68	70	75	75	77
Interquartile range	16	15	16	13	14	13

Figure 23 Mean age on admission to hospital following a second AMI in men 1990-2000

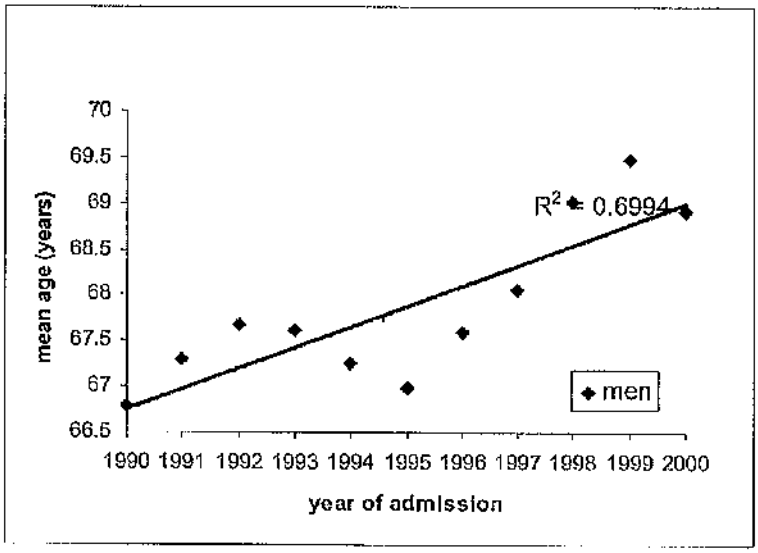
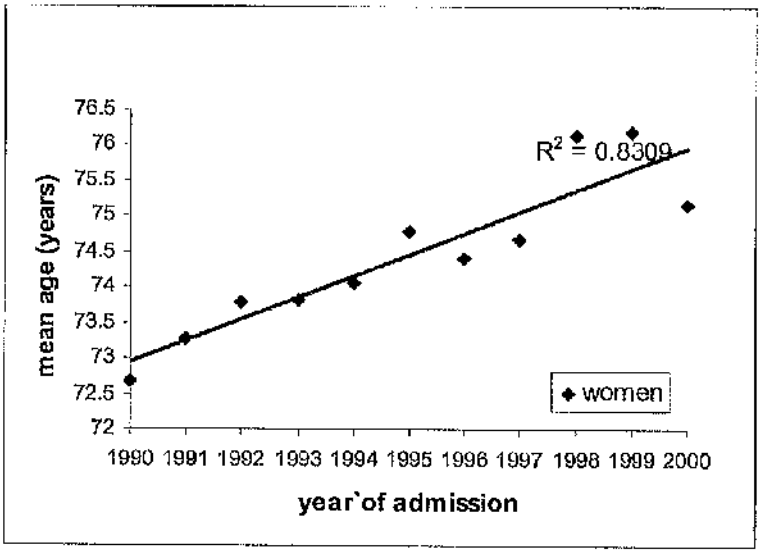


Figure 24 Mean age on admission to hospital following a second AMI in women 1990-2000



10.1.2 Comorbidity

As for first AMI, the proportion of men and women with comorbid conditions increased over the study period for most diagnoses and in most age groups (Figure 25). However, fewer of the trends reached statistical significance, especially in younger age groups (Table 88).

The proportion of men with a diagnosis of diabetes increased across all age groups between 1990-1992 and 1997-2000. 4% of men aged less than 55 years had a diagnosis of diabetes in 1990-1992. By 1997-2000 this had risen to 8.8%. Other age groups demonstrated changes of a similar magnitude. These trends were all significant. In women the proportion of individuals with a diagnosis of diabetes was greater than in men and increased in all but the very elderly. These trends did not however reach statistical significance.

The proportion of individuals with a diagnosis of cancer increased in men in all but the very elderly. These trends did not reach significance except in the under 55 year olds in whom the relative change was greatest. In this age group, 2.9% of men had a cancer diagnosis in 1990-1992 and this rose to 7.7% in 1997-2000. In women, the greatest changes occurred between 1993-1996 and 1997-2000. In 1993-1996, 8.3% of women aged 55-64 years had a diagnosis of cancer and this rose to 19.4% in 1997-2000. Trends over time however were not statistically significant.

As for first AMI, cerebrovascular disease and peripheral vascular disease exhibited less clear trends in prevalence over time in both men and women. There were no obvious patterns for cerebrovascular disease and changes were not significant except in men and women aged 75 to 84 years in whom the prevalence rose. In women the prevalence of cerebrovascular disease increased from 8.2% to 13.4% over the study period. None of the trends were significant for peripheral vascular disease.

The prevalence of heart failure increased substantially in men except in those aged less than 55 years. 23.1% of men aged 65-74 years had a diagnosis of heart failure in 1990-1992. By 1997-2000 this had risen to 34.9%. Similar increases were seen for first AMI. In women the trends were less clear. Only women aged 65-74 years experienced a significant increase in the prevalence of heart failure. In this age group the proportion with

a heart failure diagnosis increased from 26.8% to 42%. This contrasted with first AMI in which similar increases were seen in men and in women.

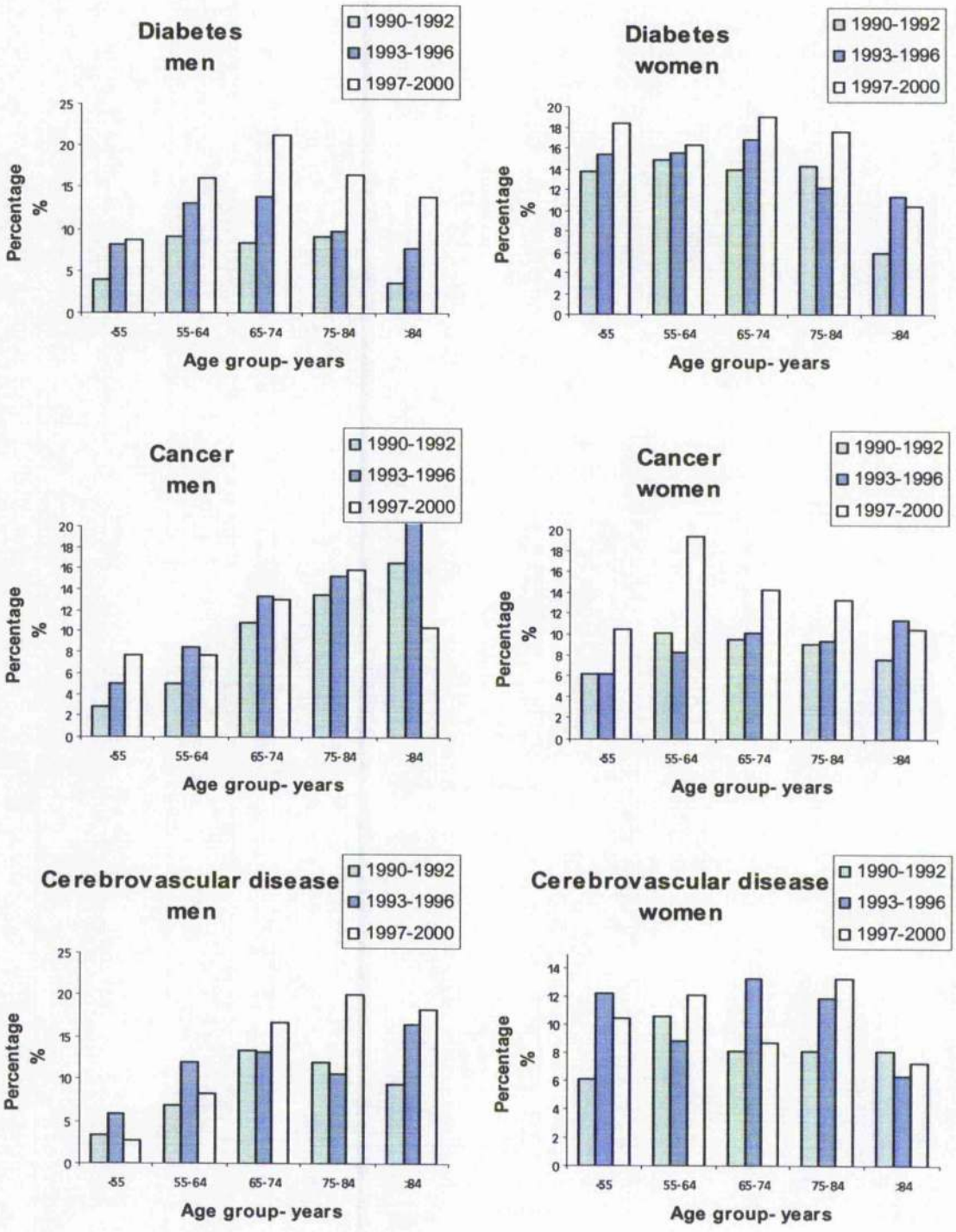
Coding for atrial fibrillation increased substantially over the study period. In 1990-1992 7.8% of women aged 65-74 years had a diagnosis of atrial fibrillation. By 1997-2000 this figure had risen to 18.6%. Increases were seen across all age groups although these were greater in the elderly and did not reach statistical significance in those aged less than 65 years. In men the relative changes were more consistent across age groups and the trends all reached significance. The proportion of men aged 65-74 years with a diagnosis of atrial fibrillation increased from 8.6% in 1990-1992 to 14.5% in 1997-2000. These changes were similar to those observed for first AMI.

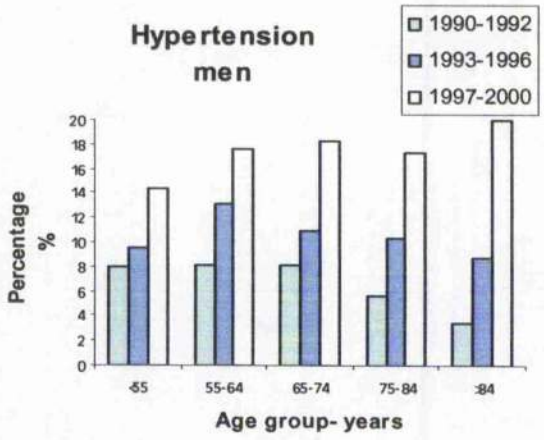
Hypertension also increased in prevalence over time. The changes occurred across all age groups except in women aged less than 55 years. Again this pattern was similar to that observed for first AMI. For example the proportion of women aged 75-84 years with a diagnosis of hypertension increased from 9.8% in 1990-1992 to 24.9 in 1997-2000. The equivalent figures in men were 5.7% and 17.4%.

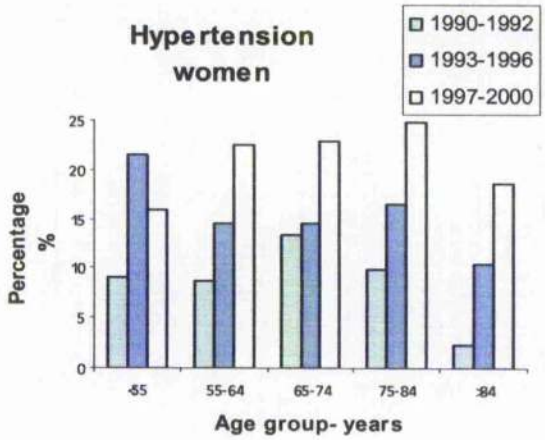
As for first AMI, trends in previous coronary heart disease excluding AMI were smaller in magnitude when compared to other diagnoses. Prevalence of previous coronary heart disease decreased in women aged less than 55 years, falling from 35.4% in 1990-1992 to 23.7% in 1997-2000. In older women prevalence demonstrated modest increases. For example in women aged 65-74 years the prevalence increased from 21.8% to 26.4%. None of these trends were significant in women. In men, older age groups experienced significant increases in the prevalence of previous coronary heart disease, especially in men aged greater than 84 years in whom the prevalence rise from 9.4% in 1990-1992 to 34.8% in 1997-2000.

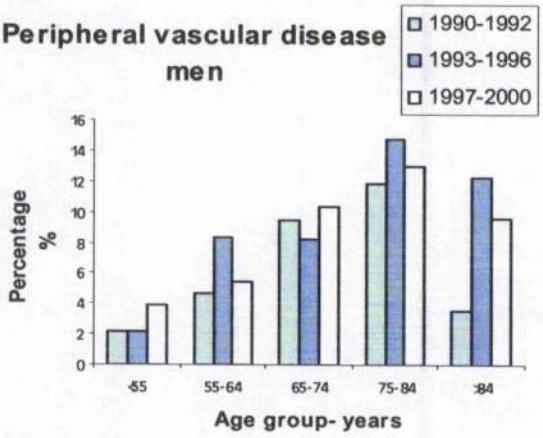
Overall the proportion of men and women with at least one comorbid diagnosis increased in men and women of all ages although these trends were not significant in women aged less than 65 years and in men aged less than 55 years. In 1990-1992, 55.3% of men aged greater than 84 years had one or more comorbid diagnoses. By 1997-2000, this figure had increased to 85.2%. The equivalent figures in women were 75.9% and 81.3%.

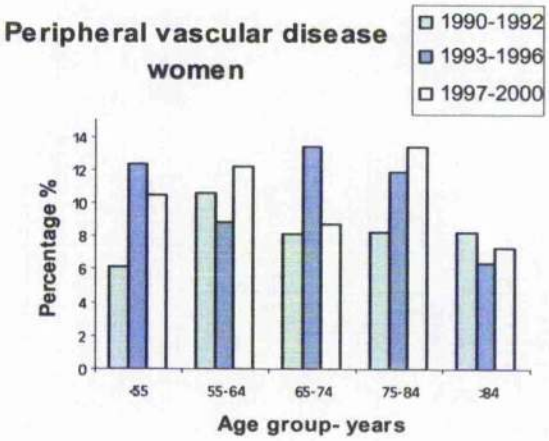
Figure 25 Distribution of comorbid diagnoses by age group and time period for men and women

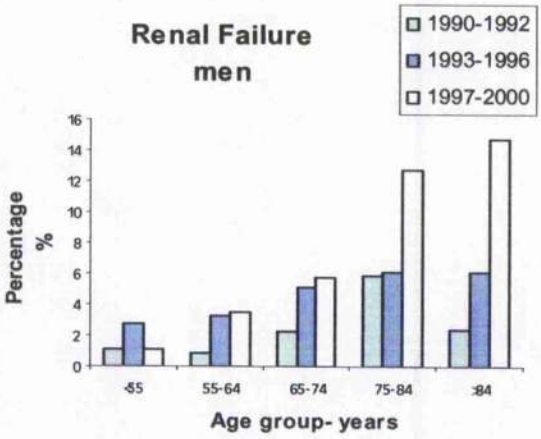



Hypertension
men
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Hypertension
women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Peripheral vascular disease
men
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Peripheral vascular disease
women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Renal Failure
men
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
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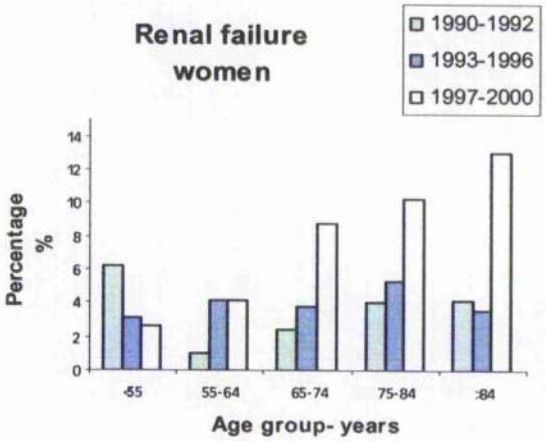
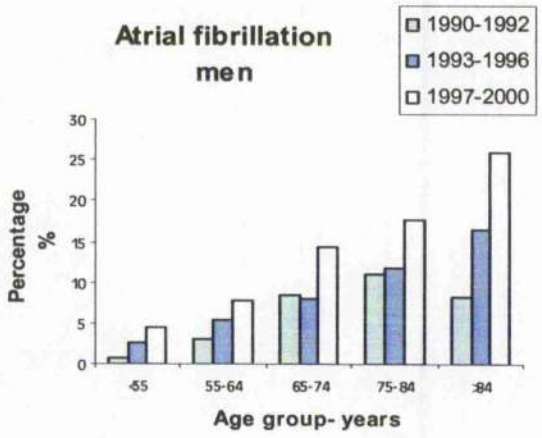
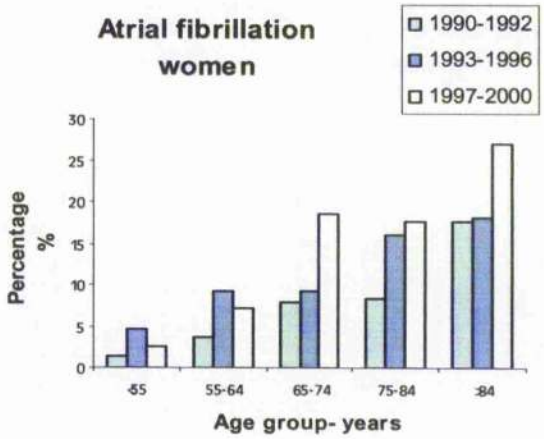
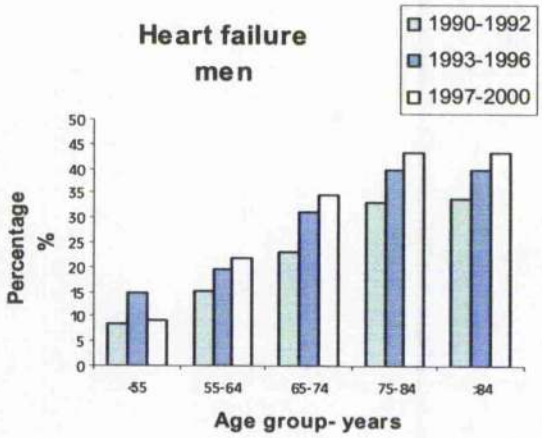
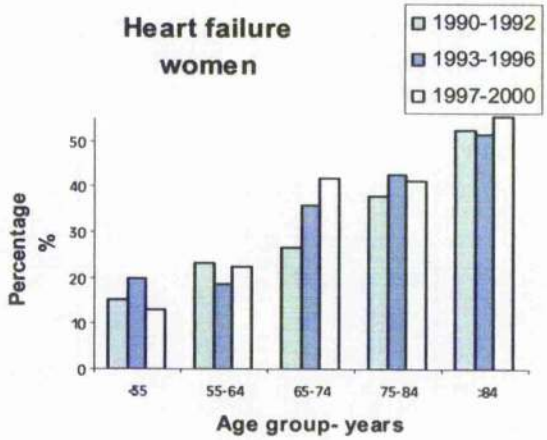

Renal failure
women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Atrial fibrillation
men
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Atrial fibrillation
women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Heart failure
men
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Heart failure
women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
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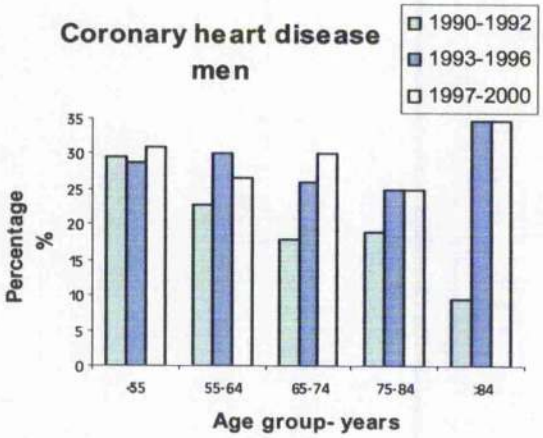
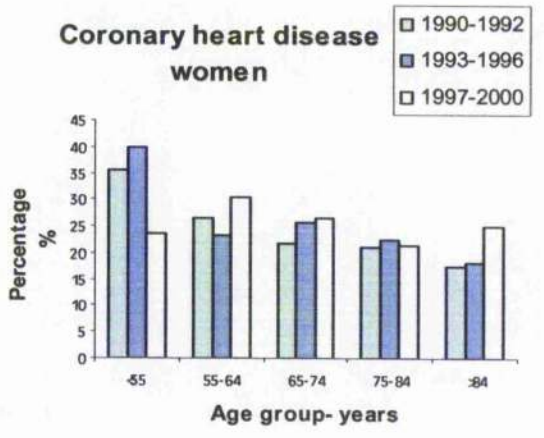
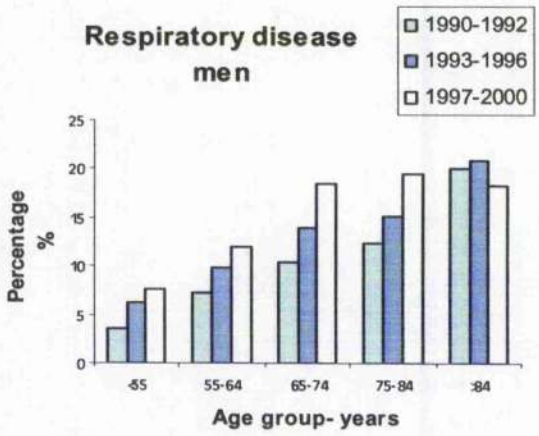
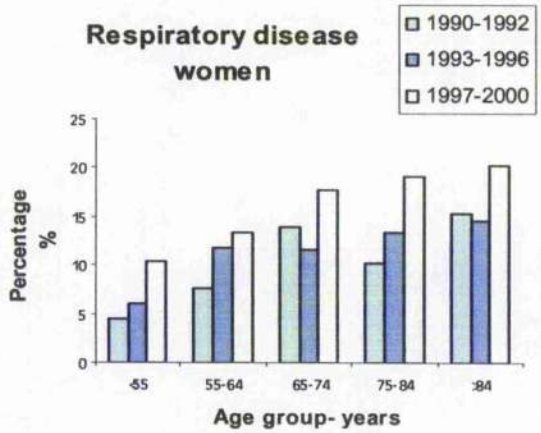

Coronary heart disease
men
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Coronary heart disease
women
1990-1992
1993-1996
1997-2000
Percentage %
Age group- years
-55
55-64
65-74
75-84
:84


Respiratory disease men
1990-1992
1993-1996
1997-2000
Percentage %
25
20
15
10
5
0
-55
55-64
65-74
75-84
:84
Age group- years


Respiratory disease women
1990-1992
1993-1996
1997-2000
Percentage %
25
20
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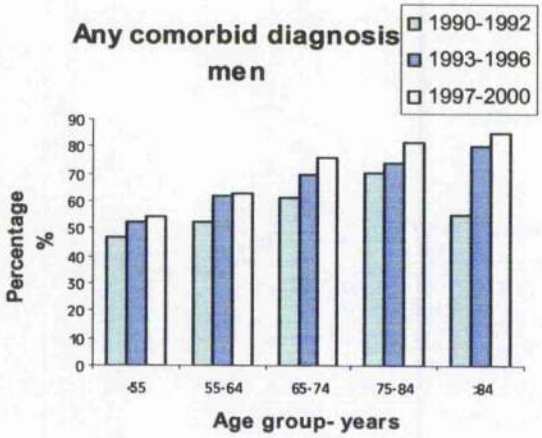
55-64
65-74
75-84
:84
Age group- years


Any comorbid diagnosis men
1990-1992
1993-1996
1997-2000
Percentage %
90
80
70
60
50
40
30
20
10
0
-55
55-64
65-74
75-84
:84
Age group- years

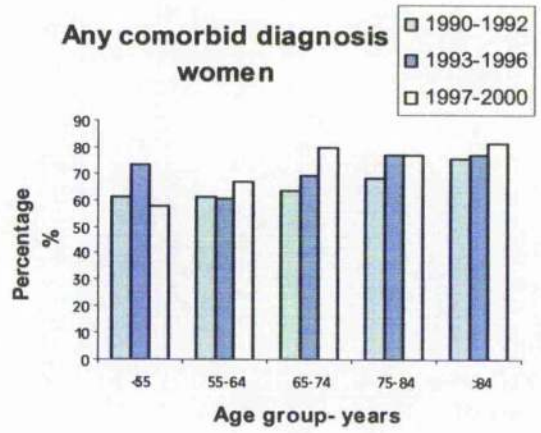

Any comorbid diagnosis women
1990-1992
1993-1996
1997-2000
Percentage %
90
80
70
60
50
40
30
20
10
0
-55
55-64
65-74
75-84
:84
Age group- years

Table 87 Chi square test for trend between year of admission and comorbid condition within age groups

	CHI SQUARE TEST FOR TREND, p value									
	Age <55 years		**55-64 years**		**65-74 years**		**75-84 years**		**>84 years**	
Comorbidity	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
Diabetes	P=0.032	P=0.545	P=0.003	P=0.745	P<0.001	P=0.083	P=0.001	P=0.266	P=0.010	P=0.160
Cancer	P=0.020	P=0.452	P=0.088	P=0.051	P=0.220	P=0.080	P=0.318	P=0.048	P=0.186	P=0.408
Respiratory disease	P=0.056	P=0.261	P=0.18	P=0.099	P<0.001	P=0.329	P=0.005	P<0.001	P=0.733	P=0.196
Cerebrovascular disease	P=0.992	P=0.379	P=0.253	P=0.807	P=0.132	P=0.445	P=0.001	P=0.009	P=0.095	P=0.737
Peripheral vascular disease	P=0.308	P=0.279	P=0.398	P=0.877	P=0.770	P=0.935	P=0.567	P=0.146	P=0.183	P=0.295
Atrial fibrillation	P=0.011	P=0.635	P=0.002	P=0.133	P=0.003	P<0.001	P=0.006	P<0.001	P=0.001	P=0.027
Hypertension	P=0.034	P=0.246	P<0.001	P<0.001	P<0.001	P=0.003	P<0.001	P<0.001	P<0.001	P<0.001
Renal failure	P=0.811	P=0.346	P=0.010	P=0.067	P=0.002	P=0.001	P<0.001	P<0.001	P=0.001	P=0.001
Heart failure	P=0.483	P=0.893	P=0.016	P=0.702	P<0.001	P<0.001	P=0.002	P=0.239	P=0.186	P=0.544
Coronary heart disease	P=0.777	P=0.323	P=0.123	P=0.602	P<0.001	P=0.146	P=0.032	P=0.803	P<0.001	P=0.081
Any comorbdity	P=0.093	P=0.946	P=0.001	P=0.368	P<0.001	P<0.001	P<0.001	P=0.001	P<0.001	P=0.203

10.2 Discussion regarding temporal trends in baseline characteristics of second AMI

10.2.1 Age and sex

Individuals hospitalised with a second AMI increased in age between 1990 and 2000. The median age on admission increased from 68 to 70 years in men and from 75 to 77 years in women. The increase in age was therefore similar in men and women and comparable to the change observed in individuals hospitalised with a first AMI. In 1997-2000, 85.2% of women and 65.7% of men hospitalised with a second AMI were aged 65 years and over. This is a relatively elderly cohort and highlights the importance of population based studies and the limitations of age restricted studies in the description and analysis of AMI epidemiology. There are no other studies with which to compare these data. The SPRINT Registry compared the baseline characteristics and prognosis of patients hospitalised with a recurrent AMI in 1981-3 and 1992-6.[237] The mean age of patients in this study did not change significantly over time, although sex specific results were not reported. The registry only includes individuals admitted to coronary care units who are younger and more likely to be men than in a population based study. The registry is therefore subject to selection bias making it difficult to generalise results. The proportion of women decreased slightly over the study period from 40.6% in 1990 to 38.9% in 2000. Again there are no other population based studies with which to compare these results. In the SPRINT Registry the proportion of women remained stable at 21-22%, which is substantially lower than seen in the current study.[237]

10.2.2 Comorbidity

As with first AMI the proportion of men and women diagnosed with comorbid conditions increased over the study period. Overall in 1990, 59.1% of men and 66.3% of women had one or more comorbid diagnosis. By 2000 this had increased to 72.5% and 76.9% in men and women respectively. Increases occurred in most age groups and for all diagnoses. The greatest relative increases occurred with atrial fibrillation, hypertension and renal failure in both men and women and diabetes in men. The prevalence of all these diagnoses more than doubled between 1990 and 2000. These diagnoses also demonstrated the largest relative increases in prevalence over time for first AMI. The only study to report changing baseline characteristics over time in individuals hospitalised with recurrent AMI is the

SPRINT Registry.[237] This study found that patients hospitalised in 1992-1996 had a higher prevalence of diabetes and hypertension but less frequently had prior angina than individuals hospitalised in 1981-1983. Overall the prevalence of diabetes increased from 21% in 1981-1983 to 30% in 1992-1996. The reported prevalences of diabetes and hypertension were substantially higher than those reported in the current study. As discussed previously it is likely that comorbid diagnoses are underrecorded in the Scottish Morbidity Record discharge forms used in the current study. In addition the SPRINT Registry only includes individuals admitted to coronary care units and is not representative of the general population.

10.2.3 Summary

In the current study, individuals hospitalised with a second AMI increased in age between 1990 and 2000. They also were increasingly likely to be diagnosed with other comorbid conditions. These changes affected men and women of all ages and were similar to the changes observed in individuals hospitalised with a first AMI between 1990 and 2000.

11 SECOND AMI: BURDEN OF DISEASE

11.1 Results

11.1.1 Population rates for admission to hospital following a second AMI 1990-2000

The aim of this section is to describe the burden that individuals hospitalised with a second AMI place on the National Health Service. It describes the incidence of second AMI in men and women and in different age groups, their length of stay and occupied bed days as well as the proportion of individuals that undergo revascularisation procedures during their index stay.

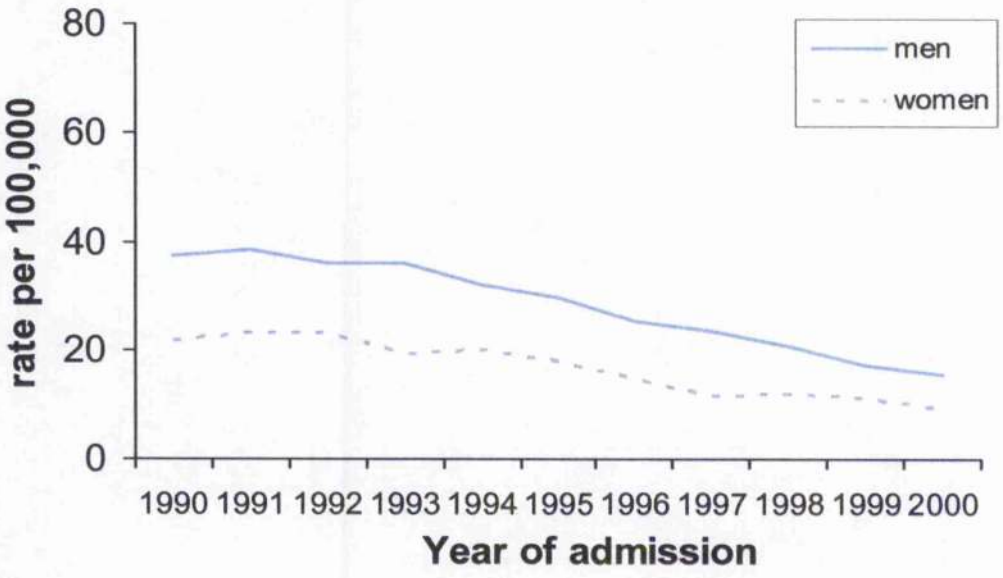
Sex

Between 1990 and 2000, the population discharge rate for second AMI fell by 58% in men, from 37 to 15 per 100,000, and by 58% in women, from 22 to 9 per 100,000 (Table 88 and Figure 26). These trends were highly significant in men and women, $p<0.001$. Population admission rates for first AMI declined by 28% in men and 30% in women and the declines observed for second AMI were therefore greater than the declines observed for first AMI.

Table 88 Annual number of cases and population rates per 100,000 for men and women admitted to hospital following a second AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	693	455	37	22
1991	714	480	38	23
1992	666	482	36	23
1993	671	406	36	19
1994	601	419	32	20
1995	555	377	30	18
1996	475	312	26	15
1997	441	239	24	11
1998	385	248	21	12
1999	325	239	17	11
2000	289	192	15	9
Crude % change	-58.30	-57.80	-58.58	-58.16
Average annual change (95% CI)	¯46 (¯ 39-¯52)	¯ 2.5 (¯2.1- ¯ 2.8)	¯31 (¯ 24-¯38)	¯ 1.5 (¯ 1.2-¯1.8)

Figure 26 Age and sex specific population rates for admission to hospital following a second AMI



Age and sex

Age and sex specific temporal trends in population rates are shown in Table 89,Table 90, Table 91, Table 92, Table 93, and Figure 27. The greatest absolute change in the number of individuals admitted to hospital following a second AMI occurred in those aged 55 to 64 years and 65-74 years, and was greater in men than in women. Between 1990 and 2000, the number of men aged 65-74 years with a discharge diagnosis of second AMI decreased by 127, a relative decline of 60%. In women the number of second AMI diagnoses in individuals aged 65-74 years, declined by 89, a relative decline of 67%. These trends were all highly significant.

Smaller absolute and relative changes were seen in men and women aged >84 years. In this age group, population rates for AMI hospitalisation declined by 39% in men and 46% in women. These trends were significant, although they represented a small reduction in second AMIs in absolute terms, a decline of only 3 cases in men and 7 cases in women. A similar pattern was observed in individuals aged <55 years. There was a decline of 61% in population rates for second AMI in men aged <55 years and a decline of 46% in women aged <55 years. These significant trends represented small changes in absolute terms.

The sex differences in population rates for second AMI hospitalisation decreased with increasing age so that the large discrepancy seen in younger people was no longer as apparent in men and women aged 75 and over. This was because the absolute decline in population rates was substantially higher in men although the relative changes were similar.

Table 89 Annual number of cases and population rates per 100,000 for men and women aged <55 years admitted to hospital following a second AMI

Aged < 55 years	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	110	22	8	2
1991	85	23	7	2
1992	80	20	6	2
1993	85	15	7	1
1994	99	19	8	1
1995	88	16	7	1
1996	62	15	5	1
1997	63	12	5	1
1998	41	7	3	1
1999	35	7	3	1
2000	42	12	3	1
Crude % change	-61.82	-45.45	-61.18	-45.90
Average annual change (95% CI)	¯6.7 (¯ 9-¯4)	¯1.5 (¯ 2- ¯ 1)	¯ 0.5 (¯0.7- ¯ 0.3)	¯0.1 (¯ 0.2- ¯0.1)

Table 90 Annual number of cases and population rates per 100,000 for men and women aged 55-64 years admitted to hospital following a second AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	174	78	68	27
1991	198	62	78	22
1992	161	68	63	24
1993	177	57	70	20
1994	126	57	49	20
1995	132	39	52	14
1996	117	40	46	14
1997	102	35	40	13
1998	84	23	33	8
1999	68	23	26	8
2000	59	17	22	6
Crude % change	-66.09	-78.21	-67.08	-78.09
Average annual change (95% CI)	¯14 (¯16-¯11)	¯6 (¯7-¯5)	¯5 (¯7-¯4)	¯2 (¯2.5-¯1.8)

Table 91 Annual number of cases and population rates per 100,000 for men and women aged 65-74 years admitted to hospital following a second AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	211	133	112	54
1991	234	153	122	61
1992	240	136	124	54
1993	211	126	107	50
1994	209	127	104	49
1995	190	110	96	44
1996	168	84	85	34
1997	133	55	67	22
1998	128	72	65	29
1999	102	60	51	24
2000	84	44	42	18
Crude % change	-60.19	-66.92	-62.19	-66.65
Average annual change (95% CI)	¯15 (¯ 19-¯11)	¯11 (¯ 14-¯3)	¯8 (¯ 10-¯6)	¯4 (¯ 5-¯3)

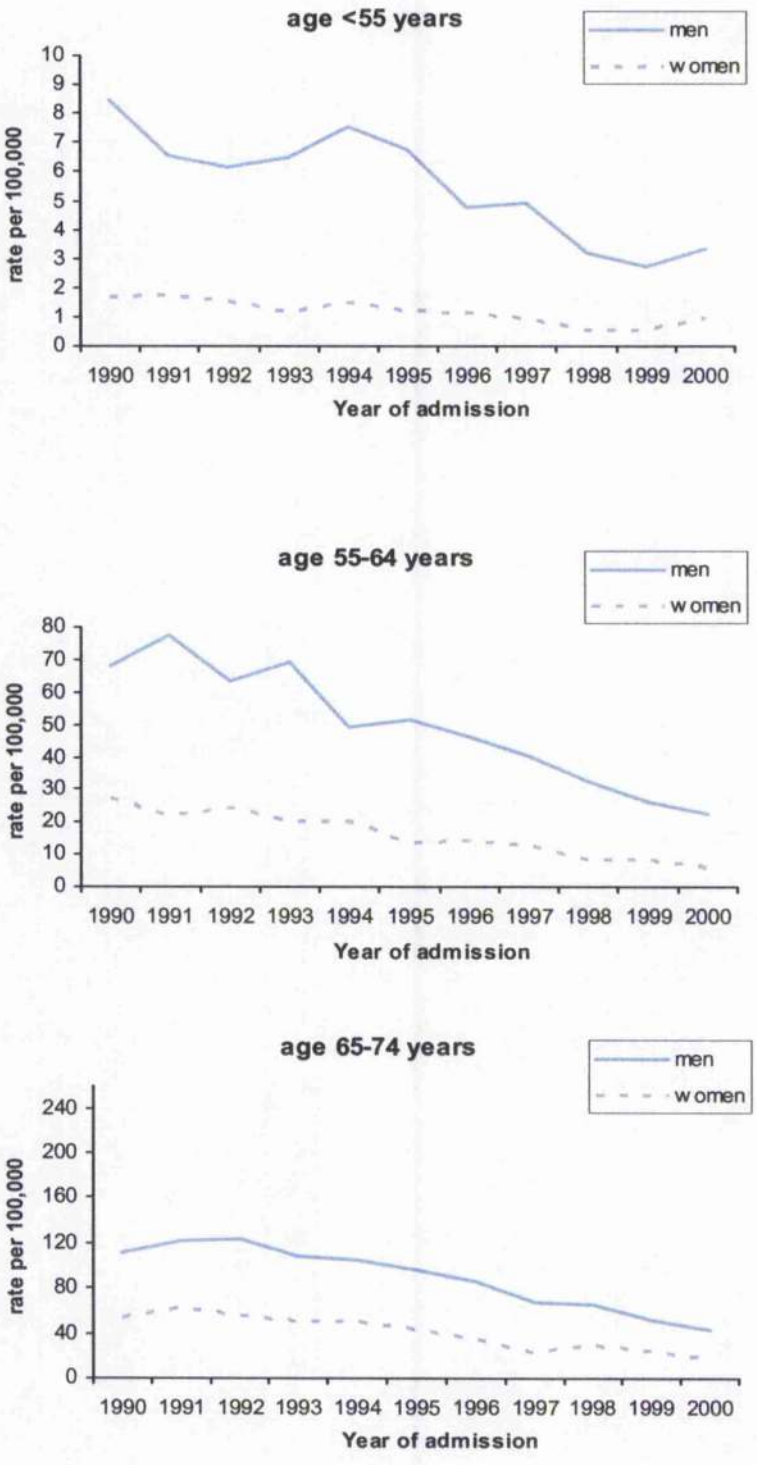
Table 92 Annual number of cases and population rates per 100,000 for men and women aged 75-84 years admitted to hospital following a second AMI

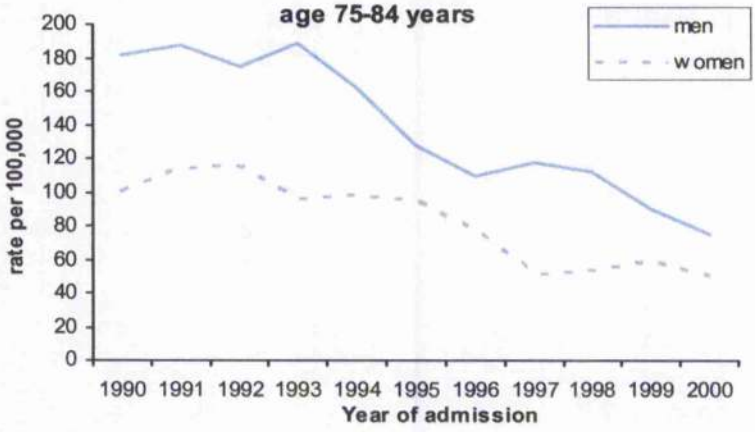
	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	166	170	182	101
1991	171	191	187	114
1992	158	191	175	116
1993	166	154	188	96
1994	140	155	162	99
1995	115	152	128	94
1996	102	128	110	78
1997	112	85	118	51
1998	108	90	112	54
1999	89	99	91	60
2000	75	84	75	50
Crude % change	-54.82	-50.59	-58.77	-49.84
Average annual change (95% CI))	¯10 (¯ 12-¯8)	¯121 (¯ 15-	¯12 (¯ 15-¯9)	¯7 (¯ 9-¯5)

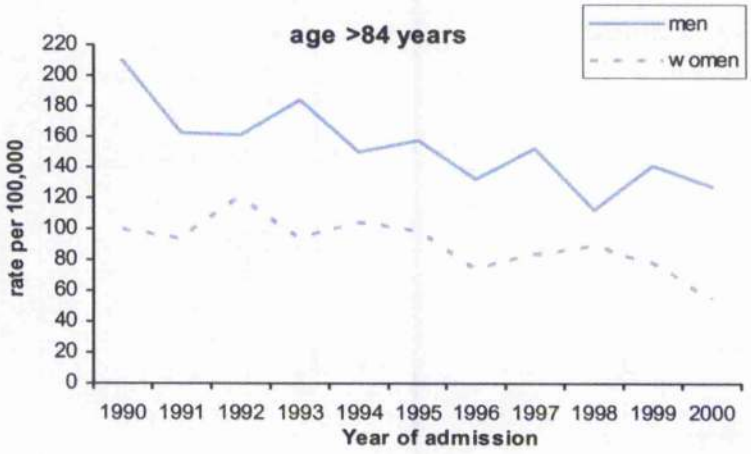
Table 93 Annual number of cases and population rates per 100,000 for men and women aged >84 years admitted to hospital following a second AMI

	Number of cases		Population rates (per 100,000)	
	Men	**Women**	**Men**	**Women**
1990	32	52	210	100
1991	26	51	163	94
1992	27	67	161	120
1993	32	54	184	94
1994	27	61	149	104
1995	30	60	158	99
1996	26	45	132	73
1997	31	52	152	83
1998	24	56	112	88
1999	31	50	141	78
2000	29	35	128	54
Crude % change	-9.38	-32.69	-39.10	-46.02
Average annual change (95% CI)	¯ 0.06 (¯0.7-0.6) NS	¯1.3 (¯ 3-0.4) NS	¯7 (¯ 10-¯3)	¯4 (¯ 7-¯1.4)

Figure 27 Age and sex specific population rates for admission to hospital following a second AMI




age 75-84 years
men
women
rate per 100,000
200
180
160
140
120
100
80
60
40
20
0
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000
Year of admission


age >84 years
men
women
rate per 100,000
220
200
180
160
140
120
100
80
60
40
20
0
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000
Year of admission

11.1.2 Length of stay and bed days occupied following admission to hospital with a second AMI 1990-2000

Length of stay in days in men and women

As for first AMI, length of stay declined steadily in men and women between 1990 and 2000 (Table 94). In 1990 the mean length of stay was 13.0 days in men and 14.1 days in women. This difference was highly significant. By 2000 the mean length of stay had declined to 8.8 days in men and 11.3 days in women. Again these changes were highly significant. These figures were very similar to those observed for first AMI. Median length of stay differed substantially from mean and was therefore a more appropriate summary measure. The median length of stay was 8 days in men and women in 1990 and declined to 6 days in men and 7 days in women by 2000. The interquartile range was greater in women than in men in each year suggesting that the distribution of length of stay was more widely spread.

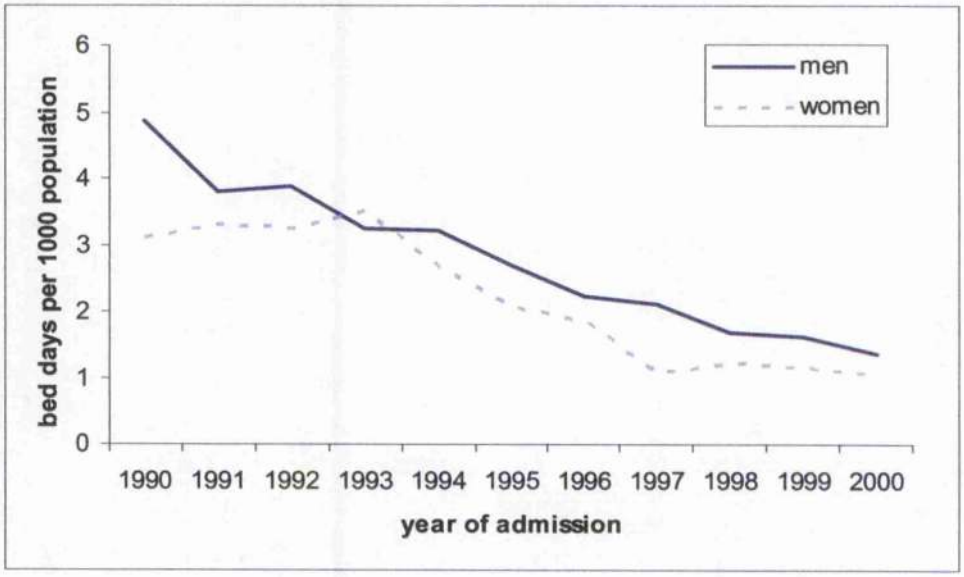
Table 94 Length of stay in men and women following a second AMI 1990-2000

	MEN			WOMEN		
year of admission	**Mean**	**Median**	**IQ range**	**Mean**	**Median**	**IQ range**
1990	13.0	8	5-8	14.1	8	6-13
1991	9.9	7	5-7	14.4	8	6-13
1992	10.8	7	5-7	13.9	8	5-12
1993	9.0	7	5-7	18.0	8	5.75-11
1994	10.0	7	5-7	13.2	8	5-14
1995	9.1	6	5-6	11.6	8	6-13
1996	8.8	7	5-7	12.3	7	5-13
1997	8.9	6	5-6	9.3	7	4-10
1998	8.1	6	4-6	10.3	7	4-11.75
1999	9.4	6	5-6	10.1	7	5-12
2000	8.8	6	4-6	11.3	7	4-14

Bed days in men and women

Figure 28 shows the bed days per 1000 population occupied by men and women following a second AMI between 1990 and 2000. As for first AMI, bed days declined substantially in men and in women. In men the number of bed days occupied per 1000 head of population fell from 4.9 in 1990 to 1.4 in 2000, a decline of 72%. The fall was slightly less in women in whom the bed days declined from 3.1 in 1990 and 1.0 in 2000, a fall of 67%. Since 1995, the occupied bed days per 1000 population has been greater in men than in women except for 1993 when occupied bed days in women exceeded that seen in men.

Figure 28 Bed days occupied by men and women following a second AMI 1990-2000



11.1.3 In-hospital revascularisation rates in men and women following a second AMI 1990-2000

Table 95 shows the number and proportion of men and women with a second AMI undergoing a revascularisation procedure during their inpatient stay.

Table 95 Numbers and rates of men and women with a second AMI undergoing revascularisation during their index hospital admission 1990-2000

	MEN			WOMEN		
	Revasc	**CABG**	**PTCA**	**Revasc**	**CABG**	**PTCA**
1990	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1991	3 (0.4%)	2 (0.3%)	1 (0.1%)	1 (0.2%)	1 (0.2%)	0 (0%)
1992	3 (0.5%)	0 (0%)	3 (0.5%)	1 (0.2%)	1 (0.2%)	0 (0%)
1993	2 (0.3%0	1 (0.1%)	1 (0.1%)	1 (0.2%)	1 (0.2%)	0 (0%)
1994	3 (0.5%)	1 (0.2%)	2 (0.3%)	1 (0.2%)	1 (0.2%)	0 (0%)
1995	3 (0.5%)	1 (0.2%)	2 (0.4%)	5 (1.3%)	2 (0.5%)	3 (0.8%)
1996	4 (0.8%)	2 (0.4%)	2 (0.4%)	4 (1.3%)	2 (0.6%)	2 (0.6%)
1997	7 (1.6%)	2 (0.5%)	5 (1.1%)	2 (0.8%)	0 (0%)	2 (0.8%)
1998	8 (2.1%)	1 (0.3%)	7 (1.8%)	5 (2.0%)	3 (1.2%)	3 (1.2%)
1999	10 (3.1%)	1 (0.3%)	9 (2.8%)	3 (1.3%)	0 (0%)	3 (1.3%)
2000	13 (4.5%)	0 (0%)	13 (4.5%)	7 (3.6%)	0 (0%)	7 (3.6%)
Total	56 (1.0%)	11 (0.2%)	45 (8%)	30 (0.8%)	11 (0.3%)	20 (3.6%)

Figure 29 Proportion of men and women undergoing a revascularisation procedure during admission following a second AMI 1990-2000

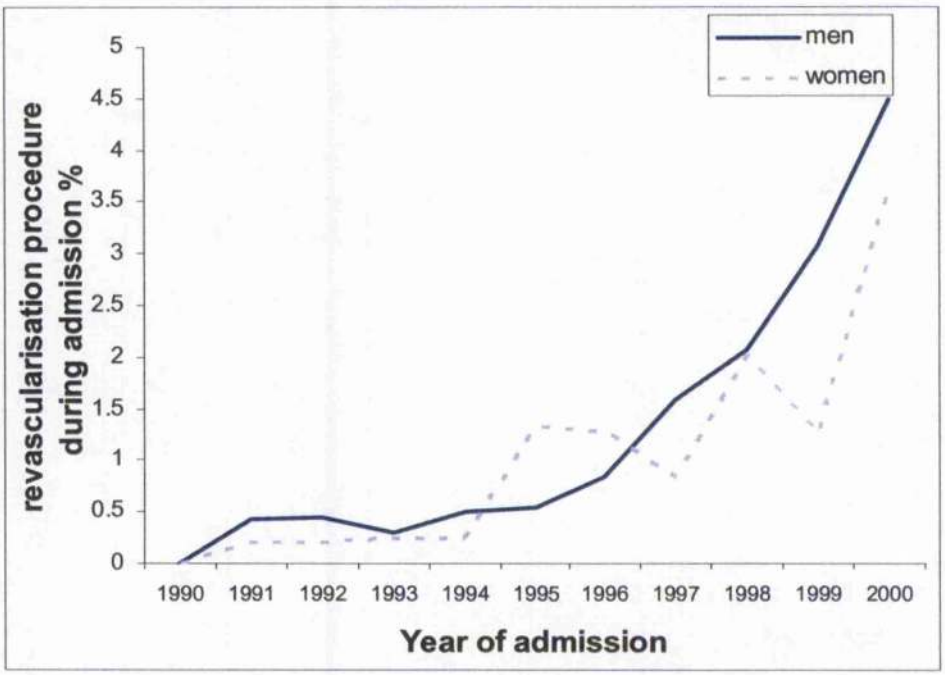


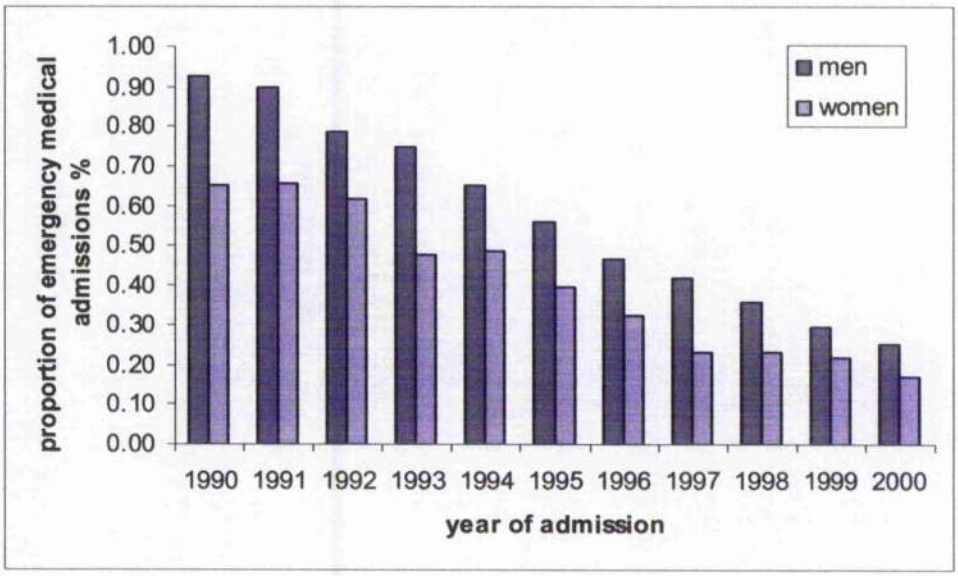
Table 96 Proportion of men and women in different age groups undergoing a revascularisation procedure during admission following a second AMI

Age group	men	women
< 55 years	18 (2.3%)	4 (2.4%)
55-64 years	20 (1.4%)	8 (1.6%)
56-74 years	14 (0.7%)	16 (1.5%)
75-84 years	3 (0.2%)	2 (0.1%)
>84 years	1 (0.3%)	0 (0%)
Total	56 (1.0%)	30 (0.8%)

11.1.4 Second AMI as a proportion of all emergency medical admissions

In 1990 hospitalisations for second AMI accounted for 0.9% of all emergency medical admissions in men and 0.7% of all emergency medical admissions in women. By 2000 these figures had fallen to 0.3% and 0.2% in men and women respectively. Second AMI accounted for a higher proportion of medical admissions in men than in women and this sex difference remained relatively stable between 1990 and 2000.

Figure 30 Barchart showing admissions for second AMI as a proportion of all emergency medical admissions in men and women 1990-2000



11.2 Discussion regarding burden of disease for second AMI

11.2.1 Population discharge rates for second AMI 1990-2000

In the current study population discharge rates for second AMI more than halved in men and women between 1990 and 2000. The relative reduction in second AMI hospitalisation rates were therefore greater than the changes observed for first AMI hospitalisation rates which declined by 28% in men and by 30% in women. Significant declines were observed in all age groups although the magnitude of these changes was slightly greater in younger compared to older individuals. The relative changes in hospitalisation rates within age groups were similar in men and women. Although there are no studies that have examined temporal trends in population rates for second AMI, a number of studies have examined temporal trends in population rates for recurrent AMI. The literature surrounding temporal trends in incidence of recurrent AMI is not consistent in its findings. The ARIC Study showed reductions in recurrent event rates in men and women although these trends only reached significance in men.[57] The Toulouse-Monica Study and NHANES Study reported declines only in men and in NHANES incidence rates of recurrent AMI increased in women.[58;60] The disagreement is therefore mainly centred around women. In the current study both men and women have experienced similar declines in the incidence of recurrent events. Recurrence rates should fall as a result of effective secondary prevention. It has been suggested that the less marked reductions in recurrent rates in women observed in some studies may be due to either a lower level of secondary prevention in this group or more severe coronary disease in women than in men.[58;83;173;238] In addition none of these studies included individuals over the age of 74 years. Given that in the current study over 70% of women hospitalised with a second AMI were aged 75 years and over, these studies are likely to have excluded the majority of their target population making it difficult to generalise results to the general population. The larger decline in numbers of second, compared to first, infarctions may reflect a greater benefit from population-based secondary, compared to primary, prevention measures.

11.2.2 Length of stay and bed days in men and women

Median length of stay declined significantly in men and women between 1990 and 2000. Median length of stay was 8 days in men and women in 1990 and declined to 6 days in

men and 7 days in women in 2000. The declines were very similar to those observed for first AMI. Median length of stay for second AMI was also similar to the length of stay observed for first AMI. This is perhaps surprising given that individuals hospitalised with a second AMI are on average older and more likely to have other comorbid conditions than individuals hospitalised with a first AMI. It may in part reflect a bias arising as a result of the increased in-hospital case fatality that occurs in individuals hospitalised with a second AMI. This could offset an increased length of stay occurring in a smaller proportion of individuals resulting in a similar overall length of stay.

11.2.3 In-hospital revascularisation rates in men and women 1990-2000

In contrast to the declining incidence of second AMI there was a dramatic increase in the number of men and women undergoing a revascularisation procedure between 1990 and 2000. In 1990 less than 1% of men or women underwent revascularisation whilst in 2000 this figure had increased to 4.5% in men and 3.7% in women. Most of this increase was accounted for by a rising rate of percutaneous angioplasty procedures. As with first AMI there was a strong age effect and revascularisation was more likely to be carried out in younger men and women than in older men and women. As discussed for first AMI these intervention rates are much lower than those reported by other studies. These findings are not felt to be representative of clinical practice and are thought to reflect deficiencies in the coding or the extraction of the data

11.2.4 Proportion of all emergency medical admissions

In 1990 hospitalisations for second AMI accounted for less than 1% of all emergency medical admissions. This figure was much lower than for first AMI which accounted for 9% of all emergency medical admissions in men and 7% of all emergency medical admissions in women. By 2000 these figures had fallen in line with first AMI and accounted for only 0.3% of male emergency medical admissions and 0.2% of female emergency medical admissions. There are no other studies with which to compare these data.

11.2.5 Summary

The incidence of first MI has fallen substantially in recent years in Scotland, as in most other industrialised countries and the current study confirms this ubiquitous trend. In addition, however, we have now shown that there has been an even more striking reduction in admissions for second infarctions, falling by nearly 60% in both men and women. Length of stay has also declined and hence the burden of second AMI on the health service has fallen between 1990 and 2000. Revascularisation rates have however increased so that a smaller number of individuals are exerting a greater pressure on the health service.

12 SURVIVAL FOLLOWING ADMISSION TO HOSPITAL WITH A SECOND AMI

12.1 Results of unadjusted survival analyses

This section describes the unadjusted case fatality of men and women hospitalised in Scotland with a second AMI. As for first AMI case fatality has been examined at 30 days, six months, one year, two years and five years in men and women. Analyses have also been stratified according to age, socioeconomic deprivation, year of admission and the presence of comorbid diagnoses. The aim is to provide detailed mortality data and to gain insight into the survival of men and women and the factors that affect survival before carrying out more sophisticated multivariate analyses.

12.1.1 Unadjusted case fatality from life tables

As for first AMI, the overall unadjusted case fatality rates were higher in women than in men at all of the time periods examined. In men the overall case fatality rates at 30 days, six months, one year, two years and five years were 22.4%, 30.2%, 35.1%, 41.4% and 55.9% respectively. In women the equivalent rates were 27.7%, 37.6%, 43.2%, 51.1% and 66.7%. These sex differences were all statistically significant. As for first AMI, prognosis following a second AMI was worse in women than in men. Case fatality was also substantially higher than for first AMI, and this excess was most apparent in men and in the elderly. For example in men, case fatality following a first AMI was 16.3% in those aged <55 years and 39.0% in those aged >84 years. Case fatality rose to 22.4% and 55.9% respectively in men following their second AMI.

Table 97 Unadjusted case fatality rates in men and women following admission to hospital with a second AMI

	CASE FATALITY % (95%CI)	
	MEN	**WOMEN**
30 days	22.4	27.7
Six months	30.2	37.6
One year	35.1	43.2
Two years	41.4	51.1
Five years	55.9	66.7

12.1.1.1 Age

30 day and six months case fatality

The effect of age on case fatality was powerful in men and in women. 30 day case fatality was 6.6% in men and 9.5% in women aged less than 55 years. It increased to 40.0% in men and 38.9% in women aged greater than 84 years (Table 98Table 97). By six months case fatality had risen to 10.0% in men and 12.5% in women aged <55 years (Table 99). There was an interaction between age and sex so that case fatality was greater in young women than in young men but less in older women than in older men at 30 days and six months. The effect of age on case fatality was slightly less marked than for first AMI, especially in the very elderly. In all but the very elderly, case fatality following a second AMI was significantly greater than case fatality following a first AMI, although this excess was more marked in younger age groups. For example, 30 day case fatality in men aged <55 years was 3.7% following a first AMI and 6.6% following a second AMI. In men aged >84 years however, the figures were 42.6% and 40.0% respectively.

One, two and five years case fatality

By one year case fatality following a second AMI had increased to 35.1% in men and 43.2% in women. Case fatality was therefore higher than the figures seen following a first AMI; 23.9% in men and 39.3% in women. The age sex interaction remained as age appeared to have a lesser effect in women than in men (Table 100Table 100). At five years case fatality remained higher in women than in men in younger age groups, but was fairly equivocal in the older age groups. At five years, case fatality following a second AMI remained higher than case fatality following a first AMI. Again, the discrepancy was greater in younger age groups. In men aged < 55 years, case fatality was 26.6% following a second AMI and 11.5% following a first AMI, but in men aged >84 year the figures were 87.8% and 85.8% respectively.

12.1.1.2 Socioeconomic deprivation

30 day and six months case fatality

Socio-economic deprivation appeared to have a minimal effect on short-term case fatality. As for first AMI, there was a reverse socioeconomic gradient, more so in men, so that fatality was higher in the least deprived groups and lower in the most deprived categories. For example, 30 day case fatality was 24.8% in the least deprived category compared to

21.2% in the most deprived category. This gradient was not as apparent in women. The effect was not consistent however, and by six months this trend was less apparent. This was in contrast to first AMI where the reverse socioeconomic effect was greater in women than in men. Case fatality was higher in all categories in women than in men at 30 days and at six months.

One, two and five years case fatality

Socio-economic deprivation had a similar effect in the longer term. Again, there was a reverse socioeconomic gradient that was stronger in men than in women, in whom the effect of socioeconomic deprivation was less consistent. For example, five year case fatality in men decreased from 57.8% in the least deprived group to 55.1% in the most deprived group. In women, case fatality was higher in the least deprived category but similar in the remaining deprivation categories and there was no evidence of any significant differences or of trends.

12.1.1.3 Comorbidity

30 day and six months case fatality

As for first AMI, the effect of prior and concurrent diagnoses had a marked effect on case fatality at 30 days and six months. The presence of one or more diagnoses increased six month case fatality from 19.9% to 35.6% in men and from 29.4% to 41.0% in women. The greatest effects were seen with renal failure, respiratory disease, cerebrovascular disease, peripheral vascular disease and heart failure. For example, six month case fatality was 58.1% in men and 59.4% in women with a coding for renal failure, compared to an overall rate of 30.2% in men and 37.6% in women. Heart failure was associated with a six month case fatality rate of 45.5% in men and 48.8% in women. There was no consistent sex effect as it varied according to diagnosis. The magnitude of effect of different comorbid diagnoses was similar for first and second AMI. Cancer however, had less of an effect on case fatality following a second AMI than it did following a first AMI. At 30 days following a second AMI, case fatality was 21.5% in men and 29.7% in women with a coding for cancer. Following a first AMI, the figures were 34.2% and 36.0% respectively. Again, hypertension had a small effect on case fatality which increased to 28.1% in men and 36.6% in women at six months. As for first AMI, none of the comorbidies coded appeared to have a protective effect and to reduce case fatality.

One, two and five years case fatality

Similar patterns to those seen at 30 days and six months were seen at one, two and five years. Respiratory disease, renal failure, heart failure and cerebrovascular and peripheral vascular disease again carried the worst prognosis. 89.5% of men and women with renal failure and 78.1% of men and 82.6% of women with heart failure were dead within five years. The presence of any comorbid diagnosis significantly increased case fatality at five years. In men, five year case fatality was 65.3% with any comorbidity compared to 38.6% with none. The effect was not quite as marked in women; 73.2% compared to 51.0%. As for shorter term case fatality, cancer had a lesser effect following a second AMI than it did following a first AMI, especially in men. Again, hypertension and coronary heart disease appeared to have the least effect on case fatality, especially in men. For example, men with a previous admission for coronary heart disease had a five year case fatality of 58.1% compared to 66.6% in women.

12.1.1.4 Trends in unadjusted case fatality in men and women

30 day and six months case fatality

Between 1990 and 2000, in men, case fatality following a second AMI fell from 24.0% to 23.2%, a marginal decline of only 3.2%. In women, case fatality declined by 2.6%, falling from 28.4% in 1990 to 27.6% in 2000 (Table 103). Larger declines were seen at six months, when case fatality declined by 7.2% in men and by 7.6% in women. These changes contrasted with those seen for first AMI. 30 day case fatality following a first AMI declined by 19% in men and by 8% in women between 1990 and 2000.

One, two and five years case fatality

At one year case fatality in men declined from 39.5% in 1990 to 35.3% in 2000, a decline of 10.7% (Table 104). In women one year case fatality fell by 7.1%, from 43.7% to 40.6%. These falls were comparable to those seen following a first AMI. At two years however, case fatality fell by 15.9% in men but remained stable in women. Five years case fatality fell by 8.6% in men, from 59.2% to 54.1% and by 10.6% in women, from 69.5% to 65.4% (Table 105). The trends in longer term case fatality following a second AMI were therefore similar to those seen following a first AMI.

Table 98 Unadjusted 30 day case fatality rates in men and women following admission to hospital with a second AMI

	30 DAY CASE FATALITY (95%CI)	
	MEN	WOMEN
Overall	22.4	27.7
Age group		
<55	6.6 (6.6-6.6)	9.5 (9.5-9.6)
55-64	13.0 (12.9-13.0)	16.8 (16.8-16.9)
65-74	23.6 (23.5-23.6)	23.6 (23.5-23.6)
75-84	35.3 (35.3-35.3)	31.9 (31.9-31.9)
>84	40.0 (39.9-40.1)	38.9 (38.9-39.0)
Deprivation quintile		
1-least deprived	24.8 (24.7-24.8)	29.2 (29.2-29.3)
2	23.6 (23.5-23.6)	27.4 (27.3-27.4)
3	23.4 (23.3-23.4)	27.5 (27.5-27.6)
4	19.8 (19.7-19.8)	27.4 (27.4-27.4)
5-most deprived	21.2 (21.1-21.2)	27.1 (27.1-27.1)
Comorbidity		
Any comorbidity	26.0 (26.0-26.0)	26.0 (26.0-26.0)
No comorbidity	15.6 (15.6-15.7)	22.9 (22.9-22.9)
Diabetes	28.7 (28.7-28.8)	28.1 (28.0-28.1)
Cancer	21.5 (21.5-21.5)	29.7 (29.7-29.8)
Respiratory disease	28.8 (28.8-28.9)	31.4 (31.4-31.4)
Cerebrovascular disease	32.1 (32.1-32.1)	34.5 (34.4-34.5)
Peripheral vascular disease	31.6 (31.5-31.6)	30.7 (30.7-30.8)
Atrial fibrillation	29.1 (29.0-29.1)	27.7 (27.7-27.7)
Hypertension	19.9 (19.8-19.9)	26.0 (25.9-26.0)
Renal failure	42.3 (42.2-42.3)	43.7 (43.6-43.7)
Heart failure	32.5 (32.4-32.5)	35.0 (35.0-35.1)
Coronary heart disease	21.1 (21.1-21.1)	27.3 (27.2-27.3)

Table 99 Unadjusted six month case fatality rates in men and women following admission to hospital with a second AMI

	SIX MONTH CASE FATALITY (95%CI)	
	MEN	**WOMEN**
Overall	30.2	37.6
Age group		
<55	10.0 (10.0-10.0)	12.5 (12.5-12.5)
55-64	17.8 (17.8-17.8)	21.8 (21.8-21.9)
65-74	31.5 (31.5-31.5)	31.7 (31.7-31.8)
75-84	46.7 (46.7-46.7)	44.4 (44.4-44.5)
>84	54.0 (53.9-54.0)	52.1 (52.1-52.2)
Deprivation quintile		
1-least deprived	33.3 (33.3-33.4)	39.8 (39.8-39.9)
2	29.8 (29.8-29.9)	37.6 (37.6-37.6)
3	30.7(30.7-30.7)	35.6 (35.6-35.7)
4	28.7 (28.7-28.7)	38.1 (38.1-38.1)
5-most deprived	28.8 (28.8-28.8)	37.6 (37.5-37.6)
Comorbidity		
Any comorbidity	35.6 (35.6-35.6)	41.0 (41.0-41.0)
No comorbidity	19.9 (19.9-19.9)	29.4 (29.3-29.4)
Diabetes	37.7 (37.6-37.7)	41.7 (41.7-41.8)
Cancer	41.8 (41.7-41.8)	43.3 (43.3-43.4)
Respiratory disease	41.4 (41.3-41.4)	43.6 (43.6-43.6)
Cerebrovascular disease	44.3 (44.2-44.3)	46.6 (46.6-46.7)
Peripheral vascular disease	42.5 (42.4-42.5)	44.2 (44.1-44.2)
Atrial fibrillation	42.6 (42.6-42.7)	44.4 (44.3-44.4)
Hypertension	28.1 (28.0-28.1)	36.6 (36.6-36.6)
Renal failure	58.1 (58.1-58.2)	59.4 (59.3-59.5)
Heart failure	45.5 (45.4-45.5)	48.8 (48.7-48.8)
Coronary heart disease	30.0 (29.9-30.0)	36.7 (36.7-36.7)

Table 100 Unadjusted one year case fatality rates in men and women following admission to hospital with a second AMI

	ONE YEAR CASE FATALITY (95%CI)	
	MEN	**WOMEN**
Overall	35.1	43.2
Age group		
<55	12.3 (12.3-12.3)	15.5 (15.4-15.5)
55-64	21.0 (21.0-21.1)	25.5 (25.4-25.5)
65-74	36.7 (36.6-36.7)	37.0 (37.0-37.0)
75-84	53.1 (53.0-53.1)	50.5 (50.5-50.5)
>84	64.8 (64.7-64.8)	59.4 (59.3-59.4)
Deprivation quintile		
1-least deprived	37.4 (37.4-37.5)	46.1 (46.0-46.1)
2	35.4 (35.4-35.4)	43.3 (43.3-43.3)
3	36.3 (36.3-36.3)	40.8 (40.8-40.8)
4	33.3 (33.3-33.3)	44.0 (44.0-44.1)
5-most deprived	33.3 (33.3-33.3)	42.4 (42.4-42.4)
Comorbidity		
Any comorbidity	41.6 (41.6-41.6)	47.1 (47.1-47.2)
No comorbidity	22.7 (22.6-22.7)	33.4 (33.4-33.4)
Diabetes	44.8 (44.8-44.8)	49.7 (49.7-49.8)
Cancer	33.4 (33.3-33.4)	50.9 (50.8-50.9)
Respiratory disease	49.0 (49.0-49.1)	52.3 (52.3-52.4)
Cerebrovascular disease	52.5 (52.4-52.5)	52.1 (52.0-52.1)
Peripheral vascular disease	51.1 (51.1-51.2)	49.8 (49.2-50.4)
Atrial fibrillation	51.4 (51.3-51.4)	51.0 (50.6-51.5)
Hypertension	33.8 (33.8-33.9)	45.0 (44.9-45.0)
Renal failure	66.0 (66.0-66.1)	67.5 (67.4-67.6)
Heart failure	52.9 (52.8-52.9)	55.2 (55.0-55.5)
Coronary heart disease	34.5 (34.5-34.5)	42.8 (42.8-42.9)

Table 101 Unadjusted two years case fatality rates in men and women following admission to hospital with a second AMI

	TWO YEAR CASE FATALITY (95%CI)	
	MEN	**WOMEN**
Overall	41.4	51.1
Age group		
<55	15.8 (15.8-15.8)	19.3 (19.2-19.3)
55-64	26.9 (26.9-26.9)	31.1 (31.1-31.2)
65-74	42.9 (42.9-42.9)	43.6 (43.6-43.6)
75-84	46.7 (46.7-46.7)	59.2 (59.2-59.2)
>84	54.0 (53.9-54.0)	70.6 (70.5-70.6)
Deprivation quintile		
1-least deprived	43.3 (43.2-43.3)	53.4 (53.4-53.4)
2	41.5 (41.5-41.5)	52.3 (52.3-52.4)
3	42.8 (42.8-42.8)	48.9 (48.9-49.0)
4	40.2 (40.1-40.2)	50.8 (50.7-50.8)
5-most deprived	39.3 (39.3-39.4)	50.8 (50.8-50.9)
Comorbidity		
Any comorbidity	49.0 (49.0-49.0)	53.4 (53.4-53.4)
No comorbidity	27.0 (27.0-27.0)	38.3 (38.3-38.3)
Diabetes	52.5 (52.4-52.5)	65.4 (65.3-65.4)
Cancer	56.4 (56.3-56.4)	50.8 (50.8-50.9)
Respiratory disease	56.0 (55.9-56.0)	56.3 (56.2-56.3)
Cerebrovascular disease	59.6 (59.5-59.6)	38.3 (38.3-38.3)
Peripheral vascular disease	59.1 (59.1-59.2)	60.0 (59.9-60.1)
Atrial fibrillation	59.3 (59.3-59.4)	68.4 (68.3-68.4)
Hypertension	41.6 (41.6-41.7)	63.80 (63.7-63.8)
Renal failure	73.9 (73.8-73.9)	59.2 (59.1-59.2)
Heart failure	61.2 (61.2-61.2)	59.9 (59.8-59.9)
Coronary heart disease	42.3 (42.3-42.3)	61.9 (61.9-62.0)

Table 102 Unadjusted five years case fatality rates in men and women following admission to hospital with a second AMI

	FIVE YEAR CASE FATALITY (95%CI)	
	MEN	**WOMEN**
Overall	55.9	66.7
Age group		
<55	26.6 (26.6-26.6)	31.1 (31.0-31.1)
55-64	38.9 (38.9-38.9)	43.4 (43.3-43.4)
65-74	58.7 (58.7-58.7)	58.1 (58.1-58.2)
75-84	79.2 (79.2-79.3)	77.0 (76.9-77.0)
>84	87.8 (87.8-87.9)	88.2 (88.1-88.2)
Deprivation quintile		
1-least deprived	57.8 (57.8-57.9)	71.1 (71.0-71.1)
2	56.6 (56.6-56.7)	66.7 (66.6-66.7)
3	55.8 (55.7-55.8)	64.5 (64.4-64.5)
4	55.1 (55.0-55.1)	65.8 (65.7-65.8)
5-most deprived	55.1 (55.0-55.1)	67.0 (66.9-67.0)
Comorbidity		
Any comorbidity	65.3 (65.3-65.3)	73.2 (73.2-73.3)
No comorbidity	38.6 (38.6-38.6)	51.0 (51.0-51.0)
Diabetes	69.6 (69.6-69.7)	77.4 (77.4-77.5)
Cancer	53.7 (53.7-53.7)	81.7 (81.6-81.7)
Respiratory disease	73.4 (73.3-73.4)	80.3 (80.3-80.4)
Cerebrovascular disease	76.8 (76.8-76.8)	78.0 (78.0-78.1)
Peripheral vascular disease	74.9 (74.9-74.9)	78.1 (77.6-78.6)
Atrial fibrillation	75.6 (75.6-75.7)	79.1 (79.1-79.1)
Hypertension	55.8 (55.7-55.8)	73.4 (73.4-73.5)
Renal failure	89.5 (89.5-89.5)	89.5 (89.4-89.5)
Heart failure	78.1 (78.0-78.1)	82.6 (82.6-82.7)
Coronary heart disease	58.1 (58.0-58.1)	66.6 (66.6-66.6)

Table 103 Trends in unadjusted 30 day and six months case fatality rates in men and women following admission to hospital with a second AMI

	30 DAY CASE FATALITY %		SIX MONTHS CASE FATALITY %	
	MEN	**WOMEN**	**MEN**	**WOMEN**
1990	24.0 (23.9-24.0)	28.4 (28.3-28.4)	33.9 (33.9-34.0)	38.9 (38.9-38.9)
1991	25.8 (25.7-25.8)	29.0 (28.9-29.0)	33.9 (33.9-33.9)	37.9 (37.9-38.0)
1992	23.3 (23.2-23.3)	29.5 (29.4-29.5)	29.0 (28.9-29.0)	42.3 (42.3-42.4)
1993	22.7 (22.6-22.7)	27.1 (27.1-27.1)	30.7 (30.7-30.7)	36.5 (36.4-36.5)
1994	19.6 (19.6-19.7)	27.2 (27.2-27.3)	26.6 (26.6-26.7)	39.1 (39.1-39.2)
1995	19.5 (19.4-19.5)	24.9 (24.9-25.0)	28.1 (28.1-28.1)	34.8 (34.7-34.8)
1996	22.3 (22.3-22.4)	25.3 (25.3-25.4)	31.0 (30.9-31.0)	35.6 (35.5-35.6)
1997	20.4 (20.4-20.4)	29.7 (29.7-29.8)	28.3 (28.3-28.4)	36.0 (35.9-36.0)
1998	22.3 (22.3-22.4)	27.4 (27.4-27.5)	29.1 (29.0-29.1)	37.1 (37.0-37.2)
1999	24.9 (24.9-25.0)	27.6 (27.6-27.7)	28.9 (28.9-29.0)	35.6 (35.5-35.6)
2000	23.2 (23.1-23.2)	27.6 (27.5-27.7)	31.5 (31.4-31.5)	35.9(35.5-35.6)
Crude % change	¯ 3.2	¯ 2.6	¯ 7.2	¯ 7.6

Table 104 Trends in unadjusted one year and two year case fatality rates in men and women following admission to hospital with a second AMI 1990-2000

	ONE YEAR CASE FATALITY %		TWO YEARS CASE FATALITY %	
	MEN	**WOMEN**	**MEN**	**WOMEN**
1990	39.5 (39.5-39.6)	43.7 (43.7-43.8)	45.7 (45.7-45.8)	52.8 (52.7-52.8)
1991	38.5 (38.5-38.6)	44.0 (43.9-44.0)	45.2 (45.2-45.3)	52.7 (52.7-52.8)
1992	33.9 (33.9-34.0)	48.3 (47.9-48.8)	42.5 (42.5-42.5)	57.5 (57.4-57.5)
1993	35.5 (35.4-35.5)	41.4 (41.3-41.4)	41.7 (41.7-41.8)	47.0 (47.0-47.1)
1994	32.3 (32.2-32.3)	44.9 (44.8-44.9)	38.4 (38.4-38.5)	53.0 (52.9-53.0)
1995	32.8 (32.8-32.8)	40.9 (40.8-40.9)	38.6 (40.2-40.3)	47.5 (47.4-47.5)
1996	34.1 (34.1-34.2)	41.4 (41.3-41.4)	40.2 (40.2-40.3)	47.8 (47.7-47.8)
1997	32.2 (32.2-32.2)	41.8 (41.8-41.9)	38.8 (38.4-38.5)	47.7 (47.6-47.8)
1998	35.6 (35.6-35.6)	42.7 (42.7-42.8)	40.3 (40.2-40.3)	50.8 (50.7-50.9)
1999	32.9 (32.9-33.0)	40.6 (40.5-40.7)	38.5 (38.4-38.5)	52.7 (52.7-52.8)
2000	35.3 (35.2-35.3)	40.6 (40.6-40.7)		
% change	¯ 10.7	¯ 7.1	¯ 15.9	¯ 0.1

Table 105 Trends in unadjusted five year case fatality rates in men and women following admission to hospital with a second AMI 1990-2000

	FIVE YEARS CASE FATALITY %	
	MEN	**WOMEN**
1990	59.2 (59.1-59.2)	69.5 (69.4-69.5)
1991	59.2 (59.2-59.3)	68.3 (68.3-68.4)
1992	57.2 (57.2-57.2)	72.2 (72.2-72.2)
1993	56.8 (56.7-56.8)	66.5 (66.5-66.5)
1994	54.7 (54.7-54.8)	68.5 (68.5-68.5)
1995	54.1(54.0-54.1)	62.1 (62.0-62.1)
1996	54.1 (54.1-54.2)	65.4 (65.4-65.5)
Crude % change	¯ 8.6	¯ 10.6

12.1.2 Kaplan-Meier Survival Curves and median survival time

12.1.2.1 Overall

The Kaplan Meier survival curve for men and women showed an initial sharp drop in survival followed by a progressive decline in cumulative survival in both men and women (Figure 31). Survival was consistently higher in men and this difference was statistically significant ($p<0.001$). The results of the log rank tests are shown in Table 108. Median survival times for men and women are shown in Table 106 and in Table 107. Median survival following a second AMI was 3.6 years in men and 1.8 years in women. This compared to a median survival following a first AMI of 8.8 years in men and 4.3 years in women.

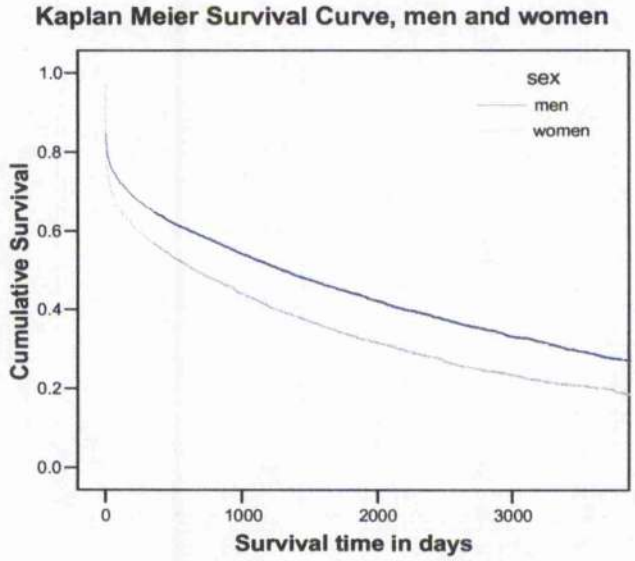
12.1.2.2 Age

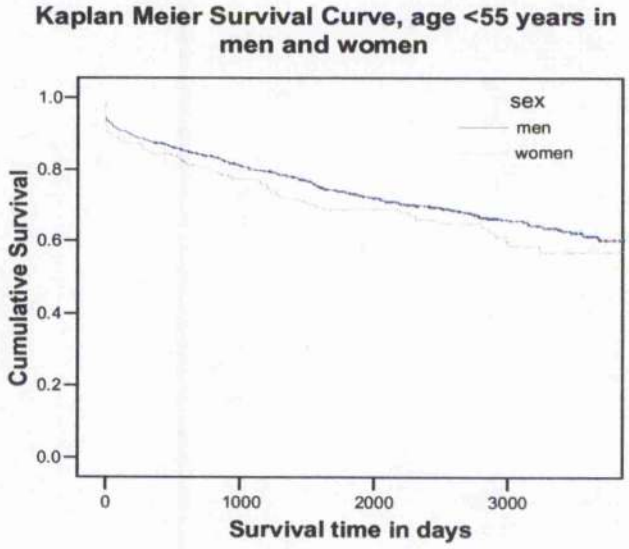
Figure 31 shows the Kaplan Meier survival curves for men and women in different age groups. As demonstrated in the life tables, age had a powerful effect on prognosis. Median survival was greater than 10 years in both men and women aged <55 years, but decreased to 0.3 years in men and 0.4 years in women aged >84 years. Prognosis was better for men than for women up to the age of 65 years, after which prognosis was better in women than in men. The interaction seen in the life table analyses was therefore evident in median survival and in the Kaplan Meier Survival Curves. In the longer term and especially in older age groups, prognosis appeared similar in men and women. The effect of sex on prognosis therefore seemed to change as survival time increased. Overall the survival curves were not significantly different in men and women in any of the age groups.

12.1.2.3 Socio-economic deprivation

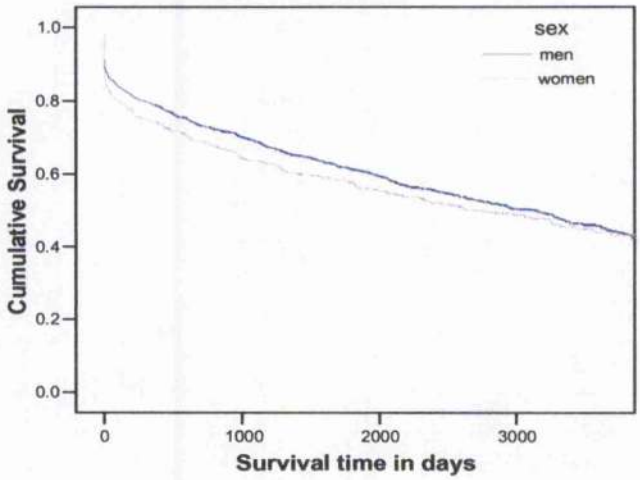
Figure 32 shows Kaplan Meier survival curves in men and women within deprivation categories. The effect of sex on survival was similar in each of the deprivation categories. Survival was significantly worse in women in all groups ($p<0.001$). In men, median survival was shorter in the least deprived category (3.2 years) when compared to other deprivation groups (3.7 years in most deprived group). There was little variation in median survival in the other categories. In women, median survival was significantly longer in the most deprived category (1.9 years) when compared to the least deprived category (1.4 years).

Figure 31 Survival by sex for all ages and by age group for second AMI

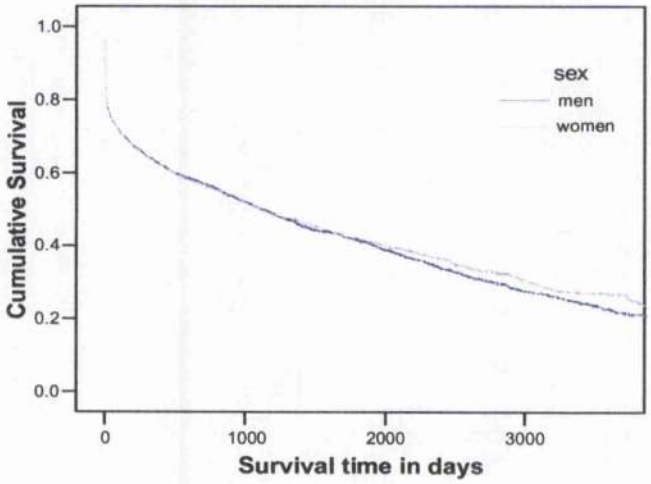




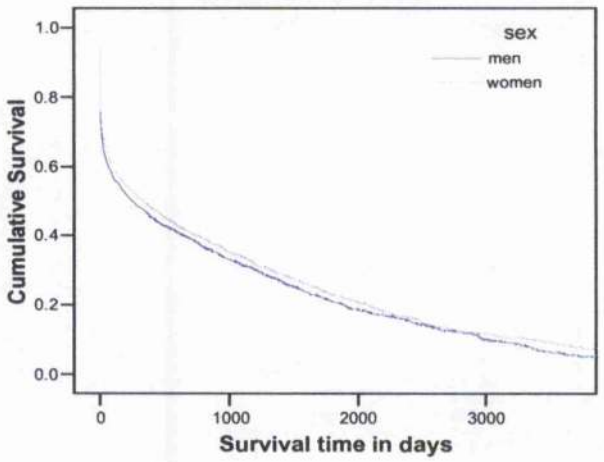
Kaplan Meier Survival Curve, age 55-64 years in men and women



Kaplan Meier Survival Curve, age 65-74 years in men and women



Kaplan Meier Survival Curve, age 75-84 years in men and women



Kaplan Meier Survival Curve, age >84 years in men and women

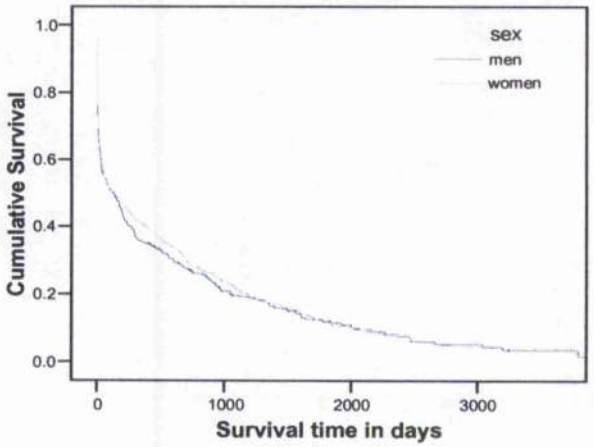
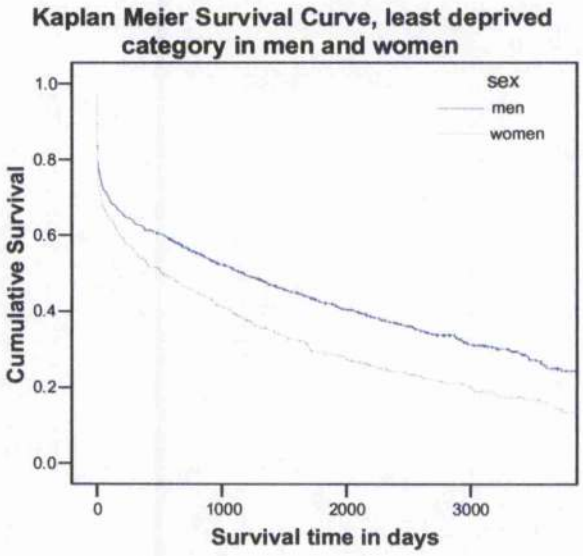
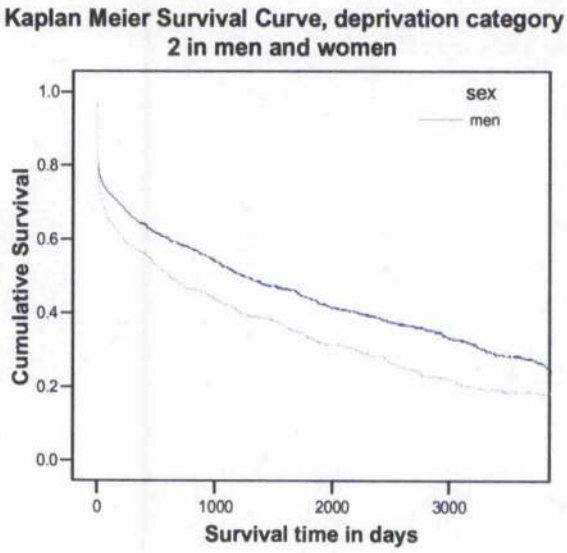
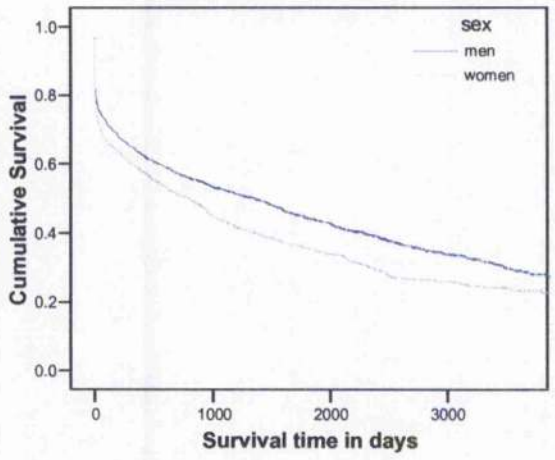


Figure 32 Survival by sex within deprivation categories for second AMI

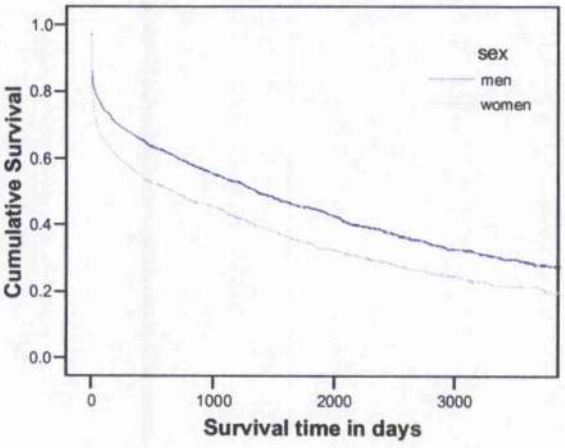




Kaplan Meier Survival Curve, deprivation category 3 in men and women



Kaplan Meier Survival Curve, deprivation category 4 in men and women



Kaplan Meier Survival Curve, most deprived category in men and women

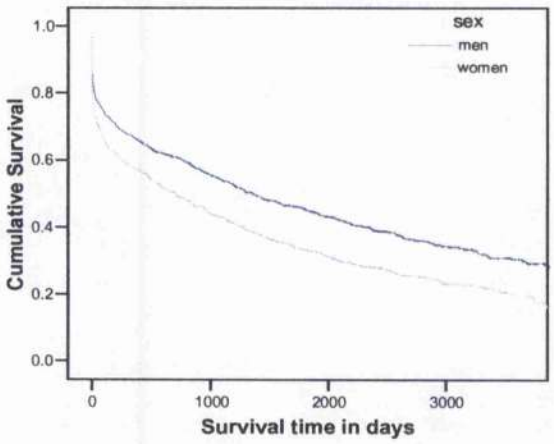


Table 106 Median survival time in years in men and women following a second AMI

	MEDIAN SURVIVAL IN YEARS (95% CI)	
	MEN	**WOMEN**
Overall	3.6 (3.3-3.8)	1.8 (1.6-2.0)
Age group		
<55	>10	11.6 (no CI)
55-64	8.6 (7.6-9.6)	7.6 (5.8-9.4)
65-74	3.1 (2.7-3.5)	3.1 (2.5-3.6)
75-84	0.7 (0.5-0.9)	0.9 (0.7-1.2)
>84	0.3 (0.1-0.5)	0.4 (0.2-0.6)
Deprivation quintile		
1-least deprived	3.2 (2.5-3.9)	1.4 (0.9-2.0)
2	3.4 (2.8-4.1)	1.7 (1.2-2.2)
3	3.7 (3.1-4.4)	2.2 (1.7-2.7)
4	3.7 (3.1-4.3)	1.9 (1.3-2.4)
5-most deprived	3.7 (3.1-4.4)	1.9 (1.5-2.4)
Comorbidity		
Any comorbidity	2.1 (1.9-2.4)	1.3 (1.1-1.5)
No comorbidity	8.1 (7.4-8.7)	4.7 (3.9-5.6)
Diabetes	1.5 (0.8-2.0)	1.1 (0.7-1.4)
Cancer	1.1 (0.8-1.4)	0.9 (0.6-1.3)
Respiratory disease	1.1 (0.7-1.6)	0.8 (0.5-1.1)
Cerebrovascular disease	0.8 (0.5-1.1)	0.8 (0.4-1.3)
Peripheral vascular disease	0.9 (0.6-1.2)	1.0 (0.4-1.6)
Atrial fibrillation	0.9 (0.6-1.2)	0.9 (0.6-1.2)
Hypertension	3.7 (2.8-4.5)	1.5 (1.0-2.0)
Renal failure	0.2 (0.1-0.3)	0.2 (0.1-0.3)
Heart failure	0.8 (0.6-0.9)	0.6 (0.4-0.7)
Coronary heart disease	3.3 (2.7-3.8)	1.9 (1.4-2.3)

Table 107 Trends in median survival time in years in men and women following a second AMI

	MEDIAN SURVIVAL IN YEARS (95% CI)	
	MEN	WOMEN
1990	2.9 (2.1-3.6)	1.7 (1.2-2.2)
1991	2.8 (2.0-3.5)	1.7 (1.2-2.2)
1992	3.4 (2.7-4.2)	1.1 (0.7-1.6)
1993	3.4 (2.6-7.0)	2.5 (1.7-3.2)
1994	4.2 (3.5-4.9)	1.5 (0.9-2.2)
1995	3.9 (2.9-4.8)	2.3 (1.4-3.2)
1996	4.0 (2.9-5.1)	2.3 (1.4-3.2)
1997	4.1 No CI	2.7 (1.0-4.3)
1998	>3	1.9 (1.2-2.7)
1999	>2	1.7 (1.2-2.3)
2000	>1	>1

Table 108 Results of log rank tests from Kaplan Meier Survival comparing men and women with a second AMI

	LOG RANK TEST, P-VALUE
Sex	P<0.001
Age group	
<55	***P=0.2157***
55-64	***P=0.2361***
65-74	***P=0.3495***
75-84	***P=0.0879***
>84	***P=0.4719***
Deprivation quintile	
1-least deprived	P<0.001
2	P<0.001
3	P=0.0001
4	P<0.001
5-most deprived	P<0.001
Comorbidity	
Any comorbidity	P<0.001
No comorbidity	P<0.001
Diabetes	P=0.0015
Cancer	P=0.0447
Respiratory disease	P=0.0075
Cerebrovascular disease	***P=0.6718***
Peripheral vascular disease	***P=0.5465***
Atrial fibrillation	***P=0.5166***
Hypertension	P<0.001
Renal failure	***P=0.7931***
Heart failure	P=0.0061
Coronary heart disease	P<0.001

Continued over…

Table 109 ***continued***

	LOG RANK TEST, P-VALUE
1990	P=0.0004
1991	P=0.0014
1992	P<0.001
1993	***P=0.046***
1994	P<0.001
1995	P=0.0028
1996	P=0.0029
1997	***P=0.0720***
1998	P=0.0041
1999	P=0.0007
2000	***P=0.2313***

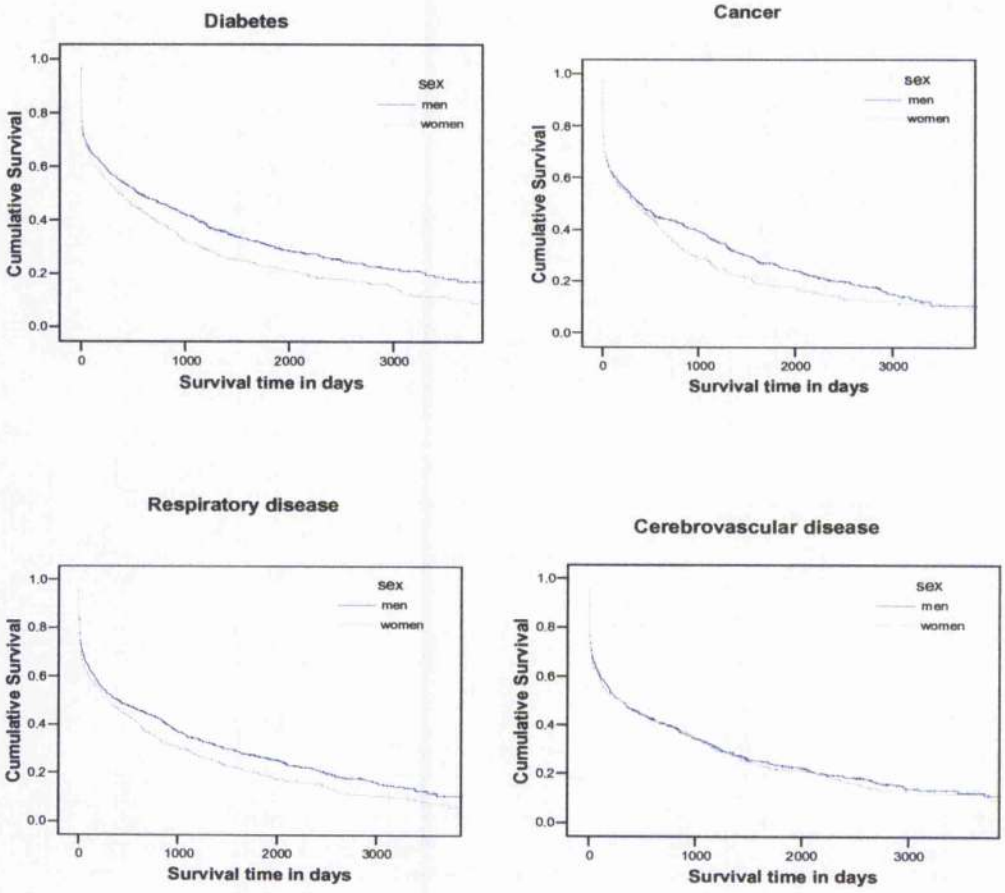
12.1.2.4 Comorbidity

The presence of any comorbid diagnosis substantially reduced median survival in men and women following a second AMI. Median survival was 8.1 years in men and 4.7 years in women who had no comorbid diagnosis but only 2.1 years in men and 1.3 years in women who had one or more comorbid diagnoses. Each of the comorbid diagnoses appeared to substantially reduce median survival. Kaplan Meier Survival Curves are shown in Figure 33. As seen in the life table analyses, the strongest effects were with renal failure, heart failure, cerebrovascular and peripheral vascular disease. Survival with any of these diagnoses was not significantly different between men and women. Sex differences in overall survival were significant with some of the comorbid diagnoses that appeared to have a lesser effect on survival. For example, hypertension and coronary heart disease ($p<0.001$). The effect of sex did not always remain constant over time so that with a cancer diagnosis, short term survival appeared similar and men and women, whilst middle and longer term survival were worse in women.

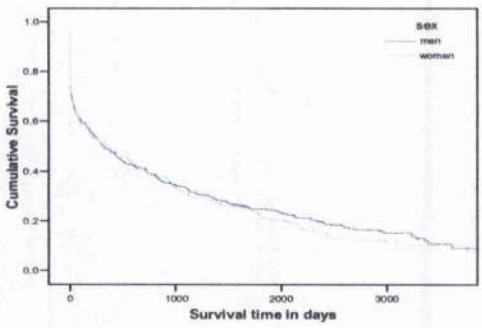
12.1.2.5 Trends in median survival following a second AMI

Median survival increased in men from 2.9 years in 1990 to 4.2 years in 1994, after which it then started to decline. A similar pattern was seen in women in whom median survival increased from 1.7 years in 1990 to 2.5 years in 1993, after which it declined reaching 1.7 years in 1999. Sex differences were not consistent and overall survival was not always significantly different in men and women.

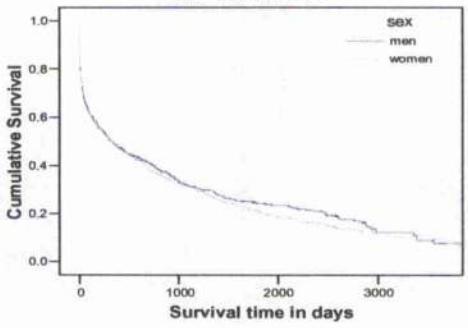
Figure 33 Kaplan Meier Survival Curves by sex within comorbid diagnoses



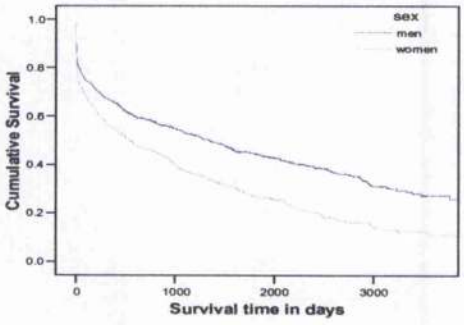
Peripheral vascular disease



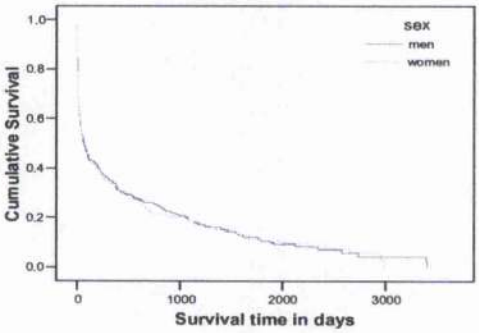
Atrial fibrillation



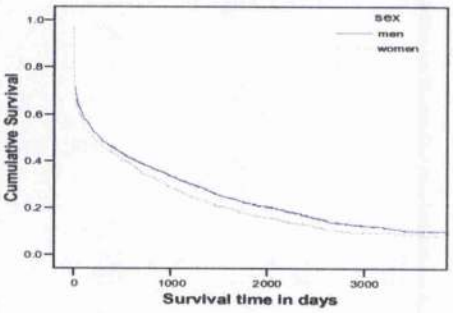
Hypertension



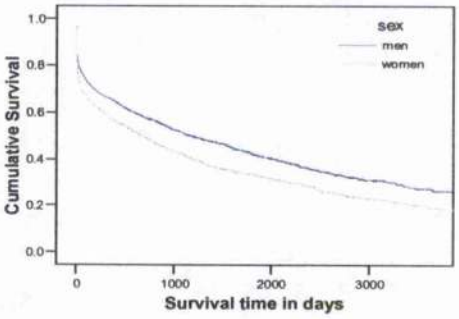
Renal failure



Heart failure



coronary heart disease



12.2 Results of adjusted survival analyses

The aim of this section is to examine the independent effect of sex on short and longer term survival following hospitalisation with a second AMI. Men and women differ in their baseline characteristics such as age and comorbid diagnoses and in order to determine whether sex has an independent effect, these varying distributions need to be accounted for using multivariate modelling techniques. The analyses also aim to examine and to quantify the independent effect of other factors such as age and comorbid diagnoses on the risk of death in men and women at different time periods.

12.2.1 Logistic regression at 30 days in men and women following a second AMI

12.2.1.1 Overall

Table 109 shows the effect of other factors on sex as a predictor of prognosis at 30 days following a second AMI. The model started with sex and added other variables, in order of decreasing significance. Without adjusting for any factors, women's odds of death at 30 days were 33% greater than for men. This sex difference was less than that seen for first AMI, where women's odds of death at 30 days were 77% greater than for men. Accounting for age differences between men and women removed almost all of this sex difference so that women's odds of death were 2% less than that of men. This difference was not statistically significant. Addition of other variables into the model slightly altered the sex difference in the odds of dying at 30 days, although sex continued to be non-significant and was not therefore a significant predictor of outcome at 30 days. The final model excluded year of admission, deprivation category, cancer, respiratory disease and previous coronary heart disease, none of which were significant predictors of outcome at 30 days. After all the variables had been included in the model, women had a non-significant survival advantage of 2% in the odds of death at 30 days. These findings contrast with first AMI where women's odds of death at 30 days were 20% greater than for men and all variables remained significant predictors of outcome and were retained in the final model. An age sex interaction term was tested but was non-significant, p=0.155.

Table 110 shows the logistic regression models carried out in men and women separately. Age was the most powerful predictor of outcome at 30 days and, as for first AMI, appeared

to have a stronger effect in men than in women. Men aged 85 years and over had a seven fold increase in the risk of death when compared to men aged < 55 years (odds ratio 7.63, 95%CI 5.27-11.05). In women the equivalent odds ratio was 6.43 (95% CI 3.59-11.51). The effect of age was not therefore as marked as for first AMI, following which men aged 85 years and over had a 15 fold increase in the risk of death when compared to men aged <55 years. Socioeconomic deprivation was not a significant predictor of outcome at 30 days in men or in women. Again this was in contrast to first AMI where socioeconomic deprivation was a significant predictor of outcome in men and in women and appeared to have a more marked effect on the odds of death in men than in women. In general, the effect of comorbid conditions on the risk of death at 30 days following a second AMI was less than that seen following a first AMI. For example a diagnosis of cancer carried an 11% increase in the odds of death in men following a second AMI and a 63% increase in the odds of death in men following a first AMI. As for first AMI, heart failure and renal failure had the strongest effect on outcome in men and in women. Previous coronary heart disease was not a significant predictor of 30 day outcome in men or in women. Atrial fibrillation and hypertension both decreased the odds of death at 30 days. Atrial fibrillation was associated a 24% reduction in the odds of death in women. The effect of atrial fibrillation did not reach significance in men. In contrast, hypertension reduced the risk of death by 28% in men and 16% in women, though this effect was only significant in men. The adjusted odds of death at 30 days decreased in men and women between 1990 and 2000, although these changes were not significant.

Table 109 Effect on sex of stepwise addition of other significant variables in logistic regression at 30 days

STEP	VARIABLE IN MODEL	ODDS RATIO (95%CI)	
		MEN	WOMEN
Enter	Sex	1.00	1.33 (1.21-1.46)
1	+ age group	1.00	0.98 (0.89-1.08)
2	+ heart failure	1.00	0.96 (0.87-1.06)
3	+ renal failure	1.00	0.97 (0.87-1.07)
4	+ time since previous AMI	1.00	0.95 (0.86-1.05)
5	+ cerebrovascular disease	1.00	0.96 (0.87-1.07)
6	+ hypertension	1.00	0.97 (0.88-1.08)
7	+ diabetes	1.00	0.97 (0.88-1.07)
8	+ atrial fibrillation	1.00	0.97 (0.88-1.07)
9	+ peripheral vascular disease	1.00	0.98 (0.88-1.08)

Table 110 Adjusted odds of death at 30 days in men and women admitted to hospital following a second AMI

	ODDS RATIO (95% CI)	
	MEN	WOMEN
Sex	1.00	0.98 (0.88-1.08)
Age group		
<55	1.00	1.00
55-64	1.85 (1.34-2.55)	2.22 (1.22-4.04)
65-74	3.57 (2.63-4.83)	3.27 (1.85-5.78)
75-84	5.93 (4.36-8.07)	4.81 (2.74-8.46)
>84	7.63 (5.27-11.05)	6.43 (3.59-11.51)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.01 (0.81-1.26)	0.95 (0.74-1.22)
3	1.12 (0.90-1.38)	1.01 (0.79-1.22)
4	0.94 (0.76-1.17)	1.01 (0.80-1.29)
5-most deprived	1.01 (0.81-1.27)	1.00 (0.78-1.27)
Comorbidity		
Diabetes	1.41 (1.16-1.71)	1.02 (0.83-1.27)
Cancer	1.11 (0.91-1.36)	1.03 (0.80-1.31)
Respiratory disease	1.10 (0.91-1.33)	1.07 (0.86-1.33)
Cerebrovascular disease	1.36 (1.12-1.65)	1.49 (1.18-1.89)
Peripheral vascular disease	1.30 (1.05-1.62)	1.04 (0.79-1.36)
Atrial fibrillation	0.98 (0.79-1.22)	0.76 (0.60-0.95)
Hypertension	0.72 (0.58-0.89)	0.84 (0.68-1.04)
Renal failure	1.83 (1.39-2.41)	1.84 (1.35-2.51)
Heart failure	1.56 (1.35-1.80)	1.52 (1.30-1.77)
Coronary heart disease	0.93 (0.80-1.09)	0.99 (0.83-1.18)

Table 111 Trends in adjusted odds of death at 30 days in men and women admitted to hospital following a second AMI

	ODDS RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	1.14 (0.88-1.48)	1.00 (0.75-1.35)
1992	0.94 (0.72-1.23)	1.01 (0.75-1.35)
1993	0.88 (0.67-1.15)	0.91 (0.67-12.4)
1994	0.75 (0.57-1.00)	0.92 (0.68-1.25)
1995	0.76 (0.56-1.01)	0.78 (0.56-1.08)
1996	0.87 (0.65-1.18)	0.84 (0.59-1.18)
1997	0.75 (0.55-1.03)	1.04 (0.72-1.49)
1998	0.80 (0.58-1.10)	0.89 (0.62-1.28)
1999	0.72 (0.51-1.01)	0.83 (0.57-1.20)
2000	0.79 (0.55-1.12)	0.83 (0.56-1.23)

12.2.1.2 Logistic regression at 30 days following a second AMI age <65 years

After adjusting for other factors, sex was not a significant predictor of outcome at 30 days in individuals aged less than 65 years hospitalised following a second AMI, p=0.17 (Table 112). This was in contrast to 30 day survival following a first AMI, in which women had a 29% increase in the odds of death after adjusting for other factors. Socioeconomic deprivation was not a significant predictor of outcome in men or women in this age group. However, in women the odds of death was greatest in the least deprived category compared to the other categories, and was significantly less in deprivation category two than in the least deprived group. This again was in contrast to outcome following a first AMI, where socioeconomic deprivation had the strongest effect in the younger age group. The presence of comorbid conditions had a more marked effect on 30 day survival in this younger age group, than in the whole cohort, however the effect of a number of these diagnoses was not significant. A diagnosis of diabetes increased the odds of death by 97% in men, p=0.001. Women with renal failure were more than six times likely to die at 30 days (odds ratio in women 46.41 95%CI 2.09-19.61). Hypertension had a protective effect but only in women in whom the odds of dying were 0.43 (0.19-0.96). Time since first AMI was a significant predictor of outcome but only in men in whom the odds of death at 30 days decreased by 6% for each additional year since the first AMI (p=0.015). Odds of dying at 30 days showed no consistent trend over time in men or in women, although year of admission was a significant predictor of outcome at 30 days in both sexes (p=0.033 in men p=0.014 in women). This contrasted with first AMI in which the odds of death fell by 59% in men and 47% in women in this younger age group.

12.2.1.3 Logistic regression at 30 days following a second AMI age 65-74 years

Sex remained a non-significant predictor of outcome in this age group (Table 114). This contrasted to first AMI in which women had a 13% increase in the odds of death at 30 days when compared to men of a similar age. Socio-economic deprivation did not have a significant effect on outcome in this age group in men or in women. The effect of comorbid diagnoses differed according to the nature of the diagnosis and sex and fewer of the diagnoses had a significant effect on outcome than demonstrated in survival following first AMI. The only diagnoses in men that were significant predictors of outcome at 30 days were heart failure, renal failure, cerebrovascular disease, hypertension and diabetes. As in the younger age group, heart failure and renal failure continued to have the strongest effects, for example men with a diagnosis of heart failure had a 70% increase in the odds of death at 30 days, whilst in women the risk was increased more than two-fold. In women,

heart failure was the only diagnosis that carried a significantly increased risk in the odds of death. Hypertension had a protective effect and lowered the odds of death by 40%, but only in men. Time since previous AMI had a similar effect as seen in the younger age group, with a 5% reduction in the odds of death at 30 days for each additional year since the first AMI. Again this was only significant in men, p=0.006. Year of admission was not a significant predictor of outcome in men or women at 30 days following a second AMI (Table 115).

12.2.1.4 Logistic regression at 30 days following a second AMI age >74 years

Sex continued to be a non-significant predictor of outcome at 30 days in this older age group (Table 116). Again this contrasts with first AMI where women had a 12% increase in the odds of death at 30 days. Socio-economic deprivation did not have a significant effect on outcome in men or in women in this older age group and this was similar to the effect seen following a first AMI. In general the presence of comorbid conditions had a lesser effect on the odds of death in this older age group than in the two younger groups. Only heart failure, renal failure and atrial fibrillation had a significant effect on outcome in men and in women. For example, heart failure increased the odds of death by 34% in men aged greater than 74 years and by 22% in women aged >74 years. In women, cerebrovascular disease also increased the odds of death, by 41%. Atrial fibrillation had a protective effect and lowered the odds of death at 30 days in men and women, by 29% in men and by 25% in women. Year if admission was not a significant predictor of outcome in men or in women (Table 117).

Table 112 Adjusted odds of death at 30 days in men and women aged < 65 years admitted to hospital following a second AMI 1990-2000

	ODDS RATIO (95% CI)	
	MEN	WOMEN
Sex	1.00	1.21 (0.92-1.59)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.46 (1.46-0.83)	0.26 (0.09-0.71)
3	1.35 (0.78-2.33)	0.65 (0.29-1.49)
4	1.08 (0.62-1.86)	0.61 (0.27-1.37)
5-most deprived	1.39 (0.80-2.40)	0.52 (0.24-1.15)
Comorbidity		
Diabetes	1.97 (1.34-1.88)	1.42 (0.75-2.70)
Cancer	1.00 (0.58-1.74)	0.73 (0.31-1.70)
Respiratory disease	1.34 (0.83-2.14)	0.99 (0.43-2.27)
Cerebrovascular disease	1.21 (0.73-1.99)	1.77 (0.89-3.54)
Peripheral vascular disease	1.67 (0.97-2.88)	1.36 (0.50-3.70)
Atrial fibrillation	1.33 (0.73-2.44)	0.80 (0.29-2.19)
Hypertension	1.06 (0.69-1.63)	0.43 (0.19-0.96)
Renal failure	2.06 (1.00-4.23)	6.41 (2.09-19.61)
Heart failure	2.06 (1.31-2.59)	2.44 (1.41-4.21)
Coronary heart disease	0.94 (0.68-1.30)	1.63 (0.97-2.74)

Table 113 Trends in adjusted odds of death at 30 days in men and women aged <65 years admitted to hospital following a second AMI

	ODDS RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	1.78 91.04-3.05)	1.90 (0.82-4.40)
1992	1.41 (0.79-2.51)	1.04 (0.42-2.55)
1993	1.02 (0.57-1.83)	0.90 (0.33-2.44)
1994	0.81 (0.42-1.57)	2.90 (1.25-6.71)
1995	0.63 (0.32-1.25)	0.34 (0.08-1.41)
1996	0.85 (0.43-1.69)	1.19 (0.43-3.28)
1997	1.40 (0.74-2.67)	0.55 (0.14-2.19)
1998	0.79 (0.37-1.72)	0.54 (0.13-2.25)
1999	0.70 (0.28-1.72)	0.23 (0.03-1.93)
2000	1.36 (0.66-2.81)	1.40 (0.39-5.10)

Table 114 Adjusted odds of death at 30 days in men and women aged 65-74 years admitted to hospital following a second AMI 1990-2000

	ODDS RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.96 (0.80-1.15)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.89 (0.61-1.29)	1.41 (0.83-2.42)
3	1.01 (0.71-1.44)	1.23 (0.73-2.06)
4	0.71 (0.49-1.02)	1.39 (0.84-2.30)
5-most deprived	0.86 (0.59-1.26)	1.67 (1.01-2.77)
Comorbidity		
Diabetes	1.52 (1.12-2.07)	0.90 (0.60-1.34)
Cancer	1.07 (0.76-1.49)	1.03 (0.64-1.65)
Respiratory disease	0.90 (0.64-1.24)	1.07 (0.70-1.64)
Cerebrovascular disease	1.72 (1.27-2.32)	1.30 (0.82-2.06)
Peripheral vascular disease	1.20 (0.83-1.74)	1.15 (0.65-2.01)
Atrial fibrillation	1.30 (0.92-1.85)	0.76 (0.47-1.24)
Hypertension	0.60 (0.41-0.88)	1.12 (0.75-1.68)
Renal failure	1.96 (1.19-3.21)	1.78 (0.92-3.44)
Heart failure	1.70 (1.34-2.16)	2.02 (1.48-2.75)
Coronary heart disease	0.92 (0.71-1.19)	0.92 (0.65-1.30)

Table 115 Trends in adjusted odds of death at 30 days in men and women aged 65-74 years admitted to hospital following a second AMI

	ODDS RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.96 (0.62-1.48)	0.89 (0.52-1.54)
1992	0.76 (0.49-1.19)	0.95 (0.54-1.67)
1993	0.91 (0.58-1.43)	0.75 (0.42-1.35)
1994	0.57 (0.35-0.92)	0.44 (0.24-0.84)
1995	0.77 (0.48-1.24)	0.53 (0.28-1.00)
1996	0.75 (0.46-1.22)	0.96 (0.50-1.84)
1997	0.51 (0.29-0.91)	0.95 (0.46-1.96)
1998	0.55 (0.31-0.97)	0.46 (0.21-0.97)
1999	0.70 (0.39-1.25)	0.61 (0.29-1.30)
2000	0.85 (0.47-1.56)	0.58 (0.24-1.37)

Table 116 Adjusted odds of death at 30 days in men and women aged >74 years admitted to hospital following a second AMI 1990-2000

	ODDS RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.88 (0.77-1.07)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.95 (0.70-1.31)	0.94 (0.69-1.26)
3	1.09 (0.80-1.50)	0.99 (0.74-1.33)
4	1.17 (0.84-1.61)	1.01 (0.75-1.36)
5-most deprived	1.04 (0.74-1.45)	0.88 (0.65-1.19)
Comorbidity		
Diabetes	1.01 (0.73-1.41)	0.97 (0.73-1.29)
Cancer	1.15 (0.86-1.54)	1.08 (0.78-1.47)
Respiratory disease	1.16 (0.88-1.54)	1.08 (0.82-1.41)
Cerebrovascular disease	1.14 (0.85-1.53)	1.41 (1.04-1.93)
Peripheral vascular disease	1.25 (0.92-1.70)	0.93 (0.67-1.31)
Atrial fibrillation	0.71 (0.52-0.96)	0.75 (0.58-0.98)
Hypertension	0.70 (0.49-1.00)	0.80 (0.61-1.06)
Renal failure	1.61 (1.11-2.33)	1.60 (1.10-2.34)
Heart failure	1.34 (1.08-1.66)	1.22 (1.01-1.48)
Coronary heart disease	0.91 (0.71-1.17)	0.94 (0.75-1.19)

Table 117 Trends in adjusted odds of death at 30 days in men and women aged >74 years admitted to hospital following a second AMI

	ODDS RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.9 (0.65-1.50)	0.95 (0.64-1.41)
1992	0.87 (0.57-1.34)	1.09 (0.75-1.61)
1993	0.73 (0.48-1.12)	1.01 (0.67-1.52)
1994	0.85 (0.54-1.33)	1.00 (0.67-1.51)
1995	0.73 (0.46-1.17)	0.98 (0.65-1.48)
1996	0.88 (0.54-1.43)	0.73 (0.46-1.14)
1997	0.69 (0.43-1.12)	1.24 (0.78-1.96)
1998	0.98 (0.61-1.59)	1.13 (0.72-1.79)
1999	0.73 (0.44-1.20)	0.99 (0.62-1.56)
2000	0.52 (0.30-0.90)	0.92 (0.56-1.51)

12.2.2 Cox's Proportional Hazards Regression in men and women at one year excluding 30 days

12.2.2.1 Overall

When no other variables were included in the model, sex was a significant predictor of outcome at one year following a first AMI ($p<0.001$) and the unadjusted hazard of death was 1.35 in women relative to men. Adjusting for age alone accounted for all of this sex difference and sex was no longer a significant independent predictor of outcome, $p=0.66$. Addition of other variables into the model had little effect on the hazard of death and did not therefore appear to account for initial sex differences. In the final model, the risk of death was similar in men and women. The adjusted hazard of death was 0.94 (0.84-1.05) so that there was no significant difference in survival between the sexes. As for survival at 30 days, not all variables were included in the final model. The model excluded; deprivation category, hypertension and previous coronary heart disease. All other variables remained significant and were included in the final model. The variables that were excluded were therefore different from those excluded from the model at 30 days which comprised: year of admission, cancer, previous coronary heart disease, respiratory disease and deprivation category. An age sex interaction term was included in the model and was not found to be significant, $p=0.44$.

Table 118 shows the Cox Proportional Hazard regression models carried out in men and women separately. Age had a less powerful effect on prognosis than at 30 days, so that the hazard of death was 5.90 times greater in men aged >84 when compared to men age <55 years. A similar effect was seen in women. The effect of age was again considerably less powerful than seen in one year survival following a first AMI. For example the hazard of death at one years was 11.61 times greater in men aged >84 years than in men aged <55 years following a first AMI. Socioeconomic deprivation was not an independent predictor of one year outcome in men or in women following a second AMI. This was in-keeping with that seen for 30 day survival following second AMI, but in contrast to one year survival following a first AMI where socioeconomic deprivation was an independent predictor of outcome in men but not in women. In general, the presence of comorbid conditions increased the hazard of death in men and women though the magnitude of effect varied according to the diagnosis and by sex. Heart failure and renal failure had the greatest effects. For example, the hazard of death was 86% greater in men and 55% greater in women who had a diagnosis of heart failure than in those individuals who did not. Hypertension, previous coronary heart disease and cancer did not have a significant

effect on prognosis in either men or women. None of the comorbid conditions had a significant protective effect. In general, the magnitude of the effect of comorbid conditions was greater at one year following a second AMI than at 30 days. For example, hazard of death was 10% greater in men with respiratory disease than in men without respiratory disease compared to 48% greater at one year. Atrial fibrillation had a protective effect on 30 day outcome which was significant in women. By one year however atrial fibrillation had an adverse effect on outcome which was significant in men and in women. Time since first AMI was a highly significant predictor of one year outcome and the hazard of death was reduced by 7% in men and 8% in women for each additional year since the first AMI. Year of admission was a significant independent predictor of outcome at one year in men and women. The adjusted hazard of death at one year fell by 50% in men and by 37% in women (Table 119). This compared to falls of 33% in men and 31% in women at one year following a first AMI. This sex difference was not significant, p=0.180.

Table 118 Hazard ratios for death at one year excluding 30 days in men and women admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.94 (0.84-1.05)
Age group		
<55	1.00	1.00
55-64	1.39 (0.98-1.98)	1.57 (0.79-3.13)
65-74	2.47 (1.78-3.42)	2.41 (1.27-4.59)
75-84	3.67 (2.64-5.11)	4.02 (2.13-7.59)
>84	5.90 (4.01-8.70)	4.82 (2.50-9.29)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.95 (0.74-1.23)	0.93 (0.71-1.39)
3	1.17 (0.91-1.49)	0.80 (0.61-1.05)
4	1.14 (0.90-1.46)	1.04 (0.80-1.35)
5-most deprived	1.02 (0.79-1.31)	0.99 (0.76-1.29)
Comorbidity		
Diabetes	1.17 (0.95-1.45)	1.38 (1.12-1.71)
Cancer	1.17 (0.95-1.44)	1.24 (0.97-1.59)
Respiratory disease	1.48 (1.22-1.79)	1.26 (1.01-1.59)
Cerebrovascular disease	1.52 (1.25-1.85)	1.15 (0.88-1.51)
Peripheral vascular disease	1.40 (1.12-1.75)	1.15 (0.86-1.54)
Atrial fibrillation	1.40 (1.13-1.73)	1.31 (1.05-1.63)
Hypertension	0.82 (0.65-1.04)	1.07 (0.86-1.34)
Renal failure	1.77 (1.34-2.34)	1.74 (1.27-2.37)
Heart failure	1.86 (1.59-2.18)	1.55 (1.31-1.84)
Coronary heart disease	1.04 (0.88-1.23)	0.90 (0.74-1.09)

Table 119 Trends in hazard ratio for death at one year excluding 30 days in men and women admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.79 (0.60-1.06)	0.99 (0.71-1.39)
1992	0.57 (0.42-0.78)	1.14 (0.83-1.57)
1993	0.72 (0.54-0.96)	0.77 (0.54-1.10)
1994	0.67 (0.50-0.91)	1.12 (0.81-1.57)
1995	0.71 (0.52-0.96)	0.88 (0.62-1.25)
1996	0.59 (0.42-0.83)	0.93 (0.64-1.35)
1997	0.60 (0.43-0.85)	0.72 (0.46-1.11)
1998	0.65 (0.46-0.92)	0.83 (0.55-1.25)
1999	0.47 (0.32-0.70)	0.63 (0.41-0.96)
2000	0.50 (0.33-0.74)	0.63 (0.39-1.00)

12.2.2.2 Cox's Proportional Hazards Regression at one year following a second AMI age <65 years excluding 30 days

Survival was similar in men and women aged less than 65 years and sex was not an independent predictor of prognosis at one year in this age group following a second AMI (Table 120). This finding was consistent with one year outcome following a first AMI. The adjusted hazard of death in women relative to men was 1.02 (0.74-1.40). As demonstrated in the whole cohort, socioeconomic deprivation was not a significant predictor of outcome in men or in women aged <65 years. Few of the comorbid conditions were significant predictors of one year outcome though the effect of these comorbid diagnoses on prognosis appeared greater in this age group than in the overall cohort. For example, heart failure was associated with 2.44 times the risk of death in the under 65 year old men compared to an increased risk of 86% in the whole cohort. In women, only heart failure carried a significant adverse effect on outcome, whilst in men, heart failure, renal failure, atrial fibrillation and diabetes were all associated with an increase in the hazard of death at one year. The adjusted hazard of death fell by 67% in men and 71% in women, though these declines were not significant (Table 121).

12.2.2.3 Cox's Proportional Hazards Regression at one year following a second AMI age 65-74 years excluding 30 days

Again, sex was not a significant predictor of one year survival in this age group (Table 122). This finding is in contrast to first AMI where the hazard of death was 8% lower in women relative to men at one year in this age group. As in the younger age group, socioeconomic deprivation was not a significant predictor of death in men or in women. Comorbid diagnoses showed similar effects to those seen in the younger age group, although the magnitude of these effects varied slightly. Heart failure, renal failure and atrial fibrillation had the strongest impact on prognosis, especially in men. For example, heart failure was associated with more than twice the risk of death in men (hazard ratio 2.02 in men and 1.63 in women). Men and women with a diagnosis of atrial fibrillation were almost twice as likely to die at one year as those without this diagnosis. Hazard of death was 1.91 in men and 1.95 in women. Following a first AMI, atrial fibrillation increased the hazard of death by 48% in men and by 53% in women in the same age group. Between 1990 and 2000 the risk of death fell by 46% in men and by 80% in women, though these trends did not reach statistical significance in men or in women (Table 123).

12.2.2.4 Cox's Proportional Hazards Regression at one year following a second AMI age >74 years excluding 30 days

As in the younger age groups, sex was not a significant predictor of outcome at one year in men and women following a second AMI, p=0.156 (Table 124). This finding was consistent with that seen at one year following a first AMI. As in the two younger age groups, socioeconomic deprivation was not a significant predictor of outcome in men or in women. Comorbid diagnoses continued to have a significant effect on prognosis, though the magnitude of these effects was generally less than that seen in younger age groups. For example, heart failure was associated with a 33% in the risk of death in women aged >74 years compared to an excess risk of 3.38 times in women aged <65 years. Atrial fibrillation continued to have an adverse effect on prognosis, but only in women. Respiratory disease, cerebrovascular disease and peripheral vascular disease all increased the risk of death in men but not in women. Time since first AMI was a significant predictor of outcome at one year in men and in women. The hazard of death declined by 6% in men and by 9% in women for each additional year since the first AMI. Year of admission was a significant predictor of one year outcome in this age group, and the hazard of death declined by 50% in men and by 12% in women (Table 125). This sex difference was significant, p=0.033.

Table 120 Hazard ratios for death one year excluding 30 days in men and women aged < 65 years admitted to hospital following a second AMI 1990-2000

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.02 (0.74-1.40)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.73 (0.83-3.60)	0.99 (0.32-3.04)
3	1.46 (0.71-3.00)	0.89 (0.29-2.69)
4	2.00 (1.00-3.97)	0.96 (0.32-2.85)
5-most deprived	1.86 (0.92-3.77)	0.72 (0.25-2.09)
Comorbidity		
Diabetes	1.60 (1.03-2.49)	1.51 (0.75-3.05)
Cancer	1.66 (0.96-2.86)	1.51 (0.67-3.43)
Respiratory disease	1.09 (0.63-1.88)	1.21 (0.49-2.98)
Cerebrovascular disease	1.34 (0.80-2.24)	1.83 (0.81-4.16)
Peripheral vascular disease	1.37 (0.74-2.54)	1.21 (0.49-2.98)
Atrial fibrillation	1.97 (1.08-3.54)	0.31 (0.07-1.47)
Hypertension	0.62 (0.35-1.09)	0.82 (0.36-1.86)
Renal failure	3.29 (1.67-6.45)	2.82 (0.81-9.77)
Heart failure	2.44 (1.70-3.50)	3.38 (1.74-6.57)
Coronary heart disease	1.07 (0.75-1.53)	1.01 (0.53-1.91)

Table 121 Trends in hazard ratios of death at one year excluding 30 days in men and women aged <65 years admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.86 (0.47-1.57)	0.63 (0.21-1.87)
1992	0.64 (0.33-1.23)	0.62 (0.22-1.72)
1993	1.14 (0.66-1.97)	1.03 (0.38-2.78)
1994	0.69 (0.36-1.30)	0.44 (0.11-1.67)
1995	0.57 (0.29-1.12)	1.17 (0.39-3.49)
1996	0.60 (0.30-1.20)	0.58 (0.16-2.13)
1997	0.53 (0.23-1.18)	0.58 (0.16-2.13)
1998	0.53 (0.23-1.20)	0.82 (0.21-3.20)
1999	0.21 (0.05-0.90)	0.46 (0.09-2.25)
2000	0.33 (0.11-0.96)	0.29 (0.03-2.50)

Table 122 Adjusted hazard ratios for death at one year excluding 30 days in men and women aged 65-74 years admitted to hospital following a second AMI 1990-2000

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.88 (0.72-1.09)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.71 (0.44-1.14)	0.99 (0.55-1.76)
3	1.12 (0.72-1.73)	0.97 (0.56-1.68)
4	1.22 (0.80-1.86)	1.20 (0.71-2.04)
5-most deprived	1.15 (0.73-1.80)	0.83 (0.47-1.47)
Comorbidity		
Diabetes	1.02 (0.70-1.47)	1.69 (1.14-2.50)
Cancer	0.98 (0.69-1.41)	1.22 (0.73-2.03)
Respiratory disease	1.42 (1.03-1.95)	1.69 (1.09-2.63)
Cerebrovascular disease	1.57 (1.13-2.47)	1.18 (0.70-2.00)
Peripheral vascular disease	1.41 (0.94-2.09)	1.59 (0.89-2.85)
Atrial fibrillation	1.91 (1.36-2.71)	1.95 (1.25-3.02)
Hypertension	0.82 (0.55-1.22)	1.15 (0.73-1.81)
Renal failure	1.87 (1.12-3.12)	1.56 (0.76-3.20)
Heart failure	2.02 (1.56-2.63)	1.63 (1.14-2.31)
Coronary heart disease	1.13 (0.85-1.50)	0.83 (0.56-1.24)

Table 123 Trends in adjusted hazard ratios for death at one year excluding 30 days in men and women aged 65-74 years admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.65 (0.39-1.07)	0.63 (0.30-1.32)
1992	0.52 (0.31-0.87)	1.19 (0.63-2.28)
1993	0.59 (0.35-0.99)	0.90 (0.45-1.80)
1994	0.63 (0.38-1.03)	1.08 (0.56-2.08)
1995	0.74 (0.45-1.23)	0.71 (0.34-1.48)
1996	0.81(0.48-1.34)	0.78 (0.34-1.48)
1997	0.53 (0.28-0.99)	0.99 (0.43-2.26)
1998	0.59 (0.32-1.07)	0.80 (0.36-1.79)
1999	0.37 (0.18-0.76)	0.66 (0.28-1.58)
2000	0.54 (0.26-1.11)	0.20 (0.05-0.91)

Table 124 Adjusted hazard ratios for death at one year excluding 30 days in men and women aged >74 years admitted to hospital following a second AMI 1990-2000

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.89 (0.77-1.04)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.90 (0.64-1.26)	0.94 (0.68-1.30)
3	1.12 (0.81-1.56)	0.73 (0.52-1.02)
4	0.93 (0.65-1.34)	1.09 (0.79-1.50)
5-most deprived	0.80 (0.55-1.15)	1.14 (0.83-1.56)
Comorbidity		
Diabetes	1.09 (0.77-1.54)	1.15 (0.86-1.52)
Cancer	1.20 (0.89-1.63)	1.25 (0.91-1.71)
Respiratory disease	1.65 (1.25-2.18)	1.17 (0.88-1.56)
Cerebrovascular disease	1.46 (1.09-1.94)	1.05 (0.74-1.49)
Peripheral vascular disease	1.45 (1.06-1.98)	0.99 (0.69-1.43)
Atrial fibrillation	1.06 (0.79-1.44)	1.30 (1.01-1.68)
Hypertension	0.99 (0.70-1.44)	1.12 (0.85-1.48)
Renal failure	1.37 (0.70-1.41)	1.67 (1.15-2.43)
Heart failure	1.53 (1.21-1.92)	1.33 (1.08-1.64)
Coronary heart disease	0.88 (0.67-1.16)	0.90 (0.70-1.15)

Table 125 Trends in adjusted hazard ratios for death at one year excluding 30 days in men and women aged >74 years admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.82 (0.53-1.27)	1.25 (0.83-1.90)
1992	0.51 (0.32-0.83)	1.29 (0.86-1.93)
1993	0.55 (0.35-0.87)	0.68 (0.42-1.10)
1994	0.63 (0.39-1.02)	1.34 (0.88-2.03)
1995	0.72 (0.45-1.17)	0.98 (0.63-1.530
1996	0.32 (0.17-0.59)	1.02 (0.65-1.62)
1997	0.68 (0.41-1.11)	0.66 (0.37-1.18)
1998	0.75 (0.45-1.24)	0.89 (0.53-1.49)
1999	0.57 (0.34-0.97)	0.66 (0.38-1.12)
2000	0.50 (0.28-0.87)	0.88 (0.52-1.50)

12.2.3 Cox's Proportional Hazards in men and women at five years following a second AMI excluding 30 days

12.2.3.1 Overall

At five years and excluding the first 30 days, women had an increased risk of death at five years (hazard ratio 1.39) before adjusting for any other prognostic factors. Accounting for the age differences between men and women removed this sex difference and sex was no longer a significant independent predictor of outcome (hazard ratio 1.01, 95% CI 0.93-1.09, p=0.82). Addition of other variables into the model had a marginal effect on this hazard ratio, and men and women continued to have a similar prognosis after adjusting for other prognostic factors (hazard ratio 0.97, 95% CI 0.89-1.05). Socioeconomic deprivation and previous coronary heart disease excluding AMI were not significant predictors of outcome and were not retained in the final model. All other variables were retained in the final model.

Table 126 shows the result of the Cox Proportional Hazard regression models carried out in men and women separately at five years following a second AMI and excluding the first 30 days. Age had a similar effect in men and women and again was the most powerful predictor of outcome. As at 30 days and one year, age had a less powerful effect on prognosis than following first AMI. At five years the hazard of death in men aged greater than 84 years was 5.07 following a second AMI compared to 11.38 following a first AMI. Socioeconomic deprivation was not a significant predictor of outcome in men or in women at five years. This was in contrast to five year survival following first AMI in which socioeconomic deprivation was a significant predictor of outcome in men and in women and men in the most deprived category had a 26% increase in the hazard of death at five years than men in the least deprived category. The presence of comorbid diagnoses had a similar effect in men and women, but was more likely to be significant in men than in women. Heart failure had the most powerful effect and increased the hazard of death by 78% in men and by 67% in women. In men, cancer was the only diagnosis that that did not have a significant effect on outcome. Hypertension had a protective effect in men and reduced the hazard of death at five years (hazard ratio 0.73 95%CI 0.61-0.88). All other diagnoses significantly increased the hazard of death in men. Excluding hypertension and cancer, the effect of comorbid diagnoses was similar in men following a first and second AMI. In women, fewer comorbid diagnoses had a significant effect on prognosis. Diabetes, cancer, respiratory disease, cerebrovascular disease, renal failure and heart

failure all significantly increased the hazard of death at five years. Heart failure and diabetes had the most powerful effect on prognosis. Between 1990 and 1996, the five year hazard of death declined significantly by 29% in men. There was a non-significant decline of 17% in women over the same time period (Table 127). This sex difference was not significant, p=0.316. These declines were similar to those seen following a first AMI (27% in men and 23% in women).

Table 126 Hazard ratios for death at five years excluding 30 days in men and women admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.97 (0.89-1.05)
Age group		
<55	1.00	1.00
55-64	1.36 (1.10-1.68)	1.21 (0.81-1.80)
65-74	2.27 (1.86-2.77)	1.76 (1.21-2.56)
75-84	3.38 (2.75-4.17)	3.22 (2.23-4.65)
>84	5.07 (3.83-6.72)	4.34 (2.94-6.40)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.92 (0.77-1.10)	0.90 (0.74-1.10)
3	1.03 (0.86-1.22)	0.89 (0.73-1.08)
4	1.05 (0.89-1.25)	0.92 (0.76-1.12)
5-most deprived	1.06 (0.88-1.26)	1.02 (0.84-1.23)
Comorbidity		
Diabetes	1.40 (1.19-1.64)	1.45 (1.24-1.70)
Cancer	1.11 (0.94-1.32)	1.37 (1.13-1.66)
Respiratory disease	1.32 (1.12-1.54)	1.37 (1.15-1.62)
Cerebrovascular disease	1.54 (1.32-1.80)	1.33 (1.10-1.61)
Peripheral vascular disease	1.44 (1.21-1.71)	1.09 (0.87-1.36)
Atrial fibrillation	1.39 (1.17-1.66)	1.14 (0.96-1.36)
Hypertension	0.73 (0.61-0.88)	1.10 (0.93-1.3)
Renal failure	1.70 (1.32-2.19)	1.38 (1.03-1.84)
Heart failure	1.78 (1.59-2.00)	1.67 (1.47-1.89)
Coronary heart disease	1.17 (1.04-1.32)	0.92 (0.80-1.06)

Table 127 Trends in hazard ratio for death at five years excluding 30 days in men and women admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.95 (0.79-1.14)	0.97 (0.79-1.19)
1992	0.85 (0.71-1.02)	1.00 (0.82-1.23)
1993	0.83 (0.69-1.00)	0.78 (0.63-0.97)
1994	0.84 (0.69-1.02)	0.95 (0.77-1.18)
1995	0.83 (0.68-1.01)	0.73 (0.59-0.92)
1996	0.71 (0.58-0.88)	0.83 (0.66-1.06)

12.2.3.2 Cox's Proportional Hazards Regression at five years following a second AMI age <65 years excluding 30 days

As in the whole cohort, sex was not a significant independent predictor of outcome at five years in individuals aged less than 65 years, p=0.97. Socioeconomic deprivation remained non-significant in men and in women (Table 128). This contrasted with first AMI in which socioeconomic deprivation was a relatively powerful predictor of outcome especially in younger men. As seen in shorter term survival, the presence of comorbid conditions had a marked impact on prognosis at five years in this younger age group, especially in men. Men and women with renal failure and heart failure had almost twice the increased risk of death at five years as those without these conditions. For example, the hazard of death at five years in individuals with a diagnosis of heart failure was increased 2.12 times in women aged less than 65 years and by 96% in men. Hypertension had a protective effect in men with a hazard ratio of 0.56 (95% CI interval, 0.38-0.81, p<0.001). All other diagnoses carried an adverse effect. Comorbid diagnoses were more likely to carry a significant adverse effect in men than in women. In women only heart failure, diabetes, respiratory disease and cerebrovascular disease were significant independent predictors of outcome. The magnitude of effect was however greater in women than in men for a number of diagnoses including cerebrovascular disease and respiratory disease. In men respiratory disease was not a significant predictor of outcome but in women the hazard ratio was 2.32 (95% CI 1.40-3.83, P=0.001). Time since previous AMI was not a significant predictor in women but was in men in whom the risk of death decreased by 7% for each additional year since the first AMI. The risk of death fell by 41% in men and 50% in women between 1990 and 1996 (Table 129). This decline was only significant in men, p=0.009.

12.2.3.3 Cox's Proportional Hazards Regression at five years following a second AMI age 65-74 years excluding 30 days

Hazard of death at five years and excluding the first 30 days was 16% lower in women than in men in this age group following a second AMI (Table 130). This sex effect was significant, p=0.020. Sex was not a significant predictor of outcome in younger men and women or in the whole cohort. It was however significant in this age group at five years following a first AMI. The effect of socioeconomic deprivation was significant but only in men in whom the overall effect was significant, p=0.027 although individual deprivation categories did not vary significantly from the reference category. Men in the most deprived category had a 27% increase in the hazard of death relative to individuals in the

least deprived category. The presence of comorbid diagnoses had a variable effect on outcome which differed in men and women. Heart failure again carried the worst prognosis. In men the hazard of death was increased two-fold and in women by 76% in those with a diagnosis of heart failure compared to those without. Renal failure and previous coronary heart disease were not significant independent predictors of outcome in men or in women. In women diabetes, cancer, respiratory disease, hypertension and heart failure were all significant predictors of outcome at five years in this age group. A diagnosis of diabetes increased the hazard of death by 68% (95% CI 1.36-2.24). In men, the conditions that had a significant association with outcome included respiratory disease, cerebrovascular disease, peripheral vascular disease, atrial fibrillation and heart failure. Time since first AMI was a significant predictor of outcome in men and in women and each additional year decreased the hazard of death by 8% in men and by 5% in women. This sex difference was not statistically significant. The temporal decline in the risk of death at five years was only significant in women, (hazard ratio 0.51, 95% CI 0.30-0.88) (Table 131).

12.2.3.4 Cox's Proportional Hazards Regression at five years following a second AMI age >74 years excluding 30 days

In this age group, as in the youngest age group, sex was not a significant predictor of outcome at five years, p=0.997. This contrasted with first AMI where sex was a significant predictor of outcome in all three age groups. Socioeconomic deprivation did not have a significant effect on prognosis in men or women in this age group (Table 132). Comorbid diagnoses had a less powerful effect in men and women in this age group compared to the younger age groups. The magnitude of the effects was less than that observed in younger age groups. These findings were similar to that observed following a first AMI. In women only cancer and heart failure were associated with a significant adverse prognosis. As in younger age groups, heart failure had the most powerful effect and was associated with a 58% increase in the hazard of death at five years. In men, diabetes, heart failure, peripheral vascular disease and cerebrovascular disease were all associated with a significant adverse outcome at five years. Again heart failure had the most powerful effect with a hazard ratio of 1.53. Time since first AMI was a significant predictor of outcome in men and women. Each additional year was associated with a reduction in the hazard of death of 5% in men and 10% in women. This sex difference was not significant, p=0.324. There was a significant decline in the risk of death of 47% in

men. In women, although year of admission was a significant predictor of outcome there was no clear trend in the hazard of death at five years (Table 133).

Table 128 Hazard ratios for death five years excluding 30 days in men and women aged < 65 years admitted to hospital following a second AMI 1990-2000

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	0.97 (0.79-1.19)
Deprivation quintile		
1-least deprived	1.00	1.00
2	1.60 (1.05-2.43)	0.76 0.40-1.45)
3	1.45 (0.97-2.17)	0.69 (0.36-1.32)
4	1.59 (1.08-2.36)	0.62 (0.32-1.19)
5-most deprived	1.49 (1.00-2.24)	0.77 (0.42-1.38)
Comorbidity		
Diabetes	1.85 (1.38-2.48)	1.92 (1.21-3.06)
Cancer	1.63 (1.12-2.35)	1.36 (0.79-2.32)
Respiratory disease	1.16 (0.81-1.65)	2.32 (1.40-3.83)
Cerebrovascular disease	1.45 (1.04-2.02)	2.39 (1.45-3.94)
Peripheral vascular disease	1.54 (1.04-2.27)	1.17 (0.61-2.26)
Atrial fibrillation	1.60 (1.02-2.51)	1.48 (0.74-2.97)
Hypertension	0.56 (0.38-0.81)	1.03 (0.63-1.70)
Renal failure	3.87 (2.36-6.35)	1.74 (0.67-4.54)
Heart failure	1.96 (1.54-2.48)	2.12 (1.33-3.38)
Coronary heart disease	1.24 (1.00-1.54)	0.97 (0.65-1.46)

Table 129 Trends in hazard ratios of death at five years excluding 30 days in men and women aged <65 years admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	1.01 (0.73-1.41)	0.92 (0.51-1.66)
1992	0.84 (0.60-1.19)	0.95 (0.54-1.66)
1993	0.89 (0.64-1.23)	0.89 (0.49-1.59)
1994	0.63 (0.43-0.91)	0.39 (0.18-0.83)
1995	0.61 (0.42-0.87)	0.44 (0.20-0.95)
1996	0.59 (0.39-0.88)	0.50 (0.23-1.06)

Table 130 Adjusted hazard ratios for death at five years excluding 30 days in men and women aged 65-74 years admitted to hospital following a second AMI 1990-2000

	HAZARD RATIO (95% CI)	
	MEN	WOMEN
Sex	1.00	0.84 (0.73-0.97)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.83 (0.60-1.15)	0.83 (0.55-1.26)
3	1.04 (0.77-1.41)	0.93 (0.63-1.35)
4	1.23 (0.92-1.64)	0.96 (0.66-1.40)
5-most deprived	1.27 (0.94-1.72)	0.95 (0.64-1.40)
Comorbidity		
Diabetes	1.06 (0.81-1.40)	1.68 (1.36-2.24)
Cancer	1.02 (0.78-1.33)	1.49 (1.02-2.18)
Respiratory disease	1.44 (1.13-1.84)	1.71 (1.23-2.39)
Cerebrovascular disease	1.57 (1.22-2.00)	1.38 (0.95-2.02)
Peripheral vascular disease	1.53 (1.15-2.05)	1.01 (0.63-1.62)
Atrial fibrillation	1.42 (1.06-1.90)	1.33 (0.92-1.93)
Hypertension	0.79 (0.59-1.07)	1.39 (1.00-1.93)
Renal failure	1.51 (0.99-2.31)	1.58 (0.87-2.84)
Heart failure	2.00 (1.65-2.41)	1.76 (1.37-2.26)
Coronary heart disease	1.11 (0.90-1.36)	0.95 (0.72-1.25)

Table 131 Trends in adjusted hazard ratios for death at five years excluding 30 days in men and women aged 65-74 years admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	1.05 (0.76-1.45)	0.79 (0.53-1.18)
1992	0.83 (0.60-1.16)	1.00 (0.67-1.48)
1993	0.87 (0.62-1.23)	0.74 (0.48-1.14)
1994	0.89 (0.64-1.23)	0.82 (0.55-1.23)
1995	0.97 (0.69-1.37)	0.52 (0.33-0.84)
1996	0.91 (0.64-1.29)	0.51 (0.30-0.88)

Table 132 Adjusted hazard ratios for death at five years excluding 30 days in men and women aged >74 years admitted to hospital following a second AMI 1990-2000

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Sex	1.00	1.00 (0.89-1.12)
Deprivation quintile		
1-least deprived	1.00	1.00
2	0.76 (0.58-0.99)	0.94 (0.74-1.20)
3	0.94 (0.72-1.23)	0.86 (0.67-1.10)
4	0.75 (0.57-1.00)	1.02 (0.81-1.30)
5-most deprived	0.79 (0.59-1.06)	1.08 (0.85-1.37)
Comorbidity		
Diabetes	1.42 (1.06-1.90)	1.22 (0.98-1.52)
Cancer	1.03 (0.78-1.35)	1.44 (1.12-1.85)
Respiratory disease	1.27 (0.98-1.65)	1.13 (0.90-1.42)
Cerebrovascular disease	1.41 (1.09-1.84)	1.10 (0.84-1.43)
Peripheral vascular disease	1.40 (1.06-1.84)	0.97 (0.74-1.28)
Atrial fibrillation	1.25 (0.97-1.61)	1.15 (0.93-1.43)
Hypertension	0.92 (0.66-1.28)	0.92 (0.73-1.16)
Renal failure	1.30 (0.85-2.01)	1.16 (0.80-1.68)
Heart failure	1.53 (1.27-1.84)	1.58 (1.35-1.85)
Coronary heart disease	1.20 (0.97-1.50)	0.92 (0.76-1.11)

Table 133 Trends in adjusted hazard ratios for death at five years excluding 30 days in men and women aged >74 years admitted to hospital following a second AMI

	HAZARD RATIO (95% CI)	
	MEN	**WOMEN**
Year of admission		
1990	1.00	1.00
1991	0.80 (0.58-1.09)	1.10 (0.84-1.45)
1992	0.80 (0.59-1.09)	1.08 (0.82-1.41)
1993	0.67 (0.49-0.92)	0.75 (0.56-1.00)
1994	0.86 (0.62-1.19)	1.19 (0.90-1.57)
1995	0.85 (0.61-1.20)	0.93 (0.70-1.24)
1996	0.53 (0.36-0.78)	1.03 (0.77-1.38)

12.3Discussion regarding unadjusted and adjusted survival in men and women following a second AMI

Prognosis following hospitalisation with a second AMI is poor and is worse than the prognosis seen in individuals hospitalised with a first AMI. In the current study approximately one quarter of individuals died within one month of admission and almost 40% within one year. As for first AMI, unadjusted short and long term case fatality rates were lower in men than in women. Median survival was only 1.8 years in women and 3.6 years in men compared with 4.3 years in women and 8.8 years in men following a first AMI. Long term case fatality improved in men hospitalised with a second AMI between 1990 and 1996 and displayed a non-significant trend in women. Short term case fatality following hospitalisation with a second AMI did not demonstrate similar trends over the study period.

12.3.1 Sex

Short term case fatality

In the current study overall 30 day case fatality in individuals hospitalised with a second AMI was 22.4% in men and 27.7% in women. One-year case fatality was also higher in individuals hospitalised with a second AMI compared to those with a first AMI. There are few other data with which to compare these figures. In the 60 Minutes Myocardial Infarction Project unadjusted in-hospital case fatality was significantly higher in individuals hospitalised with a recurrent AMI compared to those with a first AMI (23% versus 15%). Sex specific figures were not reported. The findings from the current study are not surprising given that individuals hospitalised with a second AMI are on average older and are more likely to have other comorbid diagnoses than individuals hospitalised with a first AMI. As for first AMI, short-term case fatality was consistently higher in women than in men. Whilst a number of other studies have compared survival in individuals who do and do not experience a subsequent AMI, no other studies have reported case fatality in men and women hospitalised with a second AMI. This is important because many of these studies have compared survival using a different starting point, so that for example one year case fatality rates are calculated from the date of the first AMI, rather than the reinfarction date. This means that their findings are not comparable with the findings from the current study. In the current study after adjusting for the effects of other factors, sex was not a significant predictor of short term case

fatality. The fact that women were older than men at the time of their second AMI accounted for most of the sex difference seen in unadjusted short term survival rates. There was no age sex interaction in short term survival following second AMI and sex remained a non-significant predictor of outcome in different age groups. This finding contrasted to first AMI from which women were 20% more likely to die at 30 days after adjusting for other factors, and the effect of sex was greater in younger age groups. This is a new finding and it is not clear why sex should be an independent predictor of case fatality following first AMI but not following second AMI. It is likely that some of the hypotheses that have been put forward to explain sex differences in survival following a first AMI would also be relevant to second AMI and would therefore result in similar sex differences in survival in first and second AMI. For example the suggestion that the higher risk of death seen in younger women following a first AMI may be due to a lower rate of use of established treatments for AMI in women than in men would also be relevant for second AMI. Other hypotheses are perhaps more likely therefore. For example it has been suggested that women are more likely to delay seeking treatment, thereby resulting in higher short-term case fatality. Delay in seeking treatment is less likely to occur in individuals who have already been hospitalised with a previous AMI and are more likely to recognise their symptoms.

Longer term case fatality

By two years case fatality had increased to 41.4% in men and 51.1% in women hospitalised with a second AMI. By five years these figures had risen to 55.9% and 66.7% in men and women respectively. Survival was therefore substantially worse in men and women hospitalised with a second AMI compared to those hospitalised with a first AMI. There are few data with which to compare these findings. In the Minnesota Heart Survey three year case fatality in 1990 was 27% in men and 36% in women hospitalised with a recurrent AMI compared to 18% in men and 24% in women hospitalised with a first AMI.[55] The Minnesota Heart Survey only included individuals up to the age of 74 years and was therefore a substantially younger population than the population described in the current study. In the current study men and women hospitalised with a second AMI had a similar long term prognosis after accounting for the effect of age and other factors. Sex was not therefore a significant independent predictor of long term outcome following a second AMI. This again contrasts with first AMI where women had a long term survival advantage and were less likely to die than men. If greater natural longevity is thought to contribute to the better long term survival of women following first AMI then this is also likely to apply following a second AMI. It may be that those individuals who go on to

experience subsequent AMI are a select group with particularly severe disease who are not representative of the majority of individuals who are hospitalised with an AMI. In addition those individuals who experience a second AMI are more likely to have other comorbid diagnoses and survival might therefore be worse because of competing causes that may offset women's natural survival advantage.

12.3.2 Age

Short term case fatality

As for first AMI, age was the most powerful predictor of survival in men and women hospitalised with a second AMI. 30 day case fatality rose from 6.6% in men and 9.5% in women aged less than 55 years to 40.0% in men and 38.9% in women aged greater than 84 years. There are no other data with which to compare these figures. 30 day case fatality following a first AMI rose from 3.7% in men and 5.9% in women aged less than 55 years to 42.6% in men and 44.7% in women aged greater than 84 years. Short term case fatality was therefore worse following a second AMI than following a first AMI, but only in younger patients and not in the very elderly. It is not clear why second AMI should carry a particularly adverse prognosis in younger individuals. These individuals have high rates of comorbid diagnoses which will contribute to their poor prognosis. In keeping with these findings, age had a less powerful effect on prognosis in second AMI than in first AMI, after adjusting for the effects of other factors. The risk of death was increased 7.6 times in men and 6.4 times in women aged greater than 84 years hospitalised with a second AMI, compared to 15.3 times in men and 12.1 times in women hospitalised with a first AMI.

Longer term case fatality

In the current study, over one half of men and two thirds of women hospitalised with a second AMI were dead within five years. As for short term case fatality, the excess risk associated with second AMI was greater in younger age groups. At five years the effect of age on prognosis was less powerful than the effect seen at 30 days. Again this contrasts with first AMI in which age continued to have a similar effect on short and longer term prognosis. This may reflect the fact that the severity of disease in these individuals is such that other factors have less of an impact on prognosis.

12.3.3 Socioeconomic deprivation

Short term case fatality

Unadjusted short term case fatality was higher in the least deprived groups and lower in the most deprived groups. This is likely to be due to the increased age of individuals in less deprived groups compared to those in more deprived groups. After adjusting for other factors in the multivariate analyses, socioeconomic deprivation was not a significant predictor of 30 day outcome in men or women or in different age groups. This finding contrasted with first AMI where socioeconomic deprivation was a significant predictor of prognosis and increased the risk of death especially in younger individuals and in men. It is not clear why socioeconomic deprivation should adversely affect outcome following a first but not a second AMI. It has been suggested that socioeconomic status may affect access to specialised cardiac services and effective secondary prevention treatments.[122;174;207;208] A delay in the diagnosis of coronary heart disease and failure to institute appropriate treatment might be associated with an adverse prognosis following a first but not a second AMI. If the survival differences seen in different socioeconomic groups following first AMI were wholly attributable to less effective treatment during hospitalisation then it would seem likely that these differences would also be present in survival following a second AMI. There are no studies that have compared the effects of socioeconomic deprivation on first and subsequent AMI.

Longer term case fatality

In the current study socioeconomic deprivation had a similar effect on short and long term case fatality following a second AMI. In the multivariate analyses socioeconomic deprivation was not a significant predictor of long term outcome in men or in women. Again this contrasted with first AMI in which socioeconomic deprivation was a significant predictor of long term outcome in men and women and men in the most deprived category had a 26% increased risk of death than men in the least deprived category. As mentioned previously it has been suggested that the longer term effects of socioeconomic deprivation may arise as a result of less efficient secondary prevention in these individuals.[174;207;209] It seems likely that these effects would apply to second as well as first AMI. It is however possible that the severity of disease in individuals hospitalised with a second AMI is such that they represent a more homogenous group with less potential for survival to be affected by individual factors such as sex, socioeconomic deprivation and comorbid diagnoses.

12.3.4 Comorbid diagnoses

Short term case fatality

In the current study, as for first AMI, comorbid diagnoses were associated with a substantially increased unadjusted case fatality in individuals hospitalised with a second AMI. Unadjusted case fatality was increased particularly in individuals with diagnoses of renal failure, heart failure, respiratory disease and cerebrovascular and peripheral vascular disease. After adjusting for the effects of other factors in the multivariate analyses, not all comorbid diagnoses were significant predictors of outcome, unlike in first AMI where all comorbid diagnoses were significant independent predictors of survival. At 30 days, only heart failure, cerebrovascular disease and renal failure were significantly associated with reduced survival in men and women and the magnitude of effect was smaller than for first AMI. In general the presence of comorbid diagnoses had a lesser effect on prognosis following hospitalisation with second than with first AMI. Again this may be due to the fact that individuals hospitalised with a second AMI have severe disease and a poor prognosis and consequently have less scope for other factors such as comorbid disease to impact upon survival. The comorbid diagnoses that remained significant predictors of outcome following hospitalisation with a second AMI were those that were associated particularly adverse outcomes following hospitalisation with a first AMI. There are no other studies with which to compare these data. Atrial fibrillation had a protective effect and was associated with a reduction in the risk of death at 30 days but only in women. Hypertension was also associated with a reduction in the risk of death although this effect was only significant in men. These findings were similar to those seen in first AMI in which both hypertension and atrial fibrillation were associated with a reduction in the risk of death at 30 days. It is not clear why atrial fibrillation should be associated with a reduction in short term case fatality following AMI. As mentioned previously there is some evidence to suggest that the prognosis following AMI may be influenced by the temporal relationship between atrial fibrillation and AMI, and whether atrial fibrillation is a pre-existing condition or whether it develops as a complication of the AMI.[98;99;139] Pre-existing atrial fibrillation is less likely to be associated with an adverse outcome following AMI than atrial fibrillation that develops as a complication of an AMI. It is not possible to determine from the current study whether the atrial fibrillation was a new or pre-existing diagnosis. It is also not clear why hypertension should be associated with a reduction in the risk of death at 30 days following a second AMI. Although the literature is not consistent in its findings, most studies have found that hypertension has an adverse effect on prognosis following AMI.[142] It is likely that the prevalence of hypertension is

underestimated in the current study and that those individuals with this recorded diagnosis represent a biased sample, perhaps including those who have been targeted for secondary prevention measures. Again there are no data with which to compare these findings. In general the magnitude of effect of different comorbid diagnoses on survival was greater in younger than in older individuals hospitalised with a second AMI. This finding was similar to that seen in first AMI.

Longer term case fatality

In the current study, comorbid diagnoses again had a marked effect on unadjusted survival and most were associated with a substantial reduction in longer term survival. In the multivariate analyses most comorbid diagnoses were significant predictors of outcome and were associated with an increase in case fatality. As for short term case fatality, heart failure and renal failure were associated with a particularly adverse prognosis. These findings are consistent with first AMI in the current study and with other studies in which these diagnoses have been consistently associated with a poor prognosis in individuals hospitalised with AMI.[90;136-138;144] Hypertension was associated with a decreased risk of death at five years but only in men hospitalised with a second AMI. Hypertension was not a significant independent predictor of long term outcome following a first AMI. Atrial fibrillation increased the risk of death at five years in men and women hospitalised with a second AMI. This contrasted with the effect on 30 day survival where atrial fibrillation was found to have a protective effect. Diabetes had a greater effect on long term survival than on short term survival. As for short term survival, the presence of comorbid diagnoses had a greater impact on prognosis in younger than in older individuals. The effect of different comorbid diagnoses on survival was not consistent between men and women or between different age groups.

12.3.5 Temporal trends in case fatality in men and women following a second AMI

Short term case fatality

In the current study there were modest declines in unadjusted 30 day case fatality in men and women which were smaller than those observed in first AMI. In the multivariate analyses there was a trend towards declining case fatality, though this did not reach statistical significance. The difference in the trends between first and second AMI may reflect the lesser potential to salvage myocardium in patients with prior ventricular damage.

Longer term case fatality

The trends in longer term case fatality following second AMI were more encouraging. In the multivariate analyses there was a significant reduction in the risk of death at five years in men overall and in women aged 65-74 years. These changes were comparable to those declines seen in case fatality following hospitalisation with first AMI.

12.3.6 Summary

In the current study, as expected, the prognosis of men and women following hospitalisation with a second AMI was worse than following a first AMI. Approximately one quarter of individuals died within one month of admission and almost 40% within one year. Unadjusted short and longer term case fatality rates were lower in men than in women. However, differences in age and baseline characteristics explained all of the differences between men and women in short and long term case fatality and sex was not therefore a significant predictor of outcome. Age was the most powerful predictor of outcome, though none of the factors examined had as strong as effect on second AMI survival as on first AMI survival. Socioeconomic deprivation was not a significant predictor of outcome. Comorbid diagnoses in general had an adverse effect on prognosis which again was not as pronounced as in first AMI. There were modest declines in short term case fatality between 1990 and 2000 which did not reach statistical significance in the multivariate analyses. There was however a significant reduction in the risk of death at five years in men overall and in women aged 65-74 years which was similar to the declines observed in longer term survival following a first AMI.

13 OVERALL DISCUSSION AND CONCLUSION

I have described and compared the baseline characteristics and survival of women and also men hospitalised with a first and a second AMI in Scotland between 1990 and 2000. Although there is already a vast literature surrounding the epidemiology of AMI, there are gaps in this literature and limitations exist regarding the generalisation of research findings to men and women in the general population. Studies examining the prognosis of individuals who have experienced an AMI date back to the 1950s. Most studies, however, have focussed on short term survival. Early studies also often focussed exclusively on men. Some later studies included women, but most did not examine characteristics or outcome in men and women separately. There has been a growing awareness in the last ten years that important sex differences in cardiovascular epidemiology exist. Consequently studies have begun to examine and report on baseline characteristics and survival in men and women separately. This is very important because those individuals who experience an AMI represent a priority target group for primary and secondary prevention. In order to reduce the incidence of AMI, we need to have a good understanding of the risk factors as well as the baseline characteristics of the men and women affected. The occurrence of AMI as well as survival following AMI is largely dependent upon the success of population and individual based prevention and treatment strategies. It is therefore crucial to be able to describe these in men and women separately. Over the past ten years there have been dramatic changes in treatment of AMI. Clinical trials provide valuable information but generally on a selected and biased sample of the population. Population based studies are essential to determine whether the benefits realised in clinical trials translate into clinical practice, and how these benefits might affect men and women of different ages.

13.1What is already known

The existing literature provides consistent evidence of an age discrepancy between men and women hospitalised with AMI. It is well known that women are on average six to ten years older than men at the time of presentation with their first AMI. AMI is therefore relatively uncommon in young women compared to young men. The risk of AMI increases dramatically with age and the majority of individuals are over the age of 65 years at the time of presentation with their first AMI. Although an important cause of premature

mortality, especially in men, AMI is occurring in increasingly older individuals. The average age of individuals hospitalised with AMI is increasing steadily in men and in women. Most studies have demonstrated declining incidence rates of first AMI. Such declines have been more clearly established in men than in women in whom reports are conflicting. In terms of baseline characteristics, it is known that both men and women hospitalised with AMI have a higher than expected prevalence rate of hypertension and diabetes when compared to the general population and that the prevalence of these factors is especially high in younger men and women.

There is significant variation in reports of prognosis following AMI. The actual survival figures vary substantially between studies although the majority of studies have shown that short term survival is worse in women compared to men. There is also a growing literature that suggests that the female survival disadvantage is confined to younger women. Longer term survival is less consistent in terms of absolute risk and sex differences. There is clear evidence of declining short term case fatality following hospitalisation with AMI in men and in women.

There are very little population based data available with which to compare the demographic characteristics of these patient cohorts. The current analysis is the only one available that allows the description of the age, sex and socioeconomic characteristics of all individuals from one country that have been hospitalised with a first or second AMI.

13.2 Findings from current study

Between 1990 and 2000, 110,226 individuals were hospitalised in Scotland with a first AMI. 9,664 men and women were hospitalised with a second AMI. This does not represent the total burden of hospitalisation for AMI which would also include individuals with more than two hospitalisations with AMI. Over half of all men and three quarters of women were aged greater than 64 years at the time of their first AMI admission. Individuals hospitalised with a second AMI were significantly older (three years on average) so that by the time of their second AMI over 60% of men and 80% of women were aged 65 years or over. Individuals hospitalised with both a first and a second AMI were more likely to come from more deprived areas than from more affluent areas and this was especially true of younger women.

In terms of baseline characteristics, almost half of all men and women hospitalised with a first AMI had one or more comorbid diagnosis. The prevalence rate of comorbid illness increased with age and younger women had high levels of comorbid illness than younger men. The most commonly recorded conditions were heart failure, hypertension, respiratory disease and diabetes. However the prevalence of different comorbid conditions varied according to age and sex. Individuals hospitalised with a second AMI had an even higher prevalence of comorbid illness. Almost three quarters of men and women hospitalised with a second AMI had one or more comorbid diagnosis. The most commonly recorded diagnoses were similar: heart failure, previous coronary heart disease (excluding AMI), diabetes, hypertension and respiratory disease. As with first AMI, younger women had particularly high levels of comorbid illness compared to younger men. The median time between first and second AMIs was 2.3 years in men and 1.8 years in women. Many of these findings are new, and very few studies have examined the distribution and prevalence of non-cardiac comorbidity in men and women hospitalised with AMI.

The average age of men and women hospitalised with a first and second AMI increased by one to two years between 1990 and 2000. Over the same period, the prevalence of comorbid illness also increased. For both first and second AMI, absolute changes over time were greater in older age groups and the diagnoses that demonstrated the greatest relative increase in prevalence were hypertension, atrial fibrillation and renal failure. No other studies have reported sex specific trends in the prevalence of cardiac and non-cardiac comorbidity in men and women hospitalised with AMI.

AMI hospitalisation rates fell dramatically over the study period, declining by about 30% in individuals hospitalised with a first AMI and by more than 50% in individuals hospitalised with a second AMI. Length of stay also demonstrated substantial declines for individuals hospitalised with both first and second AMIs. The burden placed on the health service in Scotland has consequently fallen between 1990 and 2000. There has however been a dramatic increase in the proportion and number of individuals hospitalised with a first and second AMI who underwent a coronary revascularisation procedure.

In the current study, the prognosis of men and women hospitalised with a first AMI was much worse than indicated by clinical trials. One fifth of patients died within one month of admission and almost one half by five years. Unadjusted survival was substantially better in men than in women. Much but not all of the excess short term risk in women

could be explained by the fact that women were older than men at the time of their first AMI. Women however remained at a 20% increased risk of death at 30 days after adjusting for age and other factors. There was an age sex interaction in short term survival and the excess short term risk seen in women compared to men was greater in younger women. This finding is in keeping with a growing literature that reports similar observations. After excluding early deaths, adjusted longer term case fatality was slightly greater in men than in women. The short term survival advantage seen in men was therefore no longer present. Age was the most powerful predictor of survival in men and women. Socioeconomic deprivation also had a powerful effect on survival, especially on longer term survival, in younger age groups and in men. Most comorbid diagnoses substantially increased the risk of death in the short and longer term. Heart failure, renal failure and cancer had the most powerful effects. Comorbid diagnoses tended to have a greater effect on longer term survival than on short term survival and in younger men and women than in older individuals. Atrial fibrillation and hypertension reduced the risk of death in the short term but not in the longer term. The risk of death at 30 days fell by more than one third in men and a quarter in women between 1990 and 2000. Declines were greater in younger than in older age groups.

In the current study, as expected, the prognosis of men and women following hospitalisation with a second AMI was even worse than the prognosis following a first AMI. Approximately one quarter of individuals died within one month of admission and almost 40% within one year. Unadjusted short and longer term case fatality rates were lower in men than in women. Differences in age and baseline characteristics explained all of the differences between men and women in short and long term case fatality and sex was not a significant predictor of outcome. Age was the most powerful predictor of outcome. Interestingly, none of the factors examined had as strong as effect on second AMI survival as on first AMI survival. Socioeconomic deprivation was not a significant predictor of outcome. Comorbid diagnoses in general had an adverse effect on prognosis which again was not as pronounced as in first AMI. There were modest declines in short term case fatality which did not reach statistical significance in the multivariate analyses. There was however a significant reduction in the risk of death at five years in men overall and in women aged 65-74 years which was similar to the declines observed in longer term survival following a second AMI.

13.3Limitations of data used in current study

The current study has relied on hospital discharge coding to identify cases diagnosed with AMI. Discharge coding has been found to be quite accurate in Scotland. The Information and Statistics Division, Scotland has a Scottish Morbidity Record Standards Unit, which checks a one percent sample of Scottish Morbidity Record 1 forms and compares the information with that recorded in the clinical case notes. In 1994, the accuracy of AMI as a principal diagnosis was 94 percent. The extraction method that was used to identify individuals with a principal diagnosis of AMI is likely to have missed a small number of individuals in whom AMI was coded in a secondary position. During a continuous inpatient stay, individuals may be coded with a number of different diagnostic codes. In the current study the principal diagnosis was based on the last cardiovascular diagnosis in this continuous inpatient stay. This should ensure that individuals, who are diagnosed as chest pain or angina before a definitive diagnosis of AMI is made, are included in the study. It will also ensure that those individuals, who have a non-cardiovascular diagnosis at any point during their admission, are also included in the analysis. It will however exclude those individuals hospitalised with an AMI who are subsequently transferred with a diagnosis of angina. The reason for this is that the AMI data was extracted as part of a larger cardiovascular database that included chest pain and angina as well as AMI. In order to avoid double counting of patients, each individual can be given only one diagnosis. The current study only includes patients admitted to hospital. However very few individuals with a diagnosis of AMI are now managed in the community.[107] A substantial proportion of individuals experiencing an AMI will not survive to reach hospital and these individuals have not been included in the current study.[2] As recording of secondary diagnoses can be poor, co-morbidity in this study was based on both the principal diagnoses recorded in previous admissions, and secondary diagnoses in the index admission. People with milder forms of the comorbid disease, which did not result in admission, might be missed if this condition was not recorded as a secondary diagnosis. This selection bias might therefore overestimate the true impact of the comorbid conditions. A further limitation is that population-based data from hospital discharge at present lacks treatment and clinical detail. There is currently no way of knowing whether an individual received thrombolysis or other pharmacogical therapies. Lastly, though some losses to follow-up might be expected, emigration of people of "pensionable age" from Scotland was less than 2% per decade.[239]

13.4 Remaining deficits in knowledge

I believe that my work has made a number of potentially important new additions to the existing literature regarding sex differences in the epidemiology of AMI, as well as consolidating and confirming existing findings. It has also highlighted the lack of information and data pertaining to particular issues.

There are surprisingly few data describing the baseline characteristics of men and women hospitalised with AMI. Concurrent cardiac diagnoses are well described but non-cardiac diagnoses have been rarely reported. Consequently, it is not easy to assemble a realistic picture of these patients that includes other diagnoses they are likely to have other than their presenting AMI. Sex-specific information is rarely reported, so that when baseline characteristics have been more fully described, it is usually on an aggregate basis.

There is virtually no information available regarding the socioeconomic background of men and women hospitalised with an AMI. Numerous studies have looked at the population prevalence of cardiac risk factors and the relationship between specific risk factors and cardiac outcomes. There is however very little information describing the distribution of socioeconomic factors including distribution of deprivation in population cohorts of men and women hospitalised with AMI. Many of those studies that have attempted to describe the broader socioeconomic circumstances of individuals hospitalised with AMI have excluded women or the elderly, or have looked at men and women together.[75;122-124;207]

Coronary heart disease has evolved considerably over the last decade or so in terms of diagnosis and treatment, as have the risk factors and baseline characteristics of individuals presenting with AMI. Despite this, there is minimal data available describing evolving patient characteristics and changes in risk factors over time.

The health service burden of AMI and coronary heart disease is poorly defined. This may partly reflect a difficulty in making comparisons across different health care systems. It is however surprising how little is known about the contribution of these diagnoses to the total health care burden and whether this has changed over time with the introduction of new therapies and prevention strategies.

In terms of survival, a growing literature has explored potential sex differences following hospitalisation with AMI. Most of this literature has concentrated on short term survival

and studies have adjusted for different baseline factors in their multivariate analyses. This makes comparison across studies difficult. Very few studies have described and examined longer term survival in men and women hospitalised with AMI. An idea that has begun to evolve is the realisation that men and women of different ages who are hospitalised with an AMI are different entities in terms of their baseline characteristics and prognosis. The reasons for this have not yet been well explored. and there are very few studies that have examined the distribution of risk factors and baseline characteristics in these subgroups and have attempted to determine the importance of these factors in the prognosis following hospitalisation. So for example whilst a number of studies have adjusted for diagnoses such as atrial fibrillation in their attempt to quantify sex differences in 30 day survival, very few have examined the effect of these diagnoses on survival in men and women separately. From analyses carried out in the current study it seems highly likely that interaction between different comorbid diagnoses exist and that these interactions will influence prognosis. It also seems clear that comorbid diagnoses may have a different impact upon survival of individuals depending upon their age and sex. Trends in survival following AMI have also been described but it is not clear in which groups the improvements have occurred and if disparities exist why that should be.

Most studies that have explored the epidemiology of AMI have included all AMIs. A relatively small number have looked specifically at first AMI. From the findings of the current study it is clear that the baseline characteristics, survival and prognostic factors differ in individuals presenting with first and second AMIs. It would therefore seem appropriate to examine these groups separately. Whilst there is information available describing the additional risk that previous AMI presents in individuals hospitalised with any AMI, there is virtually no information available describing the characteristics and prognosis of patients presenting with second AMIs.

13.5Further research

Using the existing dataset

Had time not been a constraining factor then some of gaps that have been identified could have been explored further using the existing dataset. It would be possible to explore the prevalence of comorbid diagnoses in different socioeconomic groups and to look at the interaction between specific comorbid diagnoses and their relationship to short and longer term survival. The relationship between comorbid diagnoses and survival in men and

women is undoubtedly a complex issue but it is an issue that is amenable to further exploration especially using large datasets that are suitable for subgroup analysis. It would also be possible to look at the role of socioeconomic deprivation in more detail. Socioeconomic deprivation appears to be related to the incidence and survival of individuals hospitalised with AMI. The relationship varies according to age and sex and is different in first and second AMI. It would be interesting to examine some of these issues further in order to gain a better understanding and overview of the role of socioeconomic deprivation and AMI epidemiology. This thesis has explored the epidemiology of first and second AMI. It has not however looked at the small number of individuals who experience more than two AMIs. Whilst these individuals account for a small proportion of all individuals hospitalised with AMI, they make a greater contribution to the number of episodes of AMI and to the total burden arising as a result of AMI. It would be useful to look at these individuals in more detail. The current study has only examined all cause death in the survival analysis. It would be interesting to look at coronary heart disease death as well as all cause death and also to explore the natural history of men and women hospitalised with AMI in terms of future hospitalisations and diagnoses.

With further development of dataset

More accurate and more detailed secondary coding on hospital discharge forms would enable researchers to gain a better understanding of the characteristics of individuals hospitalised with AMI. It would be useful if the coding could incorporate information that would indicate whether the condition is a new or long-standing diagnosis. This would allow researchers to determine the temporal relationship between diagnoses and the importance of these diagnoses to the prognosis of the patient. It would also be valuable to expand the coding of secondary diagnoses to include information on risk factors including smoking, obesity and cholesterol. Such information would allow an ongoing and detailed analysis of these factors to the development and survival from coronary heart disease. It would also allow a more accurate assessment of trends in risk factors and changing characteristics of individuals presenting with coronary heart disease.

It would be useful to routinely record information regarding the results of diagnostic tests for AMI. Development of new, more sensitive tests, such as cardiac troponins and creatine kinase (CK) - MB mass, have meant that it is now possible to identify patients who have had very small infarcts, that would not previously been considered an AMI. This means that people who were formally given a diagnosis of angina pectoris might today be diagnosed as having had a small AMI. The redefinition of myocardial infarction has

implications for individuals, for clinical practice and for the study of the epidemiology of AMI. It is estimated that the new definition for AMI will increase the number of non-ST elevation acute coronary syndromes by about 40%.[6] In theory, widespread use of a standardised definition should allow more valid epidemiological comparisons between different populations and within populations over time. Information regarding the diagnosis of AMI and results of troponin tests will be vital in order to continue monitoring trends in incidence and survival of AMI in the context of a changing diagnostic threshold.

The current study only includes information derived from secondary care. Access to primary care data would be extremely valuable, especially if linked to hospital admission data. This would enable a greater understanding of the predictors of AMI and identification of high risk groups. It would also allow greater exploration of the relationship between different diagnoses and the complex interactions that exist between them.

Information on prescribing in both primary and secondary care would be extremely useful to determine how widely available therapies are prescribed in the general population and whether their use has been associated with a reduction in incidence and case fatality following AMI across the Scottish population. It is important to know whether the benefits seen in clinical trials translate into the general population and also the factors that have contributed to declining incidence and case fatality. A number of studies have attempted to estimate the contribution of different factors, however these are estimates and analysis of real data would be preferable.

Priorities regarding data

Coding of secondary diagnoses is poor. It is clear from the literature that the majority of secondary diagnoses are under-recorded, leading to an underestimation of their prevalence. In order to maximise the potential uses of the Scottish Morbidity Record database there needs to be more accurate and more complete coding of secondary diagnoses on the hospital discharge records. In addition it is apparent that revascularisation procedures are under-recorded in this current study. It is not known whether this has arisen as a result of the extraction process or whether these procedures are under-recorded in the Scottish Morbidity Record data.

Priorities regarding clinical questions

As already mentioned there is scope to gain a better understanding as to the role of socioeconomic deprivation in the epidemiology of coronary heart disease and its association with incidence and survival. Surprisingly few studies have examined these issues in men and women and greater clarity is required.

The importance of comorbid diagnoses and the relationship between different diagnoses in men and women also requires further exploration and clarification. There is a growing interest in the relationship between abnormal renal function and coronary heart disease but surprisingly this issue has not been looked at in men and women separately.

Finally from the findings of this current study and from existing literature it is apparent that younger women represent an especially high risk group in terms of short term case fatality following AMI. The reasons for this are as yet unclear and require further investigation.

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14 Appendix 1

Job Specification

NHS SCOTLAND

Ad hoc Number: IR 2003/00992

Title: Emergency AMI, Chest Pain, Angina & 'Other CHD'

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Background to Record Linkage within ISD

The main linked data set contains linked SMR1, SMR6, SMR4 and Registrar General's death. SMR1 (Scottish Morbidity Records 1) cover all non-obstetric and non-psychiatric discharges from NHS hospitals in Scotland. SMR6 are cancer registration records and SMR4 are mental health inpatient records. All patient records including deaths for each patient are linked together using 'probability matching'. The 'probability matching' algorithm uses all available identifying information (name, date of birth, postcode, hospital patient reference number etc.) to link the records.

Within these 'patient record sets', the SMR1 records are grouped into continuous stays. A continuous stay is a continuous period of time spent as an inpatient or day case in hospital regardless of any transfers between specialties or hospitals. For example, a patient may be admitted with an Acute Myocardial Infarction in a specialty of General Medicine, be transferred to Cardiology then transferred again to Geriatric Assessment before discharge. This single continuous stay would have generated three separate SMR1 discharge records which linkage can bring together.

This linked data set currently contains SMR1, SMR6, SMR4 and death records for the period 1981 onwards and holds data on over 5 million patients with over 20 million contacts within the acute hospital sector.

Accuracy of the data

It is estimated that the probability matching algorithm links the SMR1, SMR4, SMR6 and Registrar General's death records with an accuracy of 98%.

ISD Scotland has a Data Quality Unit that checks a 1% sample of SMR1 forms and compares the information recorded on SMR1/01 with that recorded in the clinical case notes. For example, from the 1998/1999 checks it was found that the accuracy of three digit principal diagnosis and main operation coding are approximately 90% and 91% respectively.

Request Specification – Emergency chest pain, Angina, AMI & 'Other CHD'

1. Define INDEX events

For the period 1986 to 2000 (inclusive) select **emergency** diagnoses **(principal diagnostic position only)** of AMI, Chest Pain, Angina and 'Other CHD' (see table below for diagnostic codes) as defined by last named (of the above) diagnoses in CIS. For example a patient admitted as an emergency for chest pain, transferred as AMI and transferred again with hip fracture will be classified as emergency AMI.

Data number	Principal diagnosis	ICD-9 code (up to 31st March 1996)	ICD-10 code (from 1st April 1996)
1	AMI	410	I21, I22
2	Chest Pain	786.5	R07
3	Angina	411, 413	I20, I24.9
4	Other CHD	412, 414	I23, I24.0-I24.8, I25

All continuous inpatient stays for each diagnosis within this period, 1986-2000 will be included.

The following fields will be included in the final data extract:

the 1st episode of the CIS:

- Link number (to identify same individual patients)
- Month & year of admission
- Month & year of discharge
- Hospital code
- Type of admission - **Emergency only**
- Type of facility
- Specialty
- Length of stay
- Postcode Sector

- Deprivation category 5 (quintiles)
- Deprivation category 7
- Health Board of Residence
- Principal Diagnosis

the 'index' SMR1(s) record

- Month & year of admission
- Month & year of discharge
- Hospital code
- Age
- Sex
- Type of admission
- Type of facility
- Specialty
- Length of stay
- Postcode Sector
- Deprivation category 5 (quintiles)
- Deprivation category 7
- Health Board of Residence
- Diagnoses 1-6
- Operations 1-4
- Month & year of main operation
- Year of admission

Markers for the index record

- marker for a diagnosis of diabetes on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of cancer on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of respiratory on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of cerebrovascular on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of PVD on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of Atrial fibrillation on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of Hypertension on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of Renal failure on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of Heart failure on diagnosis positions 2-6 of index record (see table below for codes)
- marker for a diagnosis of Cardiogenic shock on diagnosis positions 2-6 of index record (see table below for codes)

Diagnosis in	Variable	ICD-9 code	ICD-10 code

positions 2-6 of index record	**name**		
Diabetes	comorb01	250	E10-E14
Cancer	comorb02	140-208	C00-C99
Respiratory	comorb03	480-496	J10-J18, J40-J47
Cerebrovascular disease	comorb04	430-438	I60-I69, G45
Peripheral vascular disease	comorb05	440-448	I70-I78
Atrial fibrillation	comorb06	427.3	I48
Essential hypertension	comorb07	401	I10-I13
Renal Failure	comorb08	584-586	N17-N19
Heart failure	comorb09	425.4, 425.5, 425.9, 428.0, 428.1, 428.9, 402	I50, I42.0, I42.6, I111.0
Cardiogenic shock	comorb10	785. 5	R57.0

the last episode in the CIS

- Month & year of admission
- Month & year of discharge
- Hospital code
- Type of admission
- Type of facility
- Specialty
- Length of stay
- Diagnoses 1-6
- Health Board of Residence

14.1.1.1.1.1.1.1 *Summary details (within CIS)*

- Marker for CABG operation in continuous stay (see table below for codes)
- Date of CABG operation in continuous stay
- Marker for PTCA operation in continuous stay (see table below for codes)
- Date for PTCA operation in continuous stay
- Marker for Angiography operation in continuous stay (see table below for codes)
- Date for Angiography operation in continuous stay

Operation	**OPCS3 code (up to 31st Dec 1988)**	**OPCS4 code (from 1st Jan 1989)**
CABG	304.3	K40-K46
PTCA	884.5, 884.9	K49, K50.1
Angiography	306	K63, K65

- Total Length of continuous stay (Date of Admission on 1st episode – Date of Discharge on last episode
- Marker to denote if patient was discharged dead using discharge code from last episode in the continuous stay.

2. Prior Events

Screen back to1981 for the following in a different continuous stay from the index event:

a) total number of episodes with AMI in principal position (elective, emergency and transfer together)
b) total number of episodes with angina in principal position (elective, emergency and transfer together)
c) total number of episodes with chest pain in principal position (elective, emergency and transfer together)
d) total number of episodes with other CHD in principal position (elective, emergency and transfer together)
e) total number of episodes with AMI in principal position (elective, emergency and transfer together) within five years of index event
f) total number of episodes with angina in principal position (elective, emergency and transfer together) within five years of index event
g) total number of episodes with chest pain in principal position (elective, emergency and transfer together) within five years of index event
h) total number of episodes with other CHD in principal position (elective, emergency and transfer together) within five years of index event
i) total number of episodes with AMI in principal position (elective, emergency and transfer together) within ten years of index event
j) total number of episodes with angina in principal position (elective, emergency and transfer together) within ten years of index event
k) total number of episodes with chest pain in principal position (elective, emergency and transfer together) within ten years of index event
l) total number of episodes with other CHD in principal position (elective, emergency and transfer together) within ten years of index event.

m) Marker to denote if patient had any of the diagnoses specified in the table below within 5 years of index event – flag (0-no, 1-yes). Diagnosis could be in any position.

Prior admission within 5 years	ICD-9 code	ICD-10 code
Diabetes	250	E10-E14
Cancer	140-208	C00-C99
Respiratory	480-496	J10-J18, J40-J47
Cerebrovascular disease	430-438	I60-I69, G45
Peripheral vascular disease	440-448	I70-I78
Essential hypertension	401	I10-I13
Atrial fibrillation	427.3	I48
Other forms of heart disease	415-427 429	I26-I51
Heart failure	425.4, 425.5, 425.9, 428.0, 428.1, 428.9, 402	I50, I42.0, I42.6, I111.0
Renal Failure	584-586	N17-N19
Cardiogenic shock	785.5	R570

3. **Prior or secondary Events**

Marker to denote if patient had specified diagnosis in the 5 years prior to the index record or in diagnostic positions 2-6 of the index record – flag (0-no, 1-yes). Prior diagnoses could be in any position. See table below for codes.

Prior admission within 5 years or secondary diagnosis	**Variable name**	**ICD-9 code**	**ICD-10 code**
Diabetes	coprior01	250	E10-E14
Cancer	coprior02	140-208	C00-C99
Respiratory	coprio03	480-496	J10-J18, J40-J47
Cerebrovascular disease	coprio04	430-438	I60-I69, G45
Peripheral vascular disease	coprio05	440-448	I70-I78
Atrial fibrillation	coprio06	427.3	I48
Essential hypertension	coprio07	401	I10-I13
Renal Failure	coprio08	584-586	N17-N19
Heart failure	coprio09	425.4, 425.5, 425.9, 428.0, 428.1, 428.9, 402	I50, I42.0, I42.6, I111.0
Cardiogenic shock	coprio10	785.5	**14.1.1.2 R570**

4. Subsequent Events (different CIS)

a) Count of the number of episodes after the index continuous stay with a principal diagnosis of AMI, chest pain, Angina or other CHD.

AMI

- Count of all episodes for AMI after the index cis.
- Date of first episode for AMI after the index cis.

Chest pain

- Count of all episodes for chest pain after the index cis.
- Date of first episode for chest pain after the index cis.

Angina

- Count of all episodes for Angina after the index cis.
- Date of first episode for Angina after the index cis.

Other CHD

- Count of all episodes for other CHD after the index cis.
- Date of first episode for other CHD after the index cis.

b) Marker to denote if patient had specified operations after the index continuous stay and the date of the operation. If patient had more than operation of the same type the date of the first operation will be provided.

CABG (codes as before)

- Marker to denote if patient had a CABG operation after the index cis.
- Date of CABG operation.
- Number of days between date of admission on index record and date of CABG operation.

PTCA (codes as before)

- Marker to denote if patient had a PTCA operation after the index cis.
- Date of PTCA operation.
- Number of days between date of admission on index record and date of PTCA operation

Angiography(codes as before)

- Marker to denote if patient had an Angiography operation after the index cis.

- Date of angiography operation.
- Number of days between date of admission on index record and date of angiography operation

c) Other subsequent events and time to. Markers to denote if the patient had specified principal diagnoses and the time to these diagnoses.

- Marker to denote if patient had an episode with a diagnosis of Heart failure after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent heart failure episode.
- Marker to denote if patient had an episode with a diagnosis of Cerebrovascular disease after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent cerebrovascular disease episode.
- Marker to denote if patient had an episode with a diagnosis of atrial fibrillation after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent atrial fibrillation episode
- Marker to denote if patient had an episode with a diagnosis of peripheral vascular disease after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent peripheral vascular disease episode
- Marker to denote if patient had an episode with a diagnosis of lung cancer after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent lung cancer episode.
- Marker to denote if patient had an episode with a diagnosis of breast cancer after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent breast cancer episode.
- Marker to denote if patient had an episode with a diagnosis of large bowel cancer after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent large bowel cancer episode.
- Marker to denote if patient had an episode with a diagnosis of prostate cancer after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent prostate cancer episode
- Marker to denote if patient had an episode with a diagnosis of oesophageal cancer after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent oesophageal cancer episode
- Marker to denote if patient had an episode with a diagnosis of gastric cancer after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent gastric cancer episode
- Marker to denote if patient had an episode with a diagnosis of cancer after the index cis (0-no, 1-yes).
- Number of days between date of admission on index record and date of admission for first subsequent cancer episode

- Marker to denote if patient had an episode with any other diagnosis after the index cis (0-no, 1-yes).
- Date of first diagnosis after the index cis.

Diagnostic codes to be used are provided in the table below.

Diagnosis	**ICD-9 code (up to 31st Mar 1996)**	**ICD-10 code (from 1st Apr 1996)**
Heart failure	425.4, 425.5, 425.9, 428.0, 428.1, 428.9, 402	I50, I420, I426, I110
Cerebrovascular disease	430-438	I60-I69, G45
Atrial fibrillation	427.3	I48
Peripheral vascular disease	440-448	I70-I78
Lung Cancer	162	C33, C34
Breast Cancer	174	C50
Large Bowel Cancer	153-154	C18
Prostate Cancer	185	C61
Oesophageal Cancer	150	C15
Gastric Cancer	151	C16
Any Cancer	140-208	C00-C99
Any other diagnosis	Any ICD9 code except those listed above	Any ICD10 code except those listed above

d) Subsequent non-fatal event.
- Marker to denote if the patient had a subsequent principal diagnosis of AMI and/or a PTCA operation and/or a CABG operation (codes as before).
- Number of days between date of admission on index record and date of admission of subsequent non-fatal event.

e) Subsequent events within 5 and 10 years of index admission
- Marker to denote if patient had a subsequent AMI admission diagnosis (codes as before) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of admission of first subsequent principal AMI diagnosis (codes as before).
- Marker to denote if the patient had a subsequent AMI diagnosis (codes as before) either fatal or non-fatal within 5 years of date of admission of index record.

- Number of days between date of admission on index record and date of subsequent non-fatal or fatal AMI diagnosis.
- Marker to denote if the patient had a subsequent fatal AMI diagnosis (codes as before) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of subsequent fatal AMI diagnosis
- Marker to denote if the patient had a subsequent CABG or PTCA operation (codes as before) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of subsequent CABG or PTCA operation.
- Marker to denote if the patient had a subsequent non-fatal event (definition as above) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of subsequent non-fatal event.
- Marker to denote if the patient had a subsequent AMI diagnosis (codes as before) or died (any cause) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of admission/death of first subsequent principal AMI diagnosis (codes as before) or death (any cause).
- Marker to denote if the patient had a subsequent AMI diagnosis (codes as before) or had a cerebrovascular event or died (any cause) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of admission/death of first subsequent principal AMI diagnosis (codes as before) or cerebrovascular event or death (any cause).
- Marker to denote if the patient had a subsequent AMI diagnosis (codes as before) or had a revascularisation (CABG or PTCA) or died (any cause) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of admission/death of first subsequent principal AMI diagnosis (codes as before) or revascularisation (CABG or PTCA) or death (any cause).
- Marker to denote if the patient had a subsequent AMI diagnosis (codes as before) or cerebrovascular event or had a revascularisation (CABG or PTCA) or died (any cause) within 5 years of date of admission of index record.
- Number of days between date of admission on index record and date of admission/death of first subsequent principal AMI diagnosis (codes as before) or cerebrovascular event or revascularisation (CABG or PTCA) or death (any cause).

Repeat the 5 year markers for 10 years.

f) Death information as at 31st December 2001.

- Death marker (0-no, 1-yes) as at 31st December 2001
- Month & year of death
- Cause of death
- Number of days to death or censor. Censor date is 31st December 2001.
- Markers to denote if the patient died of the specified primary causes of death – flag (0-no, 1-yes). See table below for codes:

Prior admission within 5 years or secondary diagnosis	**Variable name**	**ICD-9 code**	**ICD-10 code**
Acute myocardial infarction	dthcat01	410	I21, I22
Other Coronary Heart Disease	dthcat02	411-414	I20, I23, I24, I25
Heart failure	dthcat03	425.4, 425.5, 425.9, 428.0, 428.1, 428.9, 402	I50, I420, I426, I110
Cancer	dthcat04	140-208	C00-C99
Lung Cancer	dthcat05	162	C33, C34
Breast Cancer	dthcat06	174	C50
Large Bowel Cancer	dthcat07	153-154	C18
Prostate Cancer	dthcat08	185	C61
Gastric Cancer	dthcat09	151	C16
Oesophageal Cancer	dthcat10	150	C15
Respiratory Disease	dthcat11	480-496	J10-J18, J40-J47
Cerebrovascular Disease	dthcat12	430-438	I60-I69, G45

g) Patient's status at 30 days, 1 year, 5years and 10 years.

- Marker to denote if the patient was dead or alive/censored within 30 days of date of admission of index record (0-alive/censored, 1-dead)
- Marker to denote if the patient was dead or alive/censored within 1 year of date of admission of index record (0-alive/censored, 1-dead)
- Marker to denote if the patient was dead or alive/censored within 5 years of date of admission of index record (0-alive/censored, 1-dead)
- Marker to denote if the patient was dead or alive/censored within 10 years of date of admission of index record (0-alive/censored, 1-dead)

5. Information added in SPSS

In addition to the fields extracted in FORTRAN the following fields were created in SPSS and added to the file.

AMI

- Number of days between date of admission (index) and first episode for AMI after the index cis.

Chest pain

- Number of days between date of admission (index) and first episode for chest pain after the index cis.

Angina

- Number of days between date of admission (index) and first episode for Angina after the index cis.

Other CHD

- Number of days between date of admission (index) and first episode for other CHD after the index cis.

Any subsequent admission

- Number of days between date of admission (index) and first subsequent episode after the index cis.

Other fields

- Marker to denote which condition.

  1 = AMI

  2 = Chest Pain

  3 = Angina

  4 = Other CHD

- Counter within each of the 4 data sets