

**SERVICE USE AND SOCIOECONOMIC STATUS EXAMINATION IN  
HEART FAILURE (SUSSEX-HF) – A SINGLE-CENTRE, RETROSPECTIVE STUDY  
TO INVESTIGATE PATTERNS OF HEALTH INEQUALITY IN A CONTEMPORARY  
COHORT OF PATIENTS HOSPITALIZED WITH HEART FAILURE.**

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**A THESIS PRESENTED FOR THE DEGREE OF MD(RES) AT IMPERIAL COLLEGE LONDON,  
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## **ABSTRACT**

**OBJECTIVES:** To establish the extent to which health inequality operates in a cohort of patients admitted with heart failure to a single centre serving an elderly population.

**DESIGN:** Historical cohort study of patients admitted with a first coded presentation of heart failure.

**SETTING:** Single district general hospital on the South-East coast of England.

**PARTICIPANTS:** 883 patients admitted with a coded diagnosis of heart failure in the first or second diagnostic position.

**MAIN OUTCOME MEASURES:** Mortality, readmission rates, and proportion of patients receiving recommended care.

**RESULTS:** This was an elderly cohort, with a median age of 82.4 years. Just over half were women (51.3%), who tended to be older than men (84 vs. 80 years). Crude mortality rates at 30 days and 1 year were 17% and 38% respectively. All cause readmission at 30 days occurred in 21.3% of cases and the rate of heart failure readmission within 1 year was 35%.

The most deprived patients were younger at the time of admission than those from less deprived areas (77.9 vs. 82.3 years [ $p=0.036$ ]). No association was found between deprivation and mortality but rates of readmission at 30 days were higher in more deprived quintiles ( $p=0.01$ ).

Rates of prescription of beneficial medications were not different between quintiles of deprivation, but significantly lower rates of B-blocker and aldosterone antagonist prescription were observed in the elderly. Comorbidity and left ventricular ejection fraction were also associated with differential rates of prescribing. Provision of echocardiography and documentation of ejection fraction was strongly associated with age as was provision of specialist follow-up.

**CONCLUSIONS:** Hospitalization for heart failure appears to occur at an earlier age in individuals from more deprived areas, but subsequent specialist management is heavily dependent on age, not level of deprivation. This may contribute to poorer outcomes in older individuals admitted with heart failure.

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## **DECLARATION**

This thesis was composed by Dr Paul Michael Haydock and relates to a study designed and performed by him. It is an original piece of work and has not been accepted in any previous application for a degree. All quotations contained herein have been appropriately distinguished and all sources of information have been acknowledged.



## **ACKNOWLEDGEMENTS**

My thanks go to my supervisors, Professor Martin Cowie and Dr Hugh McIntyre, for their support, guidance, and patience. Each has taught me a great deal and I shall be forever in their debt for the opportunities that they have provided. I have no doubt that my future endeavors will be influenced by their rationality and enthusiasm in equal measure.

I am also grateful to Takeda (UK) for their financial support in funding my research and to all my colleagues at the Conquest Hospital, Hastings, who helped to make my time there enjoyable as well as rewarding.

Finally, I would like to thank Alan, without the support of whom none of this would have been possible.

## **COMMONLY USED ACRONYMS AND ABBREVIATIONS**

<b>ACEi</b>	Angiotensin Converting Enzyme Inhibitor
<b>AF</b>	Atrial Fibrillation
<b>ALP</b>	Alkaline Phosphatase
<b>ALT</b>	Alanine Aminotransferase
<b>APC</b>	Admitted Patient Care
<b>ARB</b>	Angiotensin II Receptor Antagonist (Blocker)
<b>BNP</b>	B-type Natriuretic Peptide
<b>BHF</b>	British Heart Foundation
<b>CCST</b>	Certificate of Completion of Specialist Training
<b>CRT-D</b>	Cardiac Resynchronization Therapy + Implantable Cardioverter Defibrillator
<b>CRT-P</b>	Cardiac Resynchronization Therapy (pacing function only)
<b>ESHT</b>	East Sussex Hospitals' NHS Trust
<b>Hb</b>	Haemoglobin concentration
<b>HES</b>	Hospital Episodes Statistics
<b>HFNEF</b>	Heart Failure with Normal Ejection Fraction
<b>ICD</b>	Implantable Cardioverter Defibrillator
<b>ICD-10</b>	International Classification of Diseases 10 <sup>th</sup> edition
<b>IHD</b>	Ischaemic Heart Disease
<b>IMD 2007</b>	Index of Multiple Deprivation 2007
<b>IQR</b>	Inter-quartile range
<b>JOE</b>	The electronic patient records system of Conquest Hospital (not an acronym)

<b>LSOA</b>	Lower layer Super Output Area
<b>LV</b>	Left Ventricle
<b>LVEDD</b>	Left Ventricular End Diastolic Diameter
<b>LVEF</b>	Left Ventricular Ejection Fraction
<b>MCV</b>	Mean Corpuscular Volume
<b>NHS</b>	National Health Service
<b>NICE</b>	National Institute of Health and Clinical Excellence
<b>NYHA</b>	New York Heart Association
<b>ONS</b>	Office for National Statistics (UK)
<b>PAS</b>	Patient Administration System
<b>RAAS</b>	Renin-Angiotensin-Aldosterone System
<b>SD</b>	Standard Deviation
<b>SES</b>	Socioeconomic Status
<b>U&amp;E</b>	Urea and Electrolytes
<b>UK</b>	United Kingdom
<b>WCC</b>	White Cell Count

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## **1. INTRODUCTION**

This thesis is an examination of the operation of health inequality in a contemporary UK cohort of individuals with the syndrome of heart failure. Previous work, both international and UK based, has demonstrated evidence for the existence of inequalities in several heart failure outcomes. Several themes dominate the literature and the most striking are for inequality related to differences in age, gender and various measures of socioeconomic status. I will, in this thesis, address these three factors by reviewing the existing evidence and examining these complex relationships in a well described, contemporary heart failure cohort. I will begin, however, with an introduction to health inequality and the syndrome of heart failure in order to provide a context for what follows.

## **2. THE CONCEPT OF HEALTH INEQUALITY**

Health inequality is difficult to define[1], and yet it has been the focus of extensive research in the last quarter of the 20<sup>th</sup> Century and the beginning of the new millennium[2-4]. An attempt to review the literature on the subject in its entirety is beyond the scope of this thesis, but an understanding of the concepts involved and the evolution of health inequalities research in its historical context is essential to understand both the questions that this thesis will ask and the conclusions that it will suggest.

Inequality exists in many forms and as an entity it is familiar to the casual observer.

The Cambridge Dictionary defines it thus:

“A situation in which there is no equality or fair treatment in the sharing of wealth or opportunities between different groups in society”[5]

and this captures the essence of the usual meaning in the context of health.

Fundamental to appreciating health inequality is to understand that the definition of inequality depends upon the fact that human beings can be categorized into different groups based on societal norms. So, it is apparent that inequality exists to some extent as a product of the very fact that differences exist between individuals[6].



Differences between individuals exist at the genetic level to give rise to distinct phenotypes – some of which will be grouped together on the basis of the interaction between these phenotypes and the environment and society. Therefore, when health inequality is investigated and discussed it is best qualified by a description of the grouping variable being used to define the basis of the inequality e.g. gender, race, class etc.

Because the determination of certain of these groups is ultimately dependent upon immutable genetic differences between individuals, it is to be expected that some differences in health and health outcomes are unavoidable facts of biology. Where this is true, inequality – “un-equalness” – should not concern us. Whitehead argues that “a situation where everyone in the population has the same level of health, suffers the same type and degree of illness, and dies after exactly the same lifespan” is neither “achievable nor desirable”[7], and most would agree with this. Clearly, nowhere is this inevitable variation more obvious than when considering individuals at different stages of the life-course – a sense of unfairness is an unlikely reaction to the fact that a 30 year old is less likely to suffer a stroke than an 80 year old.

Such fatalistic thinking, however, can itself lead to inequality. If it is accepted that some health outcomes are more common in certain defined groups then a situation where beneficial therapies are withheld might be generally tolerated by society on the basis that higher rates of the health outcome are to be expected[8, 9]. In the era of preventative medicine, being fair and just requires a great effort on the part of governments, health services and individual practitioners[10].

Nevertheless, there is a general acceptance that inequality can exist as a perfectly legitimate entity, insofar as unequal outcomes are determined by factors which are not fundamentally unjust. Clearly, the determination of what differences are avoidable or unnecessary requires a judgment made on the basis of the values on which the society in which the inequality operates are founded. For these reasons it is necessary to be precise when considering the literature on this subject as conclusions regarding observed inequalities must be viewed through the lens of the social model and political ideology operating in the population being studied[11].

This thesis aims to explore inequalities in the management of chronic heart failure in a single UK secondary care setting, and to what extent differences in socioeconomic status determine outcomes. What follows will include an introduction to the syndrome of heart failure and the various, evidence based interventions known to improve prognosis and reduce readmission. I will also address the specific historical literature on inequality in heart failure, before outlining the methods of the SUSSEX-HF study and presenting its results. Finally, I will present my conclusions and recommendations, based on the results in the context of previously published data, as well as addressing the limitations of the study.

### **3. THE SYNDROME OF CHRONIC HEART FAILURE**

#### **3.1. PATHOPHYSIOLOGY**

##### **3.1.i. HOW DOES HEART FAILURE START?**

Current concepts regarding the pathogenesis of heart failure involve the idea of an “index event”. This is most easily conceptualized as a discrete, definable insult affecting the structure or function of the heart. A familiar example of such an event in clinical practice is acute myocardial infarction, in which the death of an area of myocardium leads to an impairment of ventricular function as that area is rendered non contractile[12].

Such events clearly occur and lead to heart failure. However, the “index event” is often less readily identifiable and the development of left ventricular systolic dysfunction may be a chronic, insidious process which at some point tips the balance towards the development of the heart failure syndrome. Examples of these “index events” would include systemic hypertension leading to pressure overload[13], progressive valvular heart disease leading to volume overload, chronic hyperglycaemia in diabetes resulting in structural changes to the myocardium or even expression of mutated genes to produce an abnormal myocardial phenotype[14-16].

### **3.1.ii. THE CONSEQUENCES OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION**

Left ventricular dysfunction results in the activation of mechanical and biochemical homeostatic mechanisms designed to compensate for a reduction in cardiac output. Whilst these mechanisms initially produce their required effect of maintaining tissue perfusion, they are ultimately maladaptive and result in the development of heart failure[17]. The progression of heart failure is determined by a process of left ventricular remodeling in response to prolonged exposure to the maladaptive internal milieu consequent on the activation of various neurohormonal pathways[18, 19]:

#### **a. Renin-angiotensin-aldosterone System**

Decreased renal perfusion as a consequence of decreased cardiac output results in the secretion of renin from the juxtaglomerular apparatus. Concurrently, production of angiotensinogen is increased by the liver and there is, thus, an increase in circulating angiotensin I. The action of the angiotensin converting enzyme (ACE) in the lungs converts angiotensin I into the effector hormone angiotensin II. This molecule is a highly potent vasoconstrictor acting on the efferent renal arterioles and the systemic arteriolar bed via activation of the sympathetic nervous system and stimulation of endothelin release from the vasculature. Angiotensin II also stimulates aldosterone secretion from the adrenal cortex, promoting salt and water retention (and potassium loss)[20, 21]. High levels of anti-diuretic hormone (ADH / vasopressin) are also seen in heart failure, especially in those treated with diuretics and some of this increased secretion is due to direct effects of angiotensin II on the pituitary[22].

Both angiotensin II and aldosterone have direct effects on cardiac myocytes which influence ventricular remodelling. Angiotensin II causes myocyte hypertrophy and fibrosis[23], whilst aldosterone results in apoptosis of myocytes as well as fibrotic changes[24].

#### **b. Sympathetic Nervous System**

Angiotensin II stimulates release of noradrenaline (norepinephrine) from sympathetic nerve terminals and inhibits vagal tone. The sympathetic nervous system is also directly stimulated by baroreceptors in response to a fall in cardiac output. Blood pressure is, consequently, raised by peripheral vasoconstriction and heart rate rises, with concomitant increased myocardial oxygen demand. Prolonged exposure has a toxic effect on the myocardium, leading to cell death[25]. Down-regulation of heart  $\beta_1$  receptors in response to continuous stimulation does not appear to be effective at preventing autonomic dysregulation. To compound the situation further, sympathetic activity stimulates the renin-angiotensin-aldosterone system (RAAS) as part of a positive feedback loop[26].

#### **c. Natriuretic Peptides**

Wall stress in the atria and ventricles is increased in heart failure by a combination of increased preload and structural changes to the chamber walls. Stretching of the atrial and ventricular walls results in the secretion of ANP (atrial natriuretic peptide) and BNP (brain / b-type natriuretic peptide) respectively. These hormones act to promote vasodilatation and, as the names suggest, natriuresis[27]. In such, they are

antagonistic to the RAAS and the sympathetic nervous system but are overwhelmed by their activity in heart failure.

Assays are available for the detection of BNP and its inactive N-terminal cleavage fragment (NT-proBNP), which can be helpful in identifying cases of heart failure where there is diagnostic uncertainty[28].

#### **d. Cytokines**

Heart failure is an inflammatory state. Transgenic mice, bred to over-express tumour necrosis factor alpha (TNF- $\alpha$ ) in cardiac myocytes develop a heart failure syndrome as a result of myocarditis and ventricular dilatation[29]. Levels of TNF- $\alpha$ , interleukin 1 (IL-1) and interleukin 6 (IL-6) are elevated in heart failure and can result in myocyte hypertrophy and apoptosis[30]. These circulating cytokines not only affect the heart but are felt to be responsible for the cachexia associated with advanced heart failure[31].

#### **The End Result**

All of these interlinked systems act on a heart with systolic left ventricular impairment to influence adverse remodelling. The heart itself is dilated in an attempt to increase ventricular pre-load – the Frank-Starling mechanism[32] – and these various neurohormonal mechanisms influence apoptosis, dissolution of myocyte bridging collagen struts, myocyte hypertrophy, and increased production of the interstitial matrix[33].

Uncontrolled adverse remodelling leads inexorably to the development of a dilated, globular ventricle and progressive pump failure. Structural changes, combined with the abnormal internal milieu, also markedly increase the propensity for malignant dysrhythmia – both atrial[34] and ventricular[35].

### **3.I.iii. HEART FAILURE WITH NORMAL EJECTION FRACTION (HFNEF)**

The clinical presentation of HFNEF can be identical to that of heart failure with systolic left ventricular dysfunction. However, as an entity it has proved difficult to study in the real world as a clear-cut diagnosis is difficult without invasive pressure-volume relationship measurements – ideally available for both before and after the onset of the heart failure syndrome[36]. The quest continues to find a reliable and reproducible echocardiographic surrogate measure for the phenomenon, though assessment of left ventricular diastolic function and left atrial size are recommended in establishing the diagnosis[37].

The pathophysiology of the condition is typified by hypertrophy of myocytes and excessive fibrosis. This situation results in ‘stiffening’ of the left ventricle in diastole and a lack of distensibility, with consequent abnormal relaxation filling of the chamber. Well recognised causes are hypertension, chronic ischaemia and diabetes. Pressure overload hypertrophy as a result of aortic stenosis is also a prevalent causal factor[38, 39].

### **3.II. DIAGNOSIS**

Heart failure is a triad of dyspnoea, fatigue and fluid retention and patients presenting with complaints of decreased exercise tolerance or with a syndrome of fluid retention should be considered as potential cases[40, 41]. Symptoms, however, may be non-typical and include dizziness, confusion, anorexia, abdominal bloating or nocturia[42]. Often, a careful history and examination will uncover the more typical signs and symptoms of heart failure.

Various models have been employed to diagnose heart failure in the research setting and in clinical practice. Commonly cited examples are the Framingham Criteria[43] and the Boston Criteria[44]. Such models rely on features of a patient's history, examination findings and the appearances of plain chest radiography, and have been shown to have high levels of specificity and moderate levels of sensitivity for identifying persons with definite heart failure[45]. International guidelines for the diagnosis of heart failure stipulate that typical symptoms and signs should be present in combination with objective evidence of cardiac dysfunction – most commonly determined by echocardiographic assessment[41, 46].

Where symptoms and signs are present, the following tests are recommended by the UK National Institute for Health and Clinical Excellence (NICE), to either rule out common masquerading conditions or confirm heart failure and identify the underlying aetiology[40]:



- 12-lead surface electrocardiogram (ECG).
  - Where the ECG is normal, heart failure due to left ventricular systolic dysfunction is highly unlikely.
  - Where the ECG is abnormal it may provide clues to the underlying aetiology of the heart failure e.g. evidence of previous myocardial infarction or left ventricular hypertrophy.
- Chest radiograph taken in the postero-anterior projection.
  - May demonstrate cardiomegaly or pulmonary venous congestion but is most useful to exclude significant lung pathology.
- Blood analyses:
  - Serum electrolytes, urea and creatinine.
  - Full blood count.
  - Thyroid function tests.
  - Liver function tests including albumin.
  - Fasting glucose and lipid profile.
  - Assay of BNP or NT-proBNP.
- Urinalysis for proteinuria and glycosuria
- Cardiac imaging by echocardiography.
  - Information should be provided on the structure and function of all four cardiac chambers, all valves and the pericardium. If such information cannot be provided then alternative methods of cardiac imaging may be required (cardiac magnetic resonance imaging [cMRI] or gated radionuclide scanning).

### **3.III. EPIDEMIOLOGY**

Chronic heart failure represents a major burden of disease, both for society and the individual[47]. The overall 5 year mortality is estimated to be in the region of 60%[48] and UK data suggest that the 6 month mortality is in the region of 30%, with 40% of patients not surviving at 18 months following the initial diagnosis[49].

The impact of the syndrome in health economic terms is profound and estimates from the early years of the 21<sup>st</sup> Century put the percentage of all healthcare spending on heart failure in developed nations at somewhere between 1% and 2% per annum[50]. This figure is set to increase over time – predictions made in 2000 for the prevalence of heart failure by 2020 estimated a 31% increase in men and a 17% increase in women, largely as a consequence of the ageing population as a whole[51]. Overall prevalence is approximately 2%, but this rises markedly with age, and prevalence in those over 85 may be as high as 15%[52].

Life expectancy is markedly reduced in heart failure and mortality is especially high in the first year following diagnosis – estimated at 20–30%[53]. Overall in-hospital mortality for patients presenting with an acute heart failure syndrome is around 10%, but cardiogenic shock has a considerably poorer outlook [54]. Of all heart failure patients who do survive to discharge 1 in 4 will be re-admitted within 12 weeks[55], unless they are entered into a good chronic disease management programme[56].

The bulk of the economic burden of heart failure is consequent on hospital in-patient care – 60% in the most recently available costing analysis for the UK National Health Service (figure 1)[57] – and, predicting increased prevalence at the rates quoted, estimates are for a translation into increases in hospitalizations of 34% in men and 12% in women by 2020. Hospital stays are long - 9.5 days on average – and around a third of patients will be re-hospitalized within 12 months[49].

### **3.IV. DEFINING HEART FAILURE**

Despite these statistics, one of the difficulties of working in this area is that, as outlined above, heart failure itself remains difficult to define and quantify[58]. Specific guidelines on the diagnosis of heart failure are available from consensus documents published by the European Society of Cardiology and the American Heart Association and both agree that the diagnosis relies on clinical assessment coupled with objective evidence of cardiac dysfunction[41, 46, 59]. In the UK, guidance is issued by the National Institute for Health and Clinical Excellence (NICE), which specifically makes the point in its second paragraph that: “There is no single diagnostic test for heart failure...” [60].

Such reliance on clinical diagnosis introduces an element of subjectivity which does not sit well in the arena of hard science. This is made all the more difficult by the fact that, until very recently, most of the available data on heart failure has come from trials where only patients with markedly reduced left ventricular ejection fraction (LVEF) were included (‘systolic heart failure’). Up to date guidelines recognise that

the syndrome is equally common where the LVEF is preserved above a 'normal' level of 45 – 50% ('diastolic heart failure' or 'heart failure with normal ejection fraction' [HFNEF])[37, 61]. Developing a cohort to accurately and representatively describe the relationship between socioeconomic status and heart failure is therefore a major challenge.

### **3.V. DETERMINANTS OF OUTCOME IN HEART FAILURE**

Many clinical factors have been shown to affect prognosis, the most important being[62-65]:

- Age at first presentation.
- Extent of co-morbidity.
- Severity of symptoms as expressed by New York Heart Association (NYHA) grade[66].
- Severity of LV dysfunction.
- Plasma BNP or NT-proBNP concentration.
- Renal function and plasma sodium.
- Blood pressure at presentation.
- Peak oxygen consumption on cardiopulmonary exercise testing [67].

In addition to these factors, outcomes have been powerfully mediated by markedly improved management of heart failure in the era of evidence-based medicine.

### **3.VI. MODERN MANAGEMENT OF HEART FAILURE**

#### **3.VI.i. DIURETICS**

Most patients with chronic heart failure will require some oral diuretic therapy. These drugs improve symptoms by easing fluid retention[68]. However, their use may exacerbate neurohormonal activation by decreasing circulating blood volume[69]. It is therefore of paramount importance that diuretics are used at the minimum required dose and in conjunction with the disease modifying drugs described below[70]. Periods of increased tendency to fluid retention may require higher dosage of diuretic, but this can be reduced again once control has been re-established[71]. Higher diuretic doses are, therefore, often taken as a proxy of increasing disease severity, where control of the syndrome is more difficult[72, 73]. Many expert patients adjust their daily dose depending on their weight, and disease management programmes, specialist nursing support and patient education help to facilitate this[74].

Commonly used diuretics are shown in table 2. Loop diuretics are considered first line treatment as they are most effective in causing efficient diuresis. A thiazide may be added in cases of resistant fluid retention. Potassium sparing diuretics can be useful in stimulating additional fluid loss, without excessive kaliuresis[41].

Management of heart failure has improved beyond the relief of congestion by diuretics over the last 30 years due to a number of factors:

### **3.VI.ii. DISEASE MODIFYING DRUG THERAPIES**

Improved understanding of pathophysiology has allowed for the increased use of disease modifying drug therapies based on robust clinical trial evidence in systolic heart failure[75]. These include antagonists of the renin-angiotensin-aldosterone axis and selected  $\beta$ -blockers[76-78].

Trials in patients with systolic dysfunction have repeatedly confirmed the benefits of drugs which antagonise the maladaptive neurohormonal mechanisms responsible for the development of the heart failure syndrome as discussed earlier. These drugs modify disease progression and improve prognosis. They are recommended in all patients with heart failure and LV systolic dysfunction who are able to tolerate them[79]. Each agent should be introduced at a low dose and titrated towards target doses with appropriate clinical supervision of symptoms, renal function, blood pressure and side-effects.

A role for the use of these agents in HFNEF is less clear-cut, with large randomised trials of ACE inhibitors and angiotensin receptor blockers being neutral[80, 81]. This emphasizes the importance of echocardiography in the assessment of heart failure to guide optimal management of the syndrome.

### **Angiotensin Converting Enzyme Inhibitors (ACEi)**

ACEi reduce the relative risk of death by 23% and the relative risk of worsening heart failure by 35%[76, 82]. Their beneficial effects have also been seen in asymptomatic LVSD and heart failure post-MI[83, 84].

ACEi work by reducing the production of angiotensin II, a hormone which is directly toxic to myocytes and also results in deleterious peripheral and renal vasoconstriction. Several preparations are licensed for use in heart failure and are shown in table 3.

### **Angiotensin II Receptor Antagonists**

These drugs block angiotensin II at its receptor and consequently reduce the effect of the RAAS. Their clinical effect can be thought of as analogous to ACEi and they share the same side effect profile, except that they do not produce rises in bradykinin and so do not result in troublesome cough.

Of the several agents available, the evidence base is strongest for the use of candesartan in chronic heart failure [85] and valsartan for use in post-MI LV systolic dysfunction [86].

### **$\beta$ -Blockers**

$\beta$ -Blockers shown to have beneficial effects in heart failure, together with their dosing schedules, are listed in table 4[87]. Well designed clinical trials have

demonstrated  $\beta$ -blockers reduce the risk of all cause mortality and death due to heart failure by 25% and 35%, respectively [77, 88-90].

Whilst these long-term benefits are clear, introduction of  $\beta$ -Blockers can result in acute deterioration in the control of the heart failure syndrome due to abrupt changes in haemodynamic compensatory mechanisms. These agents should, therefore, be introduced and up-titrated cautiously, paying close attention to heart rate, blood pressure, fluid status and renal function[91]. If decompensation occurs with the introduction of  $\beta$ -blockade then temporary increases in diuretic dosing may improve the situation. These drugs are generally avoided in the acute setting of decompensation, particularly if the patient is fluid overloaded[92].

Side effects of  $\beta$ -Blockers include bradycardia, heart block and hypotension. Care is needed when considering the use of  $\beta$ -Blockers in patients with peripheral vascular disease and chronic airways disease. However, cardioselective agents are considered safe except in cases of definite asthma[93].

### **Aldosterone Antagonists**

Blockade of the aldosterone receptor is achieved by the use of either spironolactone or eplerenone. Experience with spironolactone in patients with moderate to severe chronic heart failure (NYHA III – IV) has revealed that use of a dose of 25mg – 50mg is associated with a 30% reduction in the relative risk of death[78]. Eplerenone is a more selective aldosterone antagonist, of proven benefit in patients with low ejection fraction and either diabetes or heart failure when used in the post-MI



setting[94]. Evidence has more recently emerged to also support its use in more mild cases of heart failure[95]. Both drugs are capable of precipitating significant hyperkalaemia and renal dysfunction, and changes in fluid status can markedly increase this effect. Consequently, close monitoring of electrolytes, urea and creatinine is required when introducing these drugs and when using them in periods of physiological instability.

### **3.VI.iii. ADJUNCTIVE DRUG THERAPIES**

Other agents are of benefit in specific situations in heart failure, particularly where comorbid conditions – most notably atrial fibrillation – complicate the syndrome.

#### **Digoxin**

Digitalis has been used historically for the treatment of congestive syndromes. There is little evidence to support its modern day use in patients with sinus rhythm but it is often added to conventional treatment in patients who have failed to respond to other therapies[96]. It can be useful in controlling ventricular rates in AF, but  $\beta$ -Blockade is preferable and digoxin is recommended as an 'add in' agent rather than first line therapy[97]. Toxicity can arise easily in the elderly, particularly with intercurrent illness and changes in renal function or electrolytes.

#### **Anticoagulants**

Vitamin K antagonists (VKA) are vital in heart failure complicated by AF to reduce thromboembolic risk. Modern guidelines recommend anticoagulation in AF according to the assessment of stroke risk using the CHA<sub>2</sub>DS<sub>2</sub>-VASc score (see table

5)[98]. Scores  $\geq 2$  are associated with adjusted stroke rates of 2.2% or greater per year and formal anticoagulation with VKA is recommended[99].

Such anticoagulants are also used where intra-cardiac thrombus has been observed on imaging, where there is evidence of left ventricular aneurysm, or in dilated cardiomyopathy with a history of thromboembolism[100].

### **Nitrate and Hydralazine Combinations**

This previously widely used combination oral therapy has been superseded by ACEi. However, benefit has been demonstrated when this combination is added to ACEi / angiotensin II receptor antagonist and  $\beta$ -Blocker in African American populations – probably due to their relative low renin phenotype[101].

### **3.VI.iv. INTEGRATED, MULTI-DISCIPLINARY DISEASE MANAGEMENT[56, 102]**

The Heart Failure Association (HFA) of the European Society of Cardiology (ESC) has published a statement setting out the standards of care that patients with heart failure should expect[103]. Key within these recommendations is the concept that optimal management should involve a seamless system of care throughout the journey of the individual heart failure patient. To achieve this, a high degree of coordination between multiple services within a health care system is required.

Evidence in this area supports the benefits of specialist follow-up and nurse led heart failure services to facilitate the adoption of beneficial lifestyle measures[104], and the safe and timely up-titration of disease modifying drug therapies, as well as improving patient education and self monitoring[105] to prevent recurrent

decompensations[56, 74, 106-121]. The majority of these data are based on small studies and benefits are largely observed in the prevention of recurrent hospitalizations. However, heart failure is a long-term, complex condition requiring close monitoring and rapid access to specialist treatment where the syndrome is unstable. The characteristics of a management programme, recommended by the HFA, clearly demonstrate that a high level of input from care providers with an expert knowledge of the syndrome, and the treatment options available, is a requirement for optimal modern management of the heart failure patient.

### **3.VI.v. IMPLANTABLE DEVICE THERAPY**

Large, randomised trials of implantable devices have demonstrated improvements in both mortality and morbidity in subsets of heart failure patients [122-124].

The benefits observed are the result of one or both of the following:

- Termination of malignant ventricular tachyarrhythmia by implantable cardioverter defibrillator (ICD) technology reduces sudden death[125].
- Correction of electromechanical dyssynchrony by atrio-biventricular pacing – “cardiac resynchronisation therapy” (CRT) – improves pump efficiency.

ICD therapy has been demonstrated to benefit patients with ischaemic heart disease, LVSD and documented evidence of ventricular arrhythmia or previous cardiac arrest[122]. In patients with no documented arrhythmia, ICD implantation is

still recommended for those with LVEF  $\leq$  35% in NYHA class II or III<sup>†</sup>. Current guidelines from the UK National Institute for Health and Clinical Excellence (NICE) state that patients should have a reasonable expectation of survival with good functional status for at least 1 year[126]. NYHA class IV patients are not considered eligible as mortality is more likely to be the result of progressive heart failure than sudden cardiac death. International guidelines suggest that the indications for ICD therapy in patients with non-ischaemic causes of heart failure should be similar[41, 59].

CRT can exist as a pacing system alone (CRT-P) or be combined with ICD technology (CRT-D) for those at particularly high risk of sudden death. Implantation is as for a standard dual chamber (atrio-right ventricular) pacemaker but with a lead to pace the left ventricle introduced via the coronary sinus. Electromechanical dyssynchrony can be corrected by adjusting the timing of pacing by the atrial and ventricular leads. Dyssynchrony is best predicted in a patient with a QRS duration prolonged beyond 120ms (left bundle branch block) and a low EF.

Currently, CRT-P insertion is recommended in patients with LVEF  $\leq$ 35% and QRS duration  $\geq$ 120ms, who have NYHA class III-IV symptoms, despite optimal medical therapy. This is supported by robust trial data demonstrating the effectiveness of such devices in reducing mortality and repeat hospitalisations[124, 127]

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<sup>†</sup> Not within 40 days of an acute myocardial infarction.

## **4. INEQUALITY IN HEART FAILURE**

### **4.1. REASONS TO SUSPECT THE OPERATION OF HEALTH INEQUALITY IN HEART FAILURE**

Where increasing and more complex options are available for the management of a condition, as outlined above for heart failure, then the propensity for phenomena of health inequality is increased[9], as has been demonstrated in ischaemic heart disease, stroke, and cancer[128-131]. The importance of close and careful monitoring in the condition is also an area where differences in care may be observed along socioeconomic lines as in the case of the monitoring of hypertension[132].

There is also reason to believe that socioeconomic factors influence outcome in heart failure based initially on the study of coronary heart disease. The Framingham Heart Study has identified those factors considered to be the classical risk factors for cardiovascular disease[133]. However, subsequent work to identify novel risk factors has resulted in the development of a new, validated model for cardiovascular risk prediction in the UK – QRISK – which includes assessment of an individual's socioeconomic status[134]. The validity of such a tool is not surprising, given the wealth of data which has been accumulated relating socioeconomic status to cardiovascular risk, and this has been well reviewed by Kaplan and Keil[135].

The Whitehall Study demonstrated that mortality rates differed markedly between UK civil servants depending on their grade. Both the original and follow up study, Whitehall II, demonstrated significantly higher rates of ischaemic heart disease in those of lower civil service job grades when compared to each grade above, even allowing for obvious confounders such as smoking[136]. This demonstrates that traditional concepts of health inequality, simply based on wealth and poverty, are not enough to explain the whole story.

This evidence for an increased cardiovascular risk in general, and increased rates of ischaemic heart disease dependent on socioeconomic status lend weight to the proposal that heart failure outcomes might be associated with similar factors.

Estimates from trial and registry data suggest that anywhere between 50% and 70% of heart failure is related to ischaemic heart disease[137]. However, these figures may not be representative of a “wild-type” heart failure population, as contemporary, real world studies of the syndrome are lacking[138].

## **4.II. A CONTEMPORARY OVERVIEW OF HEART FAILURE MANAGEMENT IN THE UK –**

### **THE NATIONAL HEART FAILURE AUDIT.**

The UK National Heart Failure Audit was established in July 2007 with the aim of monitoring the care and treatment of patients admitted to hospital in England and Wales with heart failure. The Audit is commissioned by the Healthcare Quality Improvement Partnership (HQIP), managed by the National Institute for Cardiovascular Outcomes Research (NICOR) at University College London (UCL) and collects data on acute patients discharged from hospitals in England and Wales with a coded diagnosis of heart failure in the primary position, reporting its findings on a yearly basis. Specialist knowledge and support is provided by the British Society for Heart Failure (BSH) and the Audit is part of the National Clinical Audit and Patient Outcomes Programme (NCAPOP).

The ICD-10 codes used to select patients for inclusion in the Audit are the same as those specified in the SUSSEX-HF cohort (table 8), and patients admitted for elective procedures are excluded. Data are now available for 5 one-year periods up to, and including, the data for 2011/12. For this most recent report, participation in the Audit has been mandated by the Department of Health's standard terms and conditions for acute hospitals in England, but not for those in Wales[139].

Participation is defined as an acute hospital trust submitting a minimum of 20 cases to the audit each month, or all cases of heart failure for a given month if the total number is less than 20. 12 Trusts in England and one Health Board in Wales failed to

submit data to the 2011/12 Audit, meaning that data are representative of 90% of acute care providers in England and Wales, and are based on 59% of all heart failure admissions nationally.

National Audit data are not available for the period over which the cohort for SUSSEX-HF was assembled but data contemporaneous with the end of the follow-up period for this study are available in the report of 2009/10. The primary aims of collecting such audit data are to improve standards of care and to enable effective commissioning. Therefore, with each iteration of the audit one would expect to observe improvement in care quality, and so national data for 2011/12 will be difficult to directly compare with data from SUSSEX-HF. However, I will outline here the findings of the most recent Audit to provide a frame of reference for contemporary practice in the UK, in which the results of SUSSEX-HF will be received.

#### **4.II.i. SUMMARY OF THE FINDINGS OF THE NHFA 2011/12[140]**

The most recent National Heart Failure Audit data have demonstrated improved outcomes for patients treated on cardiology wards, and for patients diagnosed with left ventricular systolic dysfunction (LVSD) as an in-patient and prescribed disease modifying drug therapy (ACEi/ARB,  $\beta$ -blocker, mineralocorticoid receptor antagonist). Survival has also been demonstrated to be improved by specialist follow-up by a consultant cardiologist. All of these factors have been shown to be influenced by the age and sex of patients admitted with heart failure, with older patients and women less likely to have access to care associated with improved outcome. The data have also demonstrated that more deprived patients are



admitted at a younger age. These findings are similar to those of previous audits, although rates of prescription of medications and specialist care have improved and what follows is an outline of the findings of this report.

Data in this, most recent audit represent findings from 37,076 submitted records – 32,906 index admissions and 4,170 readmissions. The mean age of patients on their first admission was 77.7 years (median 80.1 years) and two thirds of patients were over 75 at the time of first admission. Men were significantly younger than women at the time of first admission (75.5 years vs. 80.3 years) and the majority of patients up to the age of 85 were men (61.1%). In those over 85 there was a higher proportion of women (57.9%) but overall, more male cases of heart failure were submitted to the audit (55.2%).

Analysis of the age of patients at first admission according to their level of deprivation, ascertained by hierarchical quintile group, demonstrated a mean age of 74.5 years in the most deprived group vs. 79.6 years in the least deprived group. A clear trend for an older age at time of first admission was also observed across the quintiles (Q5: 74.5 years, Q4: 76.9 years, Q3: 78.3 years, Q2: 79.1 years, Q1: 79.6 years). The authors state that they intend to carry out further analyses on the treatment and management of patients according to their level of deprivation, but as yet no such data are available.

Just under half of all patients (48%) were treated on cardiology wards, and these patients had an average length of stay of 12.7 days – shorter than both the 13.1 day

average length of stay for the 41% of patients managed on general medical wards and the average of 14.7 days spent on other wards by the remaining 11% of patients. Treatment on a cardiology ward was associated with a significant survival advantage (21.8% of patients dying over a median follow-up period of 242 days vs. 29.8% of those treated on general medical wards and 33.4% of those treated on other wards over similar periods of follow-up). Correcting for confounding factors of age >75, NYHA class III/IV and previous myocardial infarction, a significantly lower chance of survival was associated with treatment on a non-cardiology ward (HR = 1.66 [95% C.I. 1.52-1.81; p<0.001]).

Women were more likely to be treated on general medical wards (47.9% vs 36.0% of men) and other wards (12.4% vs. 9.5% of men). Advancing age was also associated with a decreased likelihood of treatment on a cardiology ward with 76.3% of patients under 45 treated on such wards compared with 47.1% of patients aged 74-84 years and 32.1% of patients 85 years and older.

High rates of access to in-patient echocardiography were demonstrated in these audit data, with 86% of patients undergoing the test during their admission. Patients were more likely to undergo assessment by echocardiography if they were male (88.8%) than if they were female (82.6%). Age was also an important determinant of access to echocardiography, with 91.4% of those under 75 years undergoing the test compared with 83.3% of those 75 and older. Treatment on a cardiology ward was also associated with higher rates of echocardiography (92.9% vs. 80.1% of those treated on a general medical ward and 77.8% of those on other wards).

65% of patients in the audit had documented left ventricular systolic dysfunction (LVSD) and 84% of these were prescribed an ACE inhibitor or an ARB on discharge. Rates of prescription were higher in those treated on a cardiology ward (87% vs. 80% on general medical wards and 76% on other wards) and also higher in younger patients (89% in those under 75 vs. 80% in those 75 and over) and in men (85% vs 83% in women).

Similar patterns were observed in the prescription of  $\beta$ -blockers, though overall rates of prescription were lower at 78%. This figure was an improvement on the data from the previous years audit, in which rates of  $\beta$ -blocker prescription were 65%. 83% of those treated on a cardiology ward received a  $\beta$ -blocker compared with 71% of those on other wards. Age and gender again affected the likelihood of prescription with 84% of those under 75 receiving this class of medication compared with 74% of older patients, and 79% of men vs. 76% of women.

The same patterns for prescription of mineralocorticoid receptor antagonists (spironolactone and eplerenone) were observed in the audit data. Overall prescription rates were 45% of all those with LVSD and, again, rates were lower on non-cardiology wards (37% vs. 51%), lower in women (40% vs. 48%), and lower in patients over 75 (39% vs. 53%).

Rates of follow-up with heart failure liaison services were 53.7% and rates of follow-up with a consultant cardiologist were 51.7%. For both aspects of follow-up, rates

were higher in those treated on cardiology wards as an in-patient, higher in men, and higher in those under 75 years old – illustrated below.

	Heart Failure Liaison Service	Cardiology Consultant
Cardiology Ward	64.1%	69.9%
General Medical Ward	43.3%	34.4%
Other Ward	42.9%	31.7%
Male	59.0%	57.6%
Female	47.1%	44.2%
<75 years old	60.8%	67.2%
≥75 years old	49.9%	43.3%

### **4.III. ANNOTATED REFERENCES ON HEART FAILURE AND INEQUALITY**

#### **4.III.i GENERAL THEMES AND REFERENCE SELECTION**

As discussed, inequity may be observed across multiple domains. To inform the design of this study, and set it in the context of the existing, published evidence on inequality in heart failure, a systematic review of the literature has been undertaken.

A thorough search for all available articles on the subject has been made using MEDLINE, EMBASE, The Cochrane Database, Intute: Health & Life Sciences, The National Electronic Library for Health (UK), Pubmed and Stat!Ref. Cross referencing with sources quoted in scholarly articles generated by this search has also been performed and, where relevant, data from such sources has informed this chapter. Articles considered were those published in English from anywhere in the world making reference to socio-economic status, social class, deprivation, employment, level of education, income, or inequality, in combination with heart failure, ventricular dysfunction or congestive cardiac failure.

This chapter comprises a review of the relationships observed between the clinical syndrome of heart failure and various measures of socioeconomic status. Key themes, identified on review of the available literature, were of the existence of social gradients operating to determine differences in:

1. Heart failure incidence
2. Mortality rates in established heart failure

3. Readmission rates for heart failure
4. Access to various therapies and disease management programmes identified as beneficial in established heart failure.

What follows comprises a list of references which have explored each of these relationships. Each reference is accompanied by a description of the study population, the method used to determine socioeconomic status and the basis on which heart failure was diagnosed. Any significant relationship identified, as well as the authors' conclusions are presented here also.

Research in this area, by its very nature, tends to be centred around analyses of wealthy, industrialized nations. The majority of the available literature comes from the United States, Scotland, and the Scandinavian Countries of Sweden and Norway. Other data are available from studies performed in England and Australasia. Analyses of these data require an appreciation of the differing systems of health insurance and patterns of access to healthcare which exist between these nations.

#### **4.III.ii. A starting point for considering the relationship between socioeconomic status and heart failure**

Eriksson et al. writing in the European Heart Journal in 1989, were the first to observe a link between SES and incident heart failure. Their study of men born in Sweden in 1913 was designed to characterize risk factors for chronic heart failure[141]. They screened a sample drawn at random from the population of Gothenburg using census data to identify individuals born in 1913. In 1963 they were

examined by the investigators and the examination was repeated in 95% of cases in 1967. A second sample was drawn in 1973 using an identical method. These men were examined and that examination repeated in 1980.

SES was characterized in both the '63 and '73 cohorts using the official Swedish classification which ranks individuals into three groups – 1 being the highest and 3 the lowest. Essentially this classification system relies on employment to rank individuals into:

1. Employers
2. Non-manual employees
3. Manual workers

However, a closer look at the system reveals that there are subsets of individuals in each class. Farmers, for example, by virtue of being employers, are in the highest social class, whereas upper level executives in major companies are in Class 2. Specific statements regarding highest level of educational achievement are also made to subdivide the three classes, but these cannot trump the main class boundaries dependent on employment. Thus it is the case that a highly educated individual with a manual job is classed lower than an assistant non-manual employee with less than 2 years post-comprehensive school education.

Heart failure in this study was defined on the basis of a scoring system validated previously in a publication by the same authors[142]. The main inclusion criterion

was dyspnoea on exertion and patients were then subdivided into 5 categories – CHF 0-4 (see table 6).

In their discussion the authors address the definition of heart failure, especially as an end-point in studies, and the problems inherent therein. Certainly, the argument for a graded definition in an attempt to represent the heterogeneity of the condition is a persuasive one. However, some of their scoring system is based on ischaemic symptoms or dysrhythmia +/- dyspnoea and in such they may have included purely ischaemic patients or even those with lone atrial fibrillation.

The authors found the prevalence of CHF among their 67 year old cohort in 1980 to be 13%. They analyzed multiple risk factors in an attempt to target avenues for intervention to prevent the development of CHF and comment that social class at the ages of 50 and 60 correlated positively with CHF development. In their regression analysis of social class they found statistically significant differences in the number of men who developed CHF over the course of both 17 and 7 years of follow-up (regression coefficient 15.42 [p=0.0001] and 0.006 [p=0.02] respectively). Despite these convincing data the authors make no comment in their conclusions about the likely effect of social class on predicting incident heart failure.

This study is a useful starting point for considering the problems inherent in exploring the relationship between SES and heart failure, as it demonstrates both the difficulties in defining heart failure itself and the reliance on specific proxy measures when determining individual SES – in this case hierarchical employment



status. Women were not studied in this cohort, thus avoiding potential difficulty in characterising female SES in relation to spousal employment.

#### **4.III.iii. INCIDENT HEART FAILURE AND SES**

**MacIntyre K, Capewell S, Stewart S, Chalmers JW, Boyd J, Finlayson A, Redpath A, Pell JP, McMurray JJ. *Evidence of improving prognosis in heart failure: trends in case fatality in 66 547 patients hospitalized between 1986 and 1995. Circulation 2000; 102: 1126 – 1131.***

This Scottish-wide retrospective cohort study examined case fatality rates per year in patients hospitalized for the first time with heart failure according to ICD 9 coding of admissions. Data on SES were collected according to Carstairs Deprivation category based on postcode data and ranked 1 – 5.

Though the primary aim of the study was to assess case fatality rates over time, the collection of SES data provide evidence of higher incidence of heart failure in more deprived individuals. 44% of cases came from the lowest two deprivation quintiles and the admission rate was 56% higher in the most deprived quintile compared with the least deprived[143].

**He J, Ogden LG, Bazzano LA, et al. *Risk Factors for Congestive Heart Failure in US Men and Women: NHANES I Epidemiologic Follow-up Study*. Arch Intern Med. 2001; 161: 996-1002.**

The First National Health and Nutrition Examination Survey (NHANES I) allowed the authors to examine the population attributable risk for incident heart failure of various baseline characteristics in a cohort of 5545 men and 8098 women aged 25 to 74 years, recruited in the initial phase of the study in 1971-1975. The relative risk for incident heart failure associated with each factor was also examined. Follow-up data were collected in 1982-1984 and 1986, 1987 and 1992. Incident heart failure was based on one or more hospital or nursing home stays with a discharge diagnosis with ICD-9 code 428.0 – 428.9, or on a death certificate report with cause of death listed as one of the same codes.

A less than high school education was associated with a population attributable risk of 8.9% for incident heart failure and the relative risk for incident heart failure was 1.35 (95% C.I. 1.16-1.57;  $p < 0.001$ ) overall, with the effect apparently slightly more marked in women compared with men. In multivariate analysis – simultaneously including all the significant factors identified in the age, race and time dependent history of coronary heart disease adjusted model – the risk associated with a less than high school education remained statistically significant (RR 1.22 [95% C.I. 1.04-1.42]  $p = 0.01$ ).

The authors conclude that less education is an independent risk factor for congestive heart failure[144].

**McAlister FA, Murphy NF, Simpson CR, Stewart S, MacIntyre K, Kirkpatrick M, Chalmers J, Redpath A, Capewell S, McMurray JJ. *Influence of socioeconomic deprivation on the primary care burden and treatment of patients with a diagnosis of heart failure in general practice in Scotland: population based study.* BMJ 2004; 328:1110.**

This Scottish study utilised the continuous morbidity recording project to explore rates of contact with general practitioners amongst a cohort representative of the Scottish population as a whole. The authors used a quintile measure of SES based on postcode of residence – the Carstairs deprivation category – and a diagnosis of heart failure was based on Read coding of face to face consultations with general practitioners. The aim of the study was to determine whether there are socioeconomic gradients in the incidence, prevalence, treatment and follow-up of patients with heart failure in primary care.

Incident heart failure was determined by the modifier ‘first’ being associated with a diagnosis of heart failure entered at the time of the consultation. This gave results demonstrating a highly significant trend for increased incidence of heart failure when moving from the most affluent quintile of the cohort to the most deprived, when adjusted for age and sex. The odds ratio for the incidence of heart failure between the most affluent and most deprived quintile was 1.44 (p for trend across groups = 0.003).

One of the authors’ conclusions is, therefore, that socioeconomically deprived patients were 44% more likely to develop heart failure[145].

**Ingelsson E, Lind L, Ärnlöv J, Sundström J. *Socioeconomic Factors as Predictors of Incident Heart Failure*. Journal of Cardiac Failure. 2006; 12: 540-5.**

The Swedish study made use of the USLAM (Uppsala Longitudinal Study of Adult Men) cohort[146] of 2322 men aged 50 at the time of enrolment and with no previous diagnosis of heart failure. Men with prior myocardial infarction or known valvular heart disease at baseline were excluded from the cohort (7 and 1 cases respectively). Occupational classification, education level and marital status were recorded as socioeconomic variables, with each variable having three possible hierarchical values. Individuals were examined at the time of entry into the study and were followed for a median of 29.6 years. Heart failure cases were identified by linkage with the nationwide hospital discharge register, where ICD-8 codes for heart failure in any of the six diagnostic positions were accepted as evidence of heart failure.

Unadjusted Cox proportional hazard analyses revealed that lower occupational classification (HR 1.55 [95% C.I. 1.03-2.35]), lower education level (HR 1.98 [95% C.I. 1.07-3.68]) and being unmarried (HR 1.44 [95% C.I. 0.99-3.68]) increased the risk of heart failure. A clear trend across hierarchical levels of occupational class and education was not, however, evident. Adjustment for established risk factors for the development of heart failure, and for interim myocardial infarction reduced the apparent hazard associated with lower socioeconomic status and being unmarried. There were low numbers of men in the highest occupational class (14.6%), and with

higher than elementary school education (16.7%). The proportion of married men in the cohort was high at 84.8%.

The authors conclude that high occupational classification and education level decreased the risk of subsequent heart failure in middle aged men, and being unmarried increased the risk, via mechanisms largely independent of established risk factors[147].

**Stewart S, Murphy NF, McMurray JJ, Jhund P, Hart CL, Hole D. *Effect of socio-economic deprivation on the population risk of incident heart failure hospitalisation: an analysis of the Renfrew/Paisley Study*. Eur J Heart Fail 2006; 8: 856–863.**

This large, prospective, population based study recruited 15402 individuals (45.8% male) between the ages of 45 and 64 years from the industrial areas of Renfrew and Paisley in Western Scotland – representing an estimated 80% of the population in this age range. Baseline assessment of cardio-respiratory health status was carried out in all subjects and they were subsequently followed for a period of 20 years for the development of incident heart failure based on discharge diagnostic coding of ICD 9 (ICD 8 in a small number of cases) codes for heart failure in the primary position.

SES in this study was based on the Carstairs-Morris Deprivation category. This index is based upon census data at the postcode level and uses levels of employment, living conditions, car ownership, and social class to rank postcode sectors into seven

deprivation categories (1=least deprived, 7=most deprived). Data were also collected on occupation at baseline according to the Registrar General's classification, but preliminary analyses indicated that the Carstairs-Morris Deprivation category was most sensitive to heart failure related outcomes and was available in a larger number of cases, and so it was chosen as the primary measure of SES. Comparison was made of the results using the Carstairs-Morris Deprivation category with those using individual social class to examine the robustness of using this composite measure.

A total of 628 study participants (4.1%) were hospitalised with a primary diagnosis of heart failure over the 20-year follow-up period. Analyses of the baseline cardiovascular risk profile of all participants revealed a marked gradient according to SES, with a significant trend for those in the most deprived categories to have multiple markers of increased risk. A statistically significant gradient was observed in the rates of hospitalization for heart failure according to Carstairs-Morris Deprivation category (Log rank test:  $p=0.003$ ) – 6.4% of those in category 7 hospitalized vs. 3.5% of those in categories 1, 3 and 4<sup>\*</sup>, with an intermediate rate of hospitalization in categories 5 (4.2%) and 6 (4.7%). Cox proportional hazards models demonstrated that lower SES at baseline was associated with a higher risk of subsequent heart failure hospitalizations independent of age, sex and baseline cardiovascular risk ( $p<0.001$  overall). In the study population as a whole, the risk of heart failure admission in the most deprived cohort was around 40% greater than in the most affluent cohort (RR 1.39 [95% C.I. 1.04-2.01]  $p=0.044$ ). The risk associated with the

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<sup>\*</sup> No cases were defined in category 2.

highest level of deprivation appeared to be greater in men than in women (64% vs. 53%), though specific comparison between the most and least deprived categories in each sex did not reach statistical significance. Subgroup analysis of initially “healthy” subjects (those without appreciable cardiovascular risk at baseline) revealed that those in the most deprived cohorts (categories 6 and 7) were close to five times more likely to be admitted for heart failure than those in categories 1 and 2 (least deprived) – 3.8% vs. 0.8% Over 20 years of follow-up (p=0.016).

The authors conclude that these data show a link between social deprivation and the risk of developing heart failure, irrespective of baseline cardio-respiratory status and cardiovascular risk factors[148].

**Schaufelberger M, Rosengren A. *Heart failure in different occupational classes in Sweden.* Eur Heart J. 2007; 28: 212-8.**

Occupation was used in this observational case-control study of 6999 men, drawn from the population of 9998 men in the interventional cohort of the multifactor Primary Prevention Study in Goteborg, Sweden[149]. Five occupational classes were identified to stratify the sample by socioeconomic status – unskilled workers through to high officials / professionals. Notably, individuals were excluded from analysis if they could not be classified by occupation due to having taken early retirement (405 of those eligible by other criteria). Of the 6999 men studied, 1004 developed heart failure over the course of the 28-year follow-up period. Diagnosis was based on linkage with the Swedish National Register on Cause of Death, and the Swedish Hospital Discharge Register. All of the men studied returned an initial questionnaire

on occupation, smoking habits, physical activity and known hypertension or diabetes mellitus. The men were also examined for height, weight and resting blood pressure, and had blood taken for analysis of serum cholesterol concentration.

A clear trend was observed across the strata of occupational class in both age adjusted hazard ratio (HR for lowest vs. highest = 1.92 [1.50-2.45]) and multiple adjusted hazard ratio (HR for lowest vs. highest = 1.42 [1.17-1.72]) for incident heart failure. The trend was less clear when considering those with a previous diagnosis of non-fatal MI or prior coronary revascularization procedure. The highest occupational class was used as the reference group and the number of men in this group was low in comparison to those in the other four groups (e.g. 802 men vs. 1671 men in the unskilled workers group).

The authors conclude that low SES is an independent risk factor for long term risk of heart failure in men[150].

**Bahrami H, Kronmal R, Bluemke DA, Olson J, Shea S, Liu K, Burke G, Lima JAC. *Differences in the Incidence of Congestive Heart Failure by Ethnicity: The Multi-Ethnic Study of Atherosclerosis. Arch Intern Med. 2008; 168(19): 2138 – 2145.***

In a similar US study Bahrami et al. investigated the incidence of heart failure in the Multi-Ethnic Study of Atherosclerosis (MESA) cohort of 6814 individuals from four ethnicities (White [38.5%], African American [27.8%], Hispanic [21.9%, Chinese American [11.8%]), recruited between July 2000 and August 2002. After excluding those with a history of cardiovascular disease at baseline, participants were followed



for a median period of 4.0 years and incident heart failure in this period was defined by:

- a. congestive heart failure diagnosed by a physician and patient receiving medical treatment for heart failure,
- b. pulmonary oedema / congestion seen on chest radiograph, and
- c. dilated ventricle / poor LV systolic function / evidence of LV diastolic function on echocardiography.

Participants meeting criteria “a” alone were considered to have met a soft criterion for incident heart failure but these individuals were included in the analyses.

Socioeconomic status was examined in this study according to educational level (6 hierarchical categories from less than high school to graduate/professional school training) and median annual household income (<\$25000, \$25000 - \$49999, \$50000 - \$75000, and >\$75000).

The authors explore the interaction of race with the various potential mediating factors in the development of incident heart failure and give us insight into the complexity of the interplay between SES and heart failure within populations. White race is taken as the reference population and hazard ratios for incident heart failure in the other three racial groups are calculated and the effect of the addition of other covariates to the model is examined. Hazard ratios for incident heart failure in Chinese Americans and Hispanics suggest no significant differences in rates of incident heart failure in these races compared to whites, though there is a trend for lower rates in Chinese Americans and higher rates in Hispanics. However, the results signal that higher median household income is associated with a lower risk of heart

failure in Chinese Americans, and that the addition of household income to the model abolishes the increased hazard associated with black race as well as reducing the non-significant hazard associated with Hispanic race. Educational level, however, appears to be associated with no significant change in the risk of incident heart failure in any racial group[151].

**Kalogeropoulos A. et al. *Epidemiology of Incident Heart Failure in a Contemporary Elderly Cohort: the Health, Aging, and Body Composition Study. Arch Intern Med.* 2009; 169(7): 708-715**

This US study examined 2934 participants without heart failure enrolled in the Health, Aging, and Body Composition Study (Health ABC Study) – a population based study enrolling community dwelling white Medicare beneficiaries and all eligible blacks, between the ages of 70 and 79 years from April 1997 to June 1998. The mean age was 73.6 years, 52.1% of those studied were women, 41.4% were black, and the median follow-up was 7.1 years.

Incident heart failure was classified on the basis of all first admissions with an overnight stay confirmed to be related to heart failure on the basis of symptoms, signs, chest radiograph and echocardiographic findings. The criteria required at least a diagnosis of heart failure from a physician and treatment for heart failure (diuretic / digitalis or vasodilator) prior to screening of the admission by a local adjudicator. Educational status (<high school, high school, >high school) was used as a potential mediator of incident heart failure and no association with the outcome was identified in this study. Black race was associated with a higher risk of incident

heart failure and, in both blacks and whites, male sex was associated with more incident heart failure. White men were, however, at less risk of incident heart failure than black women. Risk factors in those of black race were all more prevalent than in whites and carried higher population attributable risk. No significant differences in risk factor profiles were seen, however, between sexes within each race.

This paper concludes that incident heart failure is common in older persons and that a large proportion of risk is attributable to modifiable factors. No mention is made of the lack of observed effect of education level on incident heart failure, though for the purposes of this review, these are interesting negative data[152].

**Christensen S, Mogelvang R, Heitmann M, Prescott E. *Level of education and risk of heart failure: a prospective cohort study with echocardiography evaluation. Eur Heart J* 2011;**32**:450–458.**

This Danish, prospective cohort study examined the effects of level of educational achievement (<8 years, 8-10 years and >10 years) and median household income (low, medium and high) on the risk of incident heart failure, determined by survival time free of an admission for congestive heart failure, in participants in the Copenhagen City Heart Study. 18616 participants (both men and women) were followed until July 2007, with the initial cohort, recruited between 1976 and 1978, numbering 14223. Subsequent examinations were made in the years 1981-1983, 1991-1994, and 2001-2003. At the time of each subsequent examination, new participants were recruited, primarily of younger age, in an attempt to generate a study population with representatives from all age groups. All individuals included in

the analysis were free from prior MI or congestive heart failure at the time of entry into the study.

Primary endpoint was first-ever hospitalization with a diagnosis of congestive heart failure, based on ICD8 codes until 1<sup>st</sup> January 1994 and ICD10 codes thereafter.

Analyses were restricted to age below 80 at the time of study entry, as the assumption of proportional hazards was violated with regard to the effect of education on the primary outcome above this age. Individuals, therefore, contributed to the total time at risk of developing heart failure in the model until reaching the endpoint, death, emigration, or age 80.

A subset of participants were recruited, by random sampling, at the time of the final interval examination (2001-2003) for an echocardiography sub-study (n=3589). Five indices were used to examine echocardiographic abnormalities according to level of educational achievement – LV hypertrophy, LV dilatation, LVEF < 50%, mild diastolic dysfunction, and severe diastolic dysfunction.

All analyses were adjusted for age, gender and family history as potential confounders, and potentially modifiable cardiovascular risk factors were examined and treated as mediating covariates.

The authors found that participants with the lowest level of education were 1.5 times more likely to be admitted with congestive heart failure over the course of the study when compared to those with the highest level of education. These individuals

were, on average, older at the time of entry into the study and generally had a worse risk factor profile than those with the highest level of education. Following adjustment for all potentially mediating variables found to be associated with admission for congestive heart failure in the multivariable model, however, the hazard ratio for heart failure admission associated with higher levels of education remained similar to that seen in the unadjusted and age/sex adjusted analyses. Higher median household incomes were also associated with decreased hazard ratios for heart failure admission in both men and women, but the effect was less pronounced.

The findings of the echocardiography sub-study were less clear-cut, but LV dilatation and severe diastolic dysfunction appeared to be significantly correlated with lower levels of educational achievement after adjustment for all other variables. There was also a significant trend for lower rates of LVEF < 50% and any abnormal echocardiography in those with higher levels of education.

The authors conclude that level of education was associated with cardiac dysfunction and predicted future hospital admissions for congestive heart failure, with only a minor part of the excess risk being mediated by traditional cardiac risk factors[153].

#### **4.III.iv. PREVALENCE OF HEART FAILURE AND SES**

**McAlister FA, Murphy NF, Simpson CR, Stewart S, MacIntyre K, Kirkpatrick M, Chalmers J, Redpath A, Capewell S, McMurray JJ. *Influence of socioeconomic deprivation on the primary care burden and treatment of patients with a diagnosis of heart failure in general practice in Scotland: population based study.* BMJ 2004; 328:1110.**

This, previously described, study addressed not only incidence, but also prevalence of heart failure according to deprivation category. Prevalence was estimated by examination of the number of individual patient attendances for heart failure over the year 1<sup>st</sup> April 1999 – 31<sup>st</sup> March 2000. When adjusted for age and sex prevalence was 6.4/1000 in the most affluent group and 7.2% in the most deprived group (OR 1.13). No significant trend, however, was apparent across quintiles of deprivation[145].

#### **4.III.v. MORTALITY IN HEART FAILURE AND SES**

**MacIntyre K, Capewell S, Stewart S, Chalmers JW, Boyd J, Finlayson A, Redpath A, Pell JP, McMurray JJ. *Evidence of improving prognosis in heart failure: trends in case fatality in 66 547 patients hospitalized between 1986 and 1995. Circulation 2000; 102: 1126 – 1131.***

This, previously described, study provided evidence of increased incidence of heart failure with increasing deprivation. The primary aim, however, was to describe the case fatality rate for incident heart failure. Deprivation, described by Carstairs-Morris quintile, principally increased the short term case fatality rate in an adjusted logistic regression analysis at 30 days, with the effect more marked in men than in women.

A convincing trend was seen for increased early mortality with increasing quintile of deprivation and the case fatality rate at 30 days was 26% higher in men and 11% higher in women for the most deprived quintile compared with the least deprived. Long term mortality (30 days to the end of follow up) was affected to a lesser extent, though an excess mortality of 10% in men and 6% in women was observed in the most deprived quintile[143]

**Blackledge HM, Tomlinson J, Squire IB. *Prognosis for patients newly admitted to hospital with heart failure: survival trends in 12 220 index admissions in Leicestershire 1993–2001. Heart 2003; 89: 615–620.***

This UK based retrospective cohort study made use of the comprehensive record linkage system of Leicestershire Health Authority and data from the Office of

National Statistics, which allow for follow-up of all patients registered with primary care in the region for hospitalization and mortality events. Data were obtained on residents, 40 years and older, admitted with a first presentation of heart failure according to ICD 9 or ICD 10 codes for heart failure in any discharge coding position. Mortality was identified using death certification records and survival was measured from the date of admission to the date of death or the end of follow-up (30<sup>th</sup> September 2001), or to the date of migration outside of the study area. Comorbidity was assessed on the basis of admissions in the 5 years prior to heart failure hospitalization for the management of conditions associated with the development of heart failure. Average length of stay for these prior admissions was also used as a proxy for level of comorbidity.

SES was determined for members of the cohort using the index of multiple deprivation (IMD 2000) at the electoral ward level according to the patient's postcode of residence. Each member of the cohort was assigned a quintile of deprivation according to this multi-domain measure of deprivation.

All cause mortality and cardiovascular mortality reduced significantly over the course of the study. Advancing age, male sex, and comorbidity were strongly associated with higher mortality. No association was found between deprivation and either all cause or cardiovascular mortality in this cohort, either in the univariate or multivariate analyses. The authors do note, however, that a disproportionate number of index cases came from the most deprived quintiles (62% of cases from Q4 and Q5). They hypothesize that the lack of any appreciable social gradient in



mortality might be the result of a lower threshold for hospital referral in these patients from the more deprived quintiles[154].

**Riddell T. *Heart failure hospitalisations and deaths in New Zealand: patterns by deprivation and ethnicity. New Zealand Medical Journal 2005; 118(1208):1254-1263.***

This retrospective analysis of heart failure deaths and hospitalizations in New Zealand used the National Minimum Data Set of the New Zealand Health Information Service in the period 1988 – 1998 to identify admissions and deaths according to ICD 9 codes for heart failure. A small area based measure of deprivation was used according to the domicile of residence associated with each record – the New Zealand Index of Deprivation (NZDep) – and the cohort was arranged by decile of deprivation. Deciles 1-4 (least deprived) were collapsed to form a single group as the principal aim of the study was to investigate outcomes in Maori vs. non-Maori individuals, and there was an under representation of Maori in the least deprived deciles.

8079 heart failure deaths and 66416 heart failure hospitalizations were recorded in individuals over the age of 45 during the period of interest. Poisson regression analysis of relative risk of heart failure death and hospitalization revealed an 11% increase in both deaths [95% C.I. 1.06-1.16] and hospitalizations [95% C.I. 1.09-1.14] for each decile of increasing deprivation. Within deprivation strata Maori rates of

death and hospitalization were considerably higher than non-Maori rates at all levels.

These data were an unadjusted measure of the risk of heart failure death and hospitalization according to increasing deprivation from a study primarily designed to address the interaction between socioeconomic status and race on outcomes. The author concludes that deprivation was associated with an increased chance of death and hospitalization from heart failure in New Zealand and acknowledges the limitations of the study in identifying the factors underpinning this gradient[155].

**Wen M & Christakis NA. *Correlates of Ambulatory Care. Neighborhood Effects on Posthospitalization Mortality: A Population-based Cohort Study of the Elderly in Chicago.* Health Service Research 2005; 40(4): 1108**

This US retrospective cohort study merged three data sources to ascribe neighbourhood SES (based on census data) and neighbourhood social environment (based on the Project on Human Development in Chicago Neighbourhoods – Community Survey [PHDCN-CS]) to individuals in the Care after the Onset of Serious Illness (COSI) dataset, according to ZIP code of residence (akin to UK postcode).

The primary outcome of interest was survival time after the index admission. The study examined 10557 patients admitted in 1993 for the first presentation of acute myocardial infarction, congestive heart failure, hip fracture, lung cancer, or stroke. 29% of patients in the study were admitted with congestive heart failure.

Complex analyses demonstrated that better neighbourhood SES and social environment were predictors of better outcome overall, but this effect was most marked where individual income was adequate. Analyses of individual diseases in the cohort seemed to show that neighbourhood SES and social environment were potent predictors of mortality following myocardial infarction but had little effect in the other conditions studied, including heart failure. The work therefore implies that the effect of better neighbourhood related factors on mortality was principally to improve prognosis following myocardial infarction[156].

**Rathore SS, Masoudi FA, Wang Y, Curtis JP, Foody JM, Havranek EP, Krumholz HM.**

***Socioeconomic status, treatment, and outcomes among elderly patients***

***hospitalized with heart failure: findings from the National Heart Failure Project.***

**Am Heart J 2006; 152:371–378.**

This retrospective study from the USA examined medical records of a national sample of 25086 Medicare beneficiaries, aged 65 and over, hospitalized with heart failure in a single year March 1998 – April 1999. The aim was to assess the association of SES with treatments and outcomes in heart failure. Heart failure was defined by principle discharge diagnosis of heart failure according to ICD 9 code and chart review of identified admissions was undertaken to exclude cases without any clear documentation of heart failure. SES was determined using a commercially available database linking ZIP code-level residential demographic characteristics to individual patients. The index used (ZIP Quality rating) was a composite measure derived from median household income, educational achievement of persons 25 years and over, occupation of employed persons, and home value within each ZIP

code. Patients were allocated to one of four groups according to this index in a hierarchical manner based on their score relative to the national mean score. The principal outcome measures were mortality at 30 days and 1 year post admission. All-cause readmissions within 1 year of discharge were also examined, as was quality of care, determined by documentation of left ventricular systolic function and prescription of ACE inhibitors to ideal candidates.

Crude mortality rates at 30 days and 1 year did not differ between socioeconomic groups. Following adjustment for a wide range of factors identified as being associated with patient outcomes 1 year mortality rates demonstrated a significant trend for higher rates with decreasing SES. One of the conclusions offered by the authors is that SES may influence outcomes after hospitalization for heart failure[157].

#### **4.III.vi. READMISSION AND SES IN HEART FAILURE**

**Struthers AD, Anderson G, Donnan PT, MacDonald T. *Social deprivation increases cardiac hospitalisations in chronic heart failure independent of disease severity and diuretic non-adherence.* Heart 2000;83:12–16.**

This retrospective cohort study included patients admitted to an acute hospital in the Tayside region of Scotland with an ICD 9 coded diagnosis of myocardial infarction between 1<sup>st</sup> January 1989 and 31<sup>st</sup> December 1992, and then subsequently admitted with an ICD 9 coded diagnosis of chronic heart failure in the same period. The authors hypothesized that diuretic adherence might give an insight into the

assumption that more socially deprived individuals are less health conscious if adherence were less in more deprived groups. Therefore, three or more prescriptions for diuretics had to have been dispensed to each patient in the year from January 1993 – January 1994 for them to be included in the study. Total daily diuretic dose was used as a proxy marker of disease severity.

In total, 478 patients were included (52% male, age 46 – 90 years, 80% > 65 years old) and information on all emergency admissions and deaths in the two years 1<sup>st</sup> January 1993 – 31<sup>st</sup> December 1994 was recorded. Cardiac admissions were based on ICD 9 coding for cardiac disease in the primary diagnostic position. SES was determined by Carstairs score from 1 (most affluent) to 7 (most deprived) according to postcode of residence. No patients in this study had a Carstairs score of 7.

The main findings of the study were that social deprivation was independently associated with an increase in cardiac hospitalizations in individuals who have had a previous myocardial infarction and an admission for congestive heart failure, and that this effect was independent of disease severity, measured by average diuretic dose, death rate, and duration of each hospital stay. The increase in hospitalization observed was driven by admission of a higher proportion of individuals admitted in more deprived groups rather than increased frequency of admission for individuals. The relative risk of emergency cardiac admission across all six deprivation categories was 1.11 (1.002 – 1.224) when adjusted for age and sex. All cause hospitalization in this cohort was not significantly affected by deprivation and rates of diuretic adherence did not appear to influence hospitalization. It is also worth noting that this study did not demonstrate any effect of deprivation on mortality[158].

**Philbin EF, Dec GW, Jenkins PL, DiSalvo TG. *Socioeconomic status as an independent risk factor for hospital readmission for heart failure. Am J Cardiol* 2001; 87:1367 – 1371.**

This US Study retrospectively analysed hospital discharge data collected prospectively in New York State. All patients discharged at least once in the period 1<sup>st</sup> January – 31<sup>st</sup> December 1995, with an ICD 9 code for heart failure in the principal diagnostic position on the discharge abstract, were included in the study. The cohort totalled 41776 patients with a mean age of 74 years (43% male, 18% African American). Median household income in the ZIP code of each patient's residential address (based on 1990 census data) was used to define socioeconomic status, with patients assigned to one of four income quartiles for analysis purposes.

Baseline differences in the propensity for readmission were accounted for by use of a published prediction rule by the same first author[159]. In all, 21.5% of patients experienced at least 1 readmission for recurrent heart failure.

Patients in the lowest income quartile were significantly younger than those in the highest income quartile ( $71 \pm 14$  years vs.  $75 \pm 13$  years;  $p < 0.05$ ) and more likely to be female (59% vs. 54%;  $p < 0.05$ ) or African American (39% vs. 8%;  $p < 0.05$ ). They were also significantly less likely to be treated by a cardiologist (19% vs. 22%;  $p < 0.05$ ).

There was a stepwise decrease in the crude frequency of hospital readmission for heart failure from the lowest quartile of income (23.2%) to the highest (20%)

( $p < 0.0001$  for trend and for difference between highest and lowest income quartiles). Adjusted odds ratios for heart failure related admissions in each income quartile demonstrated a similar stepwise progression for increasing risk of readmission with decreasing income with the highest income quartile used as the reference population, though the differences between the top income quartile and the next lowest failed to reach statistical significance.

The authors conclude that, whilst important clinical and demographic differences exist between patients with higher and lower incomes in New York, lower income persists as a positive predictor of readmission risk when these differences are adjusted for [160].

**Tsuchihashi M, Tsutsui H, Kodama K, Kasagi F, Setoguchi S, Mohr M, Kubota T, Takeshita A. *Medical and socioenvironmental predictors of hospital readmission in patients with congestive heart failure. Am Heart J 2001;142:E7.***

This prospective study of 230 consecutive patients discharged from 5 teaching hospitals in Fukoka, Japan used medical record review to identify cases of heart failure, based on principal discharge diagnosis in the year 1<sup>st</sup> January 1997 – 31<sup>st</sup> December 1997. The validity of the diagnosis of congestive heart failure was ascertained by thorough case note review and use of the Framingham criteria.

Presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria were accepted as evidence of definite heart failure.

Socioenvironmental factors considered were occupation, financial resources (financial support for physician visits and medications), marital status, family caregiver, professional support (weekly or biweekly home visits), and follow-up visits (outpatient attendances per month).

Mean follow-up was 2.4 years and the mean age of participants was 69 years (21%  $\geq$  80 years). 60% of patients were male and no differences were observed in readmission rates according to age or gender. Rates of death at 6 months, 1 year and 2 years were 6.1%, 8.3%, and 16.5% respectively.

Readmission rates were high at 35% within 1 year. Independent predictors of hospital admission were: less than 1 follow-up visit per month, prior admission for heart failure, no occupation, longer hospital stay during the index admission, and a history of hypertension. A significantly higher percentage of patients in the non-readmitted group received professional support, but on multivariate analysis this significance was lost.

The only significant socioeconomic variable considered in this study was occupation, treated as a binomial categorical variable - occupation or no occupation. The authors make the point that it was not possible to exclude an interaction between medical and socio-environmental variables and that there was a significant relationship between older age and no occupation. Whilst longer hospital stays were associated with increased likelihood of readmission, other markers of disease



severity – NYHA class and ejection fraction – were not associated with higher readmission rates[161].

**Riddell T. *Heart failure hospitalisations and deaths in New Zealand: patterns by deprivation and ethnicity*. New Zealand Medical Journal 2005; 118(1208):1254-1263.**

The details and findings of this New Zealand based study are outlined above in the mortality section. Similar risks were noted for crude readmission and mortality according to SES[155].

**Rathore SS, Masoudi FA, Wang Y, Curtis JP, Foody JM, Havranek EP, Krumholz HM. *Socioeconomic status, treatment, and outcomes among elderly patients hospitalized with heart failure: findings from the National Heart Failure Project*. Am Heart J 2006;152:371–378.**

This previously described study examined readmission rates as well as mortality according to SES. Crude readmission rates within 1 year of discharge demonstrated a significant trend for higher rates of readmission with decreasing socioeconomic status. Those in the lowest SES group remained at an increased risk of readmission compared with those in the highest group after multivariable adjustment (RR 1.08 [1.03-1.12]). However, after such adjustment those in the lower middle and higher middle SES groups (between the highest and lowest groups) appeared to show no significantly increased risk of readmission[157].

**Antonelli-Incalzi R, Ancona C, Forastiere F, Belleudi V, Corsonello A, Perucci C A.**

***Socioeconomic status and hospitalization in the very old: a retrospective study.***

**BMC Public Health 2007; 7:227.**

This Italian retrospective cohort study examined the rate of hospitalizations for common medical conditions amongst residents of Rome, aged 75 years or older, in the period 1997 – 2000. Income data were provided by using the median income for each census tract of Rome, applied to the individual by means of linkage with their residential address. For analysis purposes, individuals were categorized into deciles of income – 1 = very underprivileged, 10 = very well off.

Age standardized rates of hospitalization (per 1000 inhabitants) by gender and income decile were calculated for the entire cohort and also for patients 75 – 84 years old and those 85 and over (22% of the cohort). There was only a marginal increase in the hospitalization rate between those aged 75-84 and those in the older group in both men and women, and rates were generally lower in women. However, the rate of hospitalization dramatically increased with decreasing income in both sexes and age groups, and rates of hospitalization increased between age groups to a greater extent with increasing poverty. Amongst those hospitalized, higher income was associated with lower Charleson's comorbidity index, but this was not explored further in the analyses.

Analysis of admission rates for individual conditions revealed the same pattern for heart failure related admissions but, interestingly, not for the sudden acute condition of hip fracture.

The authors conclude that income deprivation is a more appropriate measure to target interventions to prevent hospital admission than age per-se in elderly men and women[162].

**Saxena S, George J, Barber J, Fitzpatrick J, Majeed A. *Association of population and practice factors with potentially avoidable admission rates for chronic diseases in London: cross sectional analysis. J.RSM 2008; 99:81-89.***

This UK based study pooled routinely collected cross sectional data sources from all primary care trusts in London for the year 2001. The fields examined to accurately describe each trust were taken from census data; IMD 2000 score; condition specific mortality rates from the Office for National Statistics; prescription dispensing data from the Department of Health, according to the Prescription Pricing Authority's Prescribing Analysis and Cost scheme data; information on individual primary care trust list sizes and services; data on hospital admissions from Hospital Episodes Statistics for five chronic diseases, including heart failure (ICD 10 code I50 alone).

There were wide variations in hospital admission rates between the 31 primary care trusts in question for all conditions studied, including heart failure. These variations in heart failure appeared to be mediated by deprivation, increased percentage of elderly living alone and higher levels of ethnic minority patients. No significant associations were noted between prescription rates and rate of admission. GP factors such as practice size and list size were not apparently associated with differences in rates of admission for any of the conditions studied. Interestingly, the provision of specialist services for diabetes management in primary care was associated with decreased hospital admission rates, although the same was not true

of asthma. No analysis of specialist heart failure services in primary care is commented upon[163].

#### **4.III.vii. TREATMENT IN HEART FAILURE AND SES**

**McAlister FA, Murphy NF, Simpson CR, Stewart S, MacIntyre K, Kirkpatrick M, Chalmers J, Redpath A, Capewell S, McMurray JJ. *Influence of socioeconomic deprivation on the primary care burden and treatment of patients with a diagnosis of heart failure in general practice in Scotland: population based study.* BMJ 2004; 328:1110.**

This study, described in detail previously, examined rates of follow-up (total contacts in the year 1<sup>st</sup> April 1999 – 31<sup>st</sup> March 2000) in general practice for patients identified as having heart failure on the basis of Read coding. Prescribing data were also available in 46% of patients in the cohort from a priori selected GP practices, and this sub-cohort had a similar age, sex and deprivation distribution when compared with the full cohort. Drugs considered were loop diuretics, angiotensin converting enzyme inhibitors,  $\beta$ -blockers, spironolactone, and digoxin. Drugs were judged to have been given if they were prescribed at least twice during the 12 months of the study.

Age and sex standardised overall rates of contact with general practitioners differed between deprivation strata but without a significant trend from least to most

deprived as there was little difference between categories 1-4. There was however, a significantly reduced rate of contact in the most deprived group when compared to the other 4 groups. Contact rates did not differ across age groups or by gender. Contact rates per individual patient did vary markedly with deprivation, and in this case a highly significant trend for reduced number of annual contacts per patient was observed as deprivation increased (2.6 contacts per year in the most affluent group vs. 2.0 contacts per year in the most deprived group).

Rates of prescription of diuretics were relatively high at 80.6%, but rates of prescription of other medications was low in the cohort where information was available (ACEi 39.3%;  $\beta$ -blockers 21.4%; digoxin 20.7%; spironolactone 8.5%). No differential prescribing rates were observed according to deprivation category but age and sex appeared to strongly influence prescription rates. The authors give the example of ACEi prescription where male sex was associated with a 42% higher likelihood of prescription and the odds ratio for receiving this class of drug was 0.60 in patients aged 75 – 84 years and 0.39 for patients over 85 years, when compared with patients under the age of 65 years[145].

**Rathore SS, Masoudi FA, Wang Y, Curtis JP, Foody JM, Havranek EP, Krumholz HM. *Socioeconomic status, treatment, and outcomes among elderly patients hospitalized with heart failure: findings from the National Heart Failure Project. Am Heart J* 2006; 152:371–378.**

This study has again been described in detail earlier. As well as investigating mortality and readmission rates, the authors also examined rates of assessment of LV systolic function and prescription of ACE inhibitors / ARB.

Crude rates of LV systolic function assessment followed a significant trend of higher rates according to higher SES (58.8% through to 75%,  $p < 0.001$ ). This trend was, however, only seen in white patients, and no differential rates of assessment were seen in black patients. This pattern of lower rates of LV systolic function assessment in those of lower SES persisted after multivariable adjustment.

Rates of ACEi / ARB prescription were not related to socioeconomic status as assessed in this study[157].

**Bongers FJ, Schellevis FG, Bakx C, van den Bosch WJ, van der ZJ. *Treatment of heart failure in Dutch general practice. BMC Fam Pract* 2006;7:40.**

This survey collected data from 195 Dutch general practitioners in 104 practices with patient lists equating to 2.5% of the population of the Netherlands. Demographic data on patients were derived from the administration of practices but socioeconomic data were collected directly by return of mailed questionnaire (response rate 76.5%). Data regarding occupational and educational level were

aggregated to subdivide the cohort into 3 hierarchical social classes, with the occupational level used as the primary marker for social class.

Patients in the study were identified as having heart failure on the basis of at least one contact with the GP coded K77 (heart failure) using the International Classification of Primary Care (ICPC). Comorbidity was based on contacts in the same year with the relevant ICPC codes.

Information on drug prescription was obtained and prescription rates were calculated as proportions of patients with heart failure.

The prevalence of heart failure was calculated at 7.4/1000 (6.7/1000 in males and 8.1/1000 in females) and the mean age of patients was 77.7 years. Women were significantly older (79.7 years vs 75.2 years) and 68% of all patients were 75 or older.

The authors defined optimal heart failure treatment as a triple combination of a diuretic, an inhibitor of the renin-angiotensin-aldosterone system (RAAS-I), and a  $\beta$ -blocker. RAAS-I were defined as ACE inhibitors or angiotensin II receptor antagonists (ARBs). Analyses were based on rates of triple treatment, rates of treatment with two of the three drug classes together, or monotherapy with one of the three drug classes. Data were also presented on rates of prescription of every drug class separately and rates of prescription of digoxin and spironolactone.

Triple treatment was observed in 18% of the cohort. There was no observable difference in the frequency of triple treatment by gender, but rates in patients under

75 years were significantly higher than those in patients 75 years and older (23.7% vs. 15.4%;  $p < 0.05$ ). Rates of triple treatment were also significantly higher in patients of high SES than those of low SES (22.1% vs. 16.7%;  $p < 0.05$ ). The authors do not provide any data on prescription rates for those 1283 patients who were in the middle stratum of SES.

Where two drugs were prescribed the combination of diuretic and RAAS-I was most common (28.2% in total), and in this case older patients had significantly higher rates of this prescription. No SES or gender related prescription differential was noted. Older patients were also significantly more commonly prescribed diuretic monotherapy, and younger patients significantly more commonly prescribed RAAS-I monotherapy.

Consideration of each drug as a separate prescription revealed significantly higher prescription rates of diuretics and digoxin in older patients.  $\beta$ -blocker prescription rates were significantly higher in those under 75 (40% vs. 29%;  $p < 0.05$ ) and in those of higher SES (39% vs. 31%;  $p < 0.05$ ).

The authors concluded that the influence of gender and SES on prescription rates was not very marked but the influence of age was considerable[164].



**Shah SM, Carey IM, DeWilde S, Richards N, Cook DG. *Trends and inequities in beta-blocker prescribing for heart failure. Br J Gen Pract* 2008; 58:862–869.**

This UK survey used repeated cross-sectional analysis of a previously validated, nationally representative primary care database from 152 practices using a specific software programme to record patient data. Morbidity and prescription data in the database were coded using Read codes and the database included a commercially available sociodemographic indicator, based on available means and linked to patient postcode – the ACORN index.

Patients aged 50 years and over in the database were included in the study and heart failure was identified by a Read code using the definition of heart failure from the 2006 revision of the Quality and Outcomes Framework (QOF). Only patients considered to be actively managed for heart failure were included in the study, and this was defined as the receipt of two prescriptions of an ACEi/ARB during the calendar year around the date of cross-sectional sampling. Sampling occurred in the years 2000 – 2005.

Age adjusted use of recommended  $\beta$ -blockers rose sharply between 2000 and 2005 but a gender gap in rates of prescription persisted (6.2% to 27% in men vs. 4.2% to 21.5% in women). Other determinants of  $\beta$ -blocker prescription included age (OR for those aged 60-64 years 3.87 vs. those aged >85 years) and residence in a postcode defined in the ACORN index as “Hard pressed” (the lowest sociodemographic stratum) – OR 0.79 for prescription of  $\beta$ -blocker compared with those in the most affluent stratum. A record of recent echocardiography also predicted  $\beta$ -blocker

prescription in a multivariable model in which age remained the dominant predictor of prescription rates. Reduced prescription rates in those of lowest SES persisted after adjustment for COPD and asthma[165].

#### **4.IV. SUMMARY OF CURRENT KNOWLEDGE**

The National Heart Failure Audit for England and Wales has recurrently reported that patients from more deprived backgrounds have been admitted at an earlier age than those with lower levels of deprivation. This tallies with numerous reports, cited above, confirming a higher incidence of heart failure in patients of lower socioeconomic status.

What is not clear from the available published data is to what extent socioeconomic status affects mortality in heart failure with conflicting reports from studies in different geographies, employing different methods to assess this issue.

Evidence for higher rates of readmission amongst heart failure patients of lower socioeconomic status does appear to be available from several studies, but these are isolated, historical reports from the UK combined with data from the USA and Italy where welfare systems and health economies are markedly different.

Lower socioeconomic status has been shown to predict lower rates of LV function assessment in the USA and lower rates of  $\beta$ -blocker prescription in the Netherlands and the UK. Lower rates of contact with general practitioners in UK heart failure patients has also been demonstrated in more deprived groups. There is, however, far more evidence from international published data and from the UK National Heart Failure Audit for the existence of lower quality care associated with older age and

female gender, than for lower quality care associated with lower socioeconomic status.

## **5. HYPOTHESES**

On the basis of the available evidence several questions remain regarding the impact of socioeconomic status on heart failure outcomes and the factors which might underpin any such association. There is strong historical evidence for a link between incidence of heart failure and socioeconomic status, but in those with known heart failure there are no contemporary published data for the NHS in England for the effect of socioeconomic status on mortality, rates of re-hospitalization, or quality of care.

This thesis is designed to test the following hypotheses:

1. Lower socioeconomic status, indicated by lower ranking in the IMD 2007 for an individual's postcode of residence is associated with higher mortality in patients admitted to hospital with a new diagnosis of heart failure.
2. In patients admitted to hospital with a new diagnosis of heart failure the readmission rate is higher in those of lower socioeconomic status measured in the same way.
3. Frequency of contacts with hospital services and with community heart failure services prior to and following an initial admission with heart failure is related to socioeconomic status measured in the same way.

4. Quality of care – assessed by prescription of evidence-based medication, access to echocardiography and rates of specialist follow-up – is related to socioeconomic status measured in the same way.

## **6. METHODS**

### **6.I. OVERVIEW OF THE STUDY DESIGN**

The project has been conducted as a historical cohort study. The cohort has been identified by retrospective identification of individuals admitted with heart failure over a designated historical period, and data pertaining to these individuals have been extracted from health records created at the time of that admission. Health records and other sources of data have subsequently been examined to identify use of secondary care services in the period 2 years prior to, and following, the date of the identified heart failure admission and also for the outcome variables of death and readmission to hospital in the 2 years following the initial admission.

### **6.II. SETTING**

#### **6.II.i. LOCAL HEALTH SERVICES & INFRASTRUCTURE**

The cohort was assembled by collection of data from a single district general hospital on the South-East coast of England – The Conquest Hospital, Hastings. The hospital forms part of the East Sussex Hospitals NHS Trust (ESHT), created by the merger of the Eastbourne Hospitals NHS Trust (EHT) and the Hastings and Rother NHS Trust (HART) in April 2002. Acute, in-patient services are provided at both Conquest Hospital and Eastbourne District General Hospital (EDGH). Outpatient services, as well as some day-surgeries and physiotherapy are provided by the Trust at several

community hospitals operated by two local primary care trusts (PCT) as shown in table 7.

Hastings & Rother PCT was formed by the amalgamation of Hastings & St. Leonards PCT and Bexhill & Rother PCT following consultation in 2005 in response to the NHS Improvement Plan. Since that time it has been responsible for the provision of health services for the population resident in the area around Conquest Hospital, numbering 170, 457 people in the 2001 census[166]. The geographic context of Conquest Hospital is demonstrated in the map – figure 2.

It can be appreciated from figure 2 that the geography and road network limit the propensity for health migration. This supposition has been supported by data demonstrating that 76% of all PCT spending on acute services in 2008 was directed towards ESHT. 98% of the remaining expenditure on acute services was for tertiary care, not available at the hospitals within ESHT[167]. There has also been evidence of significant local opposition to the relocation of services from Conquest Hospital to Eastbourne[168], suggesting that residents of Hastings & Rother PCT are most likely to access secondary care at Conquest Hospital for the reasons outlined above.

#### **6.II.II. DEFINING THE STUDY PERIOD**

The historical period defined for the identification of admitted heart failure cases was 01/01/2005 – 31/12/2007. Cases identified during this, three year, period were selected for inclusion according to the criteria outlined below. The paper and electronic hospital records of those included in the final cohort were retrospectively



examined for each hospital admission and out-patient contact in the 2 years immediately prior to and immediately subsequent to the date of the identified admission. Thus, the earliest date for which prior contact with secondary care services was identified and collected in the study was 01/01/2003 and the latest date for which a subsequent admission or out-patient appointment could be recorded was 31/12/2009. The database was closed on 01/08/2010 and all deaths were recorded up to and including this date.

### **6.III. ASSEMBLING THE COHORT**

An historical cohort of patients admitted with a first episode of heart failure requiring admission to hospital was defined according to the method outlined below.

Data on all admissions to Conquest Hospital are continuously collected for inclusion in the Hospital Episode Statistics (HES) and Admitted Patient Care (APC) datasets. A search of the APC dataset of all admissions in the period 01/01/2005 – 31/12/2007 was performed to identify all episodes where heart failure appeared in the primary or secondary diagnostic positions. Diagnoses in the APC for the period in question were coded by hospital coding department staff, to determine the tariff associated with the admission, according to the International Classification of Diseases version 10 (ICD-10)[169]. The codes selected to identify heart failure in this study were the same as those used in the National Heart Failure Audit[170] and are shown in table 8.

As a result of this search, a dataset was constructed which contained all consecutive admissions for heart failure in the period in question. Using the unique hospital identifier for each patient, this dataset was then examined for cases of multiple admissions related to a single individual. Where more than one admission with heart failure was identified for a single individual in the period of interest, these admissions were considered with reference to the formal written discharge summary for each episode. In such cases, the earliest recorded admission was considered to be the index admission unless the discharge summary clearly stated that this admission was solely as a day-case for a specific investigation or therapy other than for the primary treatment of heart failure. If the earliest admission in the dataset was such a day-case admission then that episode was excluded as an index case and the next earliest admission in the period in question was considered in the same way until an admission with heart failure was identified. Where multiple admissions of the same individual were identified then all admissions subsequent to that episode accepted as the index case were designated re-admissions and removed from the initial cohort. Because the APC defines episodes of care in the same way as the HES dataset, duplicate admissions which ran over consecutive dates were also scrutinised at this stage, with reference to the hospital notes and electronic discharge summaries. Where the duplication was found to be due to a transfer of care from one consultant/speciality to another then the admissions were amalgamated into a single episode.

The dataset generated as a result of these procedures was compared against a similar dataset, generated again from APC data, in which all admissions for heart

failure in the period 01/01/2000 – 31/12/2004 were identified using the ICD-10 codes listed in table 8 in the first and second positions. Where an individual was identified as appearing in both datasets they were excluded from the final cohort. By use of this method to exclude all those hospitalized for heart failure in the preceding five years, the final cohort was designed to contain only cases of first admission with a coded diagnosis of heart failure.

Following the identification of all consecutive patients newly admitted with a diagnosis of heart failure in the primary or secondary position as detailed above, data from the medical record and the electronic discharge summary were examined for each patient in this final dataset to corroborate the diagnosis of heart failure. The criteria used were based on the contemporary recommendations of the European Society of Cardiology[41]. However, measurement of natriuretic peptides was not routine at Conquest Hospital, or in the UK, during the period in question. Therefore, the following algorithm was used to exclude cases of unlikely heart failure:

1. A Boston Heart Failure Score (see table 9)[44] was calculated for each individual on the basis of the records of symptoms, physical examination and chest x-ray report<sup>1</sup> at the time of the admission.
2. Evidence of cardiac dysfunction (both systolic and diastolic) from any echocardiogram performed during the four-year period of interest was recorded.

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<sup>1</sup> Consultant radiologist report – available from electronic records in all cases where chest x-ray performed

3. Evidence of response to heart failure treatment (diuretics & vasodilators) was recorded.<sup>2</sup>

Where the Boston Heart Failure Score was 0 – 4 the case was excluded from the cohort unless there was clear evidence of cardiac dysfunction and response to treatment directed against heart failure.

Following the above method resulted in the generation of a cohort of patients admitted for the first in-patient management of an episode of heart failure, coded as such and confirmed on review of all of the clinical evidence recorded. Because the primary focus of the study was to describe and explore the associations between socioeconomic status and contact with secondary care services and the quality of that care, confident assessment of the number and type of contacts for each individual was required. As discussed, there is strong evidence from available data that residents of the geographic area covered by Hastings & Rother PCT access secondary care almost exclusively via the Conquest Hospital. However, the region of the South Coast encompassing Hastings and its environs is a popular holiday destination, and the area contains several holiday camps and caravan parks, anecdotally more popular with elderly holidaymakers. Specific data to support this are limited, but certainly an average of 119, 6000 holiday nights were spent in Hastings alone in 2006-2008[171]. For this reason, it was predicted that a degree of seasonal health migration would be operating within the cohort of interest for the study. Individuals were only considered eligible for inclusion in the final study cohort

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<sup>2</sup> For this criterion a statement in the discharge summary of “responded well to / improved with treatment for heart failure” (or similar) was taken as evidence.

if their primary postcode of residence, recorded on the hospital's clinical information system, was located in the area defined by Hastings & Rother PCT, and if they were registered with a general practitioner operating within the PCT at the time of the index admission.

Patients were also excluded from the final cohort if there was no evidence of registration with the hospital prior to the index admission. This was estimated by the absence of an historic patient number associated with the individual's hospital records. Such numbers contained an H as the first character (H-numbers) and were replaced by numbers containing an X as the first character (X-numbers) in May 2004. All patients registered with the Conquest hospital prior to May 2004 had individual X-numbers associated with their records in addition to the historic H-number. All patients newly registered after May 2004 had a novel X-number generated for association with their records and had no H-number associated with those same records. By excluding from the cohort those individuals with no H-number associated with their medical records, those patients migrating into the study population during the period of interest for the study were not included in the analysis, as their prior contacts with secondary care, and their socioeconomic status could not be confidently assessed. Finally, as contacts with the health service were under study it was necessary to exclude patients if it were clear from review of the medical record that their care was mainly managed by a tertiary centre or in the private sector.

#### **6.IV. DATA EXTRACTION**

All data were extracted from the continuous medical record either in its electronic or paper notes form. The electronic record at the Conquest Hospital, known as JOE, has been in continuous operation since 1998. Over this period, all correspondence, blood results, radiology and echocardiogram reports<sup>3</sup>, and the results of all special investigations have been recorded on JOE and were therefore available for immediate review at the time of data collection. No other system has been used for generating letters and where investigation results were delivered by alternative software systems, all such systems have been integrated with JOE so that a permanent and complete record has been maintained.

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<sup>3</sup> Echocardiogram reports available from 2001 onwards.

## **6.V. VARIABLES**

### **6.V.i. OUTCOME MEASURES**

The primary outcome variable was death from any cause. Death was determined as having occurred on a specific date by interrogation of the JOE clinical system, which is in turn linked to the PAS system of ESHT. Where deaths occurred in the Conquest Hospital, these were immediately recorded on these systems and were corroborated by interrogation of the database of in-patient deaths, maintained by the bereavement service at the Conquest Hospital. The PAS system has continuously been linked to the Office for National Statistics, by means of the unique patient NHS number, and is updated on a three monthly basis to identify deaths occurring outside the Conquest Hospital. A final interrogation of this system was carried out on 08/11/2010 to minimise the risk of any out of hospital deaths in the cohort not being recorded as a result of these events occurring near the database closure date of 01/08/2010.

Mortality at 30 days and at one year was defined from the date of the start of the index admission.

The secondary outcome measures were of all cause readmission and readmission with heart failure. All admissions subsequent to that used to include the case in the final cohort were identified by interrogation of the APC in the period 730 days following the date of the start of that index admission, using the unique hospital

number for each patient. In this way, a list of admissions for any cause in the period two years from the start of the index admission was generated for each member of the cohort. The primary and secondary coded diagnoses for each of the identified readmissions were recorded in every case. Where one of the ICD-10 codes used to include the case in the original cohort (listed in table 8) appeared in either the primary or secondary position, then that readmission was determined to be a heart failure readmission. Readmissions where ICD-10 codes other than those used to identify heart failure cases appeared in both the primary and secondary positions were determined to be non-heart failure admissions and were combined with heart failure readmissions to generate the list of all cause readmissions.

#### **6.V.ii. ASSIGNING SOCIOECONOMIC STATUS**

The exposure variable of interest was socioeconomic status of individuals in the cohort, determined by use of the Index of Multiple Deprivation 2007 (IMD 2007)[172]. This index is a measure of multiple deprivation at the small area level in England, constructed by the Social Disadvantage Research Centre at the Department of Social Policy and Social Work at the University of Oxford. Data on deprivation – combined across seven, weighted domains – are available at the lower layer super output area (LSOA) level (table 10). Data used to calculate the IMD 2007 were, in the main, collected in 2005, or represented the average of data collected up to 2005. For a minority of the determinants in certain domains, data were taken from the most contemporaneous (2001) census.



LSOA were designated to improve the reporting of small area statistics in England and Wales and are part of a geographical hierarchy for which population statistics are available[173]. Each LSOA is composed of four to six contiguous output areas, and they were generated by the ONS to be as consistent in population size and social homogeneity as possible. The minimum population within an LSOA is 1000 persons and the mean is reported as 1500 persons. The Organisation Data Service, provided by NHS Connecting for Health, has linked each individual postcode in England and Wales with a specific LSOA. In England alone, there are 32, 482 individual LSOA. Each of these has been assigned a specific IMD 2007 score, and subsequently ranked relative to all other LSOA in the country on the basis of this score. Thus, the most deprived LSOA in England has a rank of 1, and the least deprived has a rank of 32,482.

The score and rank of the LSOA associated with the postcode of each individual member of the final cohort was recorded and these ranks were used to divide the cohort into quintiles of deprivation, according to their overall rank within England (table 11).

### **6.V.iii. EFFECT MODIFIERS**

#### **Demographic Factors**

Age and gender of members of the cohort were considered as potential effect modifiers and were routinely recorded from the APC dataset in each case.

## **Care Quality**

Several markers of high quality care were defined for the study on the basis of what information could be reliably gathered retrospectively. These markers are based on guidelines from the UK National Institute for Health and Clinical Excellence (NICE)[60] and have also been informed by the National Service Framework for Coronary Heart Disease[174] as well as recommendations by the European Society of Cardiology[41]. The variables felt to be related to care quality were echocardiography, prescription of medications, investigations performed, and specialist care (prior to, during, and subsequent to the admission). Details of the methods used to collect these data are outlined below.

## **Echocardiography**

The JOE system was interrogated for evidence of echocardiography having been performed in the period two years prior to and two years following the date of the index admission. Echocardiogram reports were identified by accessing each individual patient record and opening the following subdirectory tree:

→ RESULTS

→ CARDIAC

→ ECHO

This generated a list of all available, typed echocardiogram reports in date order. Where echocardiography was found to have been performed during the period between the admission and discharge dates of the index episode, this was recorded as an echocardiogram performed as an in-patient during a first admission for the management of heart failure. If no echocardiogram report was identified at the time

of the index episode, but a report was available from the period of interest then the number of days (either positive or negative) between this report and the index admission was recorded. Where more than one echocardiogram had been performed in the period of interest, the date of the report most contemporary with the index admission was recorded.

Once the timing of echocardiography had been determined in this manner, the measurements of interest were extracted from the identified report. All reports were for trans-thoracic studies and were prepared by a British Society of Echocardiography certified technician or by a Consultant Cardiologist or Specialist Registrar in Cardiology training. The following measurements were recorded:

1. Left Ventricular Ejection Fraction (LVEF), measured using either Teichholz method[175] or the method of discs (modified Simpson's rule)[176].  
Where LVEF was calculated using both methods, the value given by the method of discs was recorded as it was considered to be more reliable[177].
2. Left Ventricular End Systolic and End Diastolic Diameter (LVESD & LVEDD), measured in centimeters (cm), from the trailing edge of the interventricular septum to leading edge of the posterior wall by M-mode echocardiography, just beyond the tips of the mitral valve leaflets.
3. Left Atrial Internal Diameter (LAID), measured by m-mode echocardiography, in cm at end systole. The measurement was taken from the trailing edge of the posterior aortic wall to the leading edge of the posterior wall of the left atrium, at the level of the aortic valve.

4. Subjective left ventricular systolic function, recorded according to any statement made in the free text summary provided with each echocardiogram report. The measure was treated as a discrete variable, with the following possible values:
  - a. Good / Normal.
  - b. Mild systolic dysfunction.
  - c. Mild – moderate systolic dysfunction.
  - d. Moderate systolic dysfunction.
  - e. Moderate – severe systolic dysfunction.
  - f. Severe systolic dysfunction.

### **Prescription of Medications**

The electronic discharge summary, created at the end of the index admission for each member of the cohort, was examined for details of the medications prescribed on discharge. Such summaries were only available for those patients who survived to discharge, and no data were collected on the prescription of medications to patients who died during the index admission. Prescription of each medication was considered to have occurred according to the presence or absence of a member of that class of drug on the discharge summary. The following classes of medication were recorded:

1. Loop Diuretics – record was taken of the total daily dose of diuretic prescribed in furosemide equivalents<sup>4</sup>.
2. Angiotensin Converting Enzyme Inhibitors (ACEi).

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<sup>4</sup> 1mg bumetanide = 40mg furosemide = 20mg torasemide.

3. Angiotensin II Receptor Antagonists (ARB).
4.  $\beta$ -blockers – record was taken of the specific agent where this class of medication was prescribed, according to whether or not the agent was licensed for the treatment of heart failure.
5. Aldosterone antagonists (spironolactone or eplerenone at any dose).
6. Anti-platelet agents – record was taken of prescription of aspirin (acetylsalicylic acid), clopidogrel and dipyridamole, and also of situations where combinations of these drugs were prescribed.
7. Vitamin-K antagonists.
8. Nitrate preparations.
9. HMG-CoA Reductase Inhibitors (“statins”).
10. Calcium channel antagonists (CCB) – record was taken of whether dihydropyridine or non-dihydropyridine type.
11. Non-steroidal anti-inflammatory drugs (NSAIDs) other than acetylsalicylic acid.
12. Thiazide diuretics.

### **Specialist Care**

The clinician responsible for the care of the patient during the index admission was determined to be the consultant named on the electronic discharge summary.

Patients may have been recorded as having been admitted initially under the care of another clinician, but the speciality of the clinician responsible for the patient on discharge was felt to be the best proxy for the speciality which had most impact on determining the in-patient and future management. Where patients died prior to

discharge from the index admission, then the consultant recorded as responsible for the admission on the JOE system was used to determine the speciality of care for the admission. The speciality of in-patient care was classified as a discrete variable with three possible values:

1. Cardiology
2. General Medicine (any consultant physician other than one with a CCST in cardiology or elderly medicine).
3. Elderly care / geriatrics.

One of the geriatricians responsible for the care of in-patients (HFM) was recognised as having a specialist interest in heart failure. However, during the period of the study, no specialist service for elderly in-patients with heart failure existed at the Conquest Hospital and so, for the purposes of defining the speciality of care of in-patient members of the cohort, those admitted under HFM were recorded as having received care from a geriatrician.

### **Investigations**

The JOE system was interrogated for evidence of the following investigations having been performed during the index admission:

- Full Blood Count (FBC).
- Plasma urea, creatinine and electrolytes (U&E).
- Liver Function Tests (LFT).
- Plasma glucose testing.
- Serum lipid profile testing.
- Thyroid function tests (TFT).

Note was also taken as to whether these final three investigations were performed at any time in the 6 weeks prior to the date of the index admission, as it was considered that clinicians reviewing such results at the time of the admission would not feel that repeating the tests would provide additional useful information regarding the diagnosis and management of heart failure. Once collected, these data were treated as discrete variables with the possible values:

1. Test performed during index admission (or in the 6 weeks prior to the admission date for TFT and plasma glucose and lipid testing).
2. Test not performed.

Record was also taken of the performance of a chest X-ray (CXR) during the index admission. All chest radiographs are formally reported at the hospital and so this was determined by the presence on the JOE system of a formal report, by a radiology consultant or trainee, pertaining to a CXR performed during the period of the index admission.

#### **Prior contacts with secondary care**

Prior contacts with secondary care were collected for both admissions and out-patient visits in the two years prior to the date of admission for the index episode.

For prior admissions, the APC dataset was interrogated for all admissions in the period of interest using the unique hospital number for each member of the cohort, and the total number of admissions was recorded.

For out-patient visits, the PAS system was interrogated in a similar manner, using the unique hospital number for each member of the cohort. All appointments were

identified in the period of interest and the date of the appointment, as well as the speciality of the clinic was recorded in each case. Data were available for patients who failed to attend scheduled outpatient appointments and attendance at an outpatient clinic was considered to have occurred if the outcome record of the clinic was one other than DNA (did not attend).

### **Follow-up**

Details of all out-patient appointments in the follow-up period were collected using the same method used to record prior clinic visits, outlined above.

### **Contacts with primary care**

When designing the study initially, data on contacts with primary care were planned to be collected for all members of the cohort. However, when applying for ethical approval of the original study design, it was felt by the committee that access to such records without formal written consent would not be ethically acceptable.

Application to conduct the study under Section 60 of the Health and Social Care Act was explored but not considered appropriate for data confined to a single centre, as well as being too lengthy a process to embark upon given the time constraints of this MD project. A decision was, therefore, taken to confine the research to a secondary care setting.



#### **6.V.iv. CONFOUNDERS**

Factors known to be associated with outcome, in terms of death and hospital readmission in the published literature, in heart failure were recorded, as completely as possible, for each member of the cohort. Where results of blood tests were recorded, all tests were performed by the pathology services of the study site – the Conquest Hospital, Hastings – in either the biochemistry or haematology laboratories. All values were taken from the results available on the JOE system. Results of blood tests on the system are recorded in chronological order, and the first result appearing within the date range of the index admission was taken for the admission value. Where discharge values were included, they were taken to be those of the last recorded result within the date range of the admission – i.e. the last result known by the responsible admitting clinician.

#### **Renal Function and Serum Sodium**

Both admission and discharge measures of sodium, potassium, urea and creatinine (collectively U&E) were recorded.

Renal function was determined by estimated glomerular filtration rate (eGFR), calculated from the simplified Modification of Diet in Renal Disease (MDRD) formula[178]. No adjustment for race was made when calculating these values, as this information was not collected in the study. Available data on the demography of the population from which the cohort was drawn suggests that the accuracy of this method was unlikely to have been significantly impaired by discounting race when calculating the eGFR[166]. Renal function was analyzed as a continuous variable

using the eGFR and the plasma creatinine concentration[179], but also as a categorical variable using the stages of chronic kidney disease (CKD) to sort the cohort into groups according to their eGFR (table 12).

Plasma sodium was recorded as a continuous variable. Members of the cohort were also dichotomized into groups according to the presence or absence of hyponatraemia (plasma sodium < 130mmol/l).

### **Anaemia**

Admission full blood count results were examined and the haemoglobin concentration (Hb), total white cell count (WCC), platelet count and mean corpuscular volume (MCV) were recorded for each member of the cohort.

Haemoglobin concentration was analyzed as a continuous variable but anaemia was also examined as a discrete variable. The definition of anaemia used was that of the World Health Organization – Hb < 13g/dl in men and Hb < 12g/dl in women.

### **Serum Albumin**

Liver function tests measured on admission were examined and results of plasma bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT) and albumin were recorded. Plasma albumin concentration was analyzed as both a continuous variable and a discrete variable dichotomized around a level of 35g/l[180].

### **Myocardial ischaemia**

Evidence of myocardial ischaemia during the index admission was determined by reference to the result of any troponin-T assay performed during the in-patient stay. A maximum of two troponin-T results were recorded as part of the study and any result at a level greater than 0.10µg/l was taken to be representative of significant myocardial ischaemia. Myocardial ischaemia was analyzed as a discrete variable designated either present or absent on the basis of the troponin-T result. Where no measure of troponin-T was made during the index admission myocardial ischemia was designated as having been absent at the time of the index admission.

### **Comorbidity**

The presence or absence of various comorbidities were considered as candidate confounding variables. A comorbidity was defined as having been present if it was noted in the admission documentation, discharge summary or in any previous correspondence, or if it was coded at any position in the APC dataset record of the index admission or any prior admission in the preceding two years. The comorbid conditions of interest were:

- Documented history of atrial fibrillation (AF) – ICD-10 I48X. Where AF was identified as a comorbidity, demographic data and the presence of other comorbid conditions were considered to generate a CHA<sub>2</sub>DS<sub>2</sub>VASc score (see table 5) for the patient in order to determine the recommended strategy for the prevention of arterial thromboembolism, according to the guidelines of the ESC.

- Documented history of systemic hypertension: The ICD-10 codes used to examine the APC dataset for systemic hypertension were I10, I11, I12, I13, I14, I15.
- Documented history of ischaemic heart disease: Defined as present if any history of previous myocardial infarction, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) procedure was recorded in the admission documentation, discharge summary or in any previous correspondence. Also defined as present if any ICD-10 code for myocardial infarction I24, I25 was recorded in any position in any admission in the two years up to and including the index admission, or if any of these admissions was for the purposes of either PCI or CABG.
- Documented history of chronic lung disease: Use of inhalers alone was not taken to be evidence of chronic lung disease without other mention of the diagnosis of asthma, chronic obstructive pulmonary disease (COPD) or emphysema. The ICD-10 codes used to examine the APC dataset for evidence of chronic lung disease were J40, J41, J42, J43, J44, J459, and J47.
- Documented history of drug-treated diabetes mellitus (DM): The ICD-10 codes used to examine the APC dataset were E10, E11, E12, E13, E14. DM was also defined as having been present if there was record on the discharge summary for the index admission of treatment with oral hypoglycaemic agents or insulin.
- Documented history of ischaemic stroke or transient ischaemic attack (TIA): The ICD-10 codes used to examine the APC dataset were G46, I63, I64, I67, and G459.

## **6.VI. SAMPLE SIZE CALCULATION**

For a predictive power of 80% to test the primary hypothesis at a 5% level of significance, an average mortality rate of 30% at 2 years and a hazard ratio between quintiles of socioeconomic status of 1.10 was assumed, based on figures in the available literature. These assumptions suggested a requirement for a minimum cohort of 290 patients.

## **6.VII. ANALYSIS**

### **6.VII.i. GENERAL ANALYSES**

All statistical analyses were performed using PASW Statistics 18 (SPSS version 18, IBM Corporation, release date 30 July 2009) or STATA version 10.0 (StataCorp LP, release date 2009). The analyses were conducted by myself – Dr Paul Haydock – with advice from Professor Martin Cowie. Mr Winston Banya (statistician) provided assistance with the use of the STATA software, used for modeling proportional hazards and generating standardized mortality ratios for the cohort.

The distributions of continuous data were explored for evidence of normality by eye, and by the use of both Normal and Detrended Normal Q-Q plots.

Where the distribution of data was normal, then mean and standard deviation (SD) for the variable in question were quoted and data were compared across 2 groups using the Student's t--test for equality of means, or one way analysis of variance (ANOVA) for multiple groups. Non-parametric data were quoted as median and either range or inter-quartile range (IQR). Such variables were analysed for differences between 2 groups using the Mann-Whitney U test and for differences across multiple groups using the Kruskal-Wallis test.

Discrete data were analysed as proportions in each group using contingency tables, and comparison between groups was performed using the Chi-Square ( $\chi^2$ ) test or Chi-square test for trend, as appropriate.

In all cases, a p value of 0.05 or less was taken to be evidence of a statistically significant difference between groups.

### **6.VII.ii. DEATH RATES AND SURVIVAL ANALYSIS**

Crude rates of death were determined by assessing the number of patients alive at 30 days and 1 year of follow up from the date of the first day of the index admission in the cohort as a whole, and in each subgroup of age. Advancing age at the time of admission was recognized as an obvious effect modifier and so, as well as analysis by subgroup of age, standardized mortality ratios were calculated for the cohort, stratified by five-year age groups, using mortality data for the population of England and Wales as the reference population[181]. By employing this method, the hazard associated with a first admission with heart failure was estimated in each five-year age band.

Formal survival analyses were performed using the Kaplan-Meier method and evidence of statistically significant rates of survival between groups was determined by application of the log-rank test. Individuals in the cohort were censored on the date of closure of the study database (01/08/2010) if the outcome of interest had not occurred in the period of follow-up before that time.

## **6.VIII. DATA PROTECTION AND DATA STORAGE**

All data were anonymized via the generation of a unique study identifier for each member of the cohort following the inclusion of their records in the study. All data stored on electronic media were encrypted in accordance with the standards of Imperial College London and East Sussex Hospitals' NHS Trust and data were only accessed according to the principals of the Caldicott Report. The Caldicott Guardian for the trust, Dr David Scott approved the study protocol in this respect.

All paper records pertaining to the study contained no patient identifiable data and were kept in a securely locked filing cabinet in a securely locked room at all times when not in use.



## **6.IX. ETHICAL CONSIDERATIONS**

The study was considered by the Brighton East Research Ethics Committee on behalf of the NHS National Research Ethics Service – REC reference number 09/H1107/56.

In its original form the study was not approved by the committee but in the modified form described in this thesis the study was considered by the committee to constitute an audit project, not requiring further ethical consideration.

## **6.X. SPONSORSHIP**

The study was funded by an unrestricted educational grant from Takeda Pharmaceuticals UK Ltd. The Sponsor has had no input in directing the study design or the preparation of this thesis.

## **7. RESULTS**

### **7.1. FINAL COMPOSITION OF THE COHORT**

Examination of the Admitted Patient Care (APC) dataset in the period 01/01/2005 – 31/12/2007 identified 1543 admissions where heart failure was coded in the 1<sup>st</sup> or 2<sup>nd</sup> position according to the study protocol. Of these cases, 453 (29.4%) were excluded on the basis that the episode represented a readmission with heart failure during the period of interest, or that a record of a previous admission with heart failure coded in the 1<sup>st</sup> or 2<sup>nd</sup> position was identified in the 5 years prior to the first recorded admission in the period of interest. 1090 cases remained for potential inclusion in the final dataset, of which 148 (13.6%) were inadmissible on the basis of the initial examination of the data. These 148 cases were excluded from further analysis according to the following criteria:

1. 75 cases (50.7%) were excluded on the basis that there was no clear evidence of previous registration with the Conquest Hospital due to the absence of an historical “H-number” associated with the patient records.
2. 39 cases (26.4%) were excluded on the basis that their postcode of residence was outside that defined by the study protocol.
3. 29 cases (19.6%) were excluded on the basis that the only recorded hospital admission during the period of interest was for a day case procedure.
4. 5 cases (3.4%) were excluded on the basis that it was clear from review of the medical record that the majority of their contacts with the healthcare system

were at a tertiary care heart failure centre (3 cases) or in the private sector (2 cases).

Following exclusion of these cases, 942 patients were identified for potential inclusion in the final cohort. These were screened for diagnostic evidence of heart failure during the index admission and on this basis 59 cases (6.3%) were excluded.

In total, 883 cases were considered eligible for inclusion in the final cohort for analysis. For a flow diagram illustrating these data see figure 3.

## **7.II. DEMOGRAPHICS AND CHARACTERISTICS OF THE FINAL COHORT**

883 patients were included in the final cohort, with a median age of 82.4 years (mean 80.4). Just over half of the cohort were women (51.3%) and women in the cohort were significantly older on average than men (median age 84 years vs. 80 years;  $p < 0.001$ ).

Co-morbid cardiovascular conditions were common in the cohort as a whole with rates of atrial fibrillation (AF – 50%), systemic hypertension (46%), ischaemic heart disease (IHD – 45%) and prior stroke (15%) all being high. There was no significant difference between male and female members of the cohort in rates of AF, systemic hypertension or prior stroke. However, a significantly higher proportion of male members of the cohort had a history of documented IHD (49% vs. 41% of women;  $p = 0.026$ ).

Other important chronic conditions were prevalent in the cohort with 22% of patients known to have been diabetic and 21% of patients previously having been diagnosed with chronic lung disease. Again, there was no significant difference in the rates of either diabetes mellitus or chronic lung disease when the cohort was split by gender, though a trend towards higher rates of lung disease was observed in male patients (23% vs. 19% of women).

Renal impairment, defined as  $eGFR < 60 \text{mls/min/1.73m}^2$  was observed on admission in 60% of the cohort and the median  $eGFR$  was  $54 \text{mls/min/1.73m}^2$  (median serum

creatinine 105 $\mu$ mol/l). Mean haemoglobin level was 12.3g/dl but rates of anaemia (Hb < 13g/dl in men and Hb < 12g/dl in women) were high at 51% (data unavailable in 4 cases). There was no significant difference between the rates of renal impairment or the distribution of eGFR between men and women, nor was there a difference in the average haemoglobin concentration measured on admission. However, significantly higher rates of anaemia were observed in the male portion of the cohort (60% vs. 42% of women;  $p < 0.0001$ ).

Comorbid conditions<sup>5</sup> were common and did not occur in isolation in individuals in the cohort. The modal number of comorbidities per individual was 3 (min = 0, max = 7) and only 14.3% of the cohort had fewer than 2 comorbid conditions, whilst 79.6% of individuals had 2 – 5 co-existing comorbidities. Table 13 shows the number of patients in the cohort with multiple comorbidities. No significant difference in admission free survival was noted for those with 3 or more comorbidities when compared with those patients with fewer than 3 ( $p = 0.31$ ).

Hyponatraemia ( $\text{Na}^+ < 130\text{mmol/l}$ ) on admission was present in only 9% of cases in both sexes (data unavailable in 6 cases) and the median serum sodium was 138mmol/l, with no difference observed in the distribution of serum sodium values between the two gender groups.

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<sup>5</sup> Being: AF, HTN, IHD, Chronic lung disease, Previous stroke, Anaemia on admission, eGFR < 60 on admission.  
The maximum total number was 7 – no patient had all 8 comorbidities

Serum albumin results were available for 773 members of the cohort (87.5%). Nearly a quarter of these patients (23.3%) were classified as having hypoalbuminaemia (serum albumin < 35g/l). The median serum albumin was 38 (interquartile range 32 – 44). No differences were observed between genders in terms of the frequency of albumin results being available, the rates of hypoalbuminaemia, or the distribution of albumin values.

Serum Troponin-T was measured at the time of the index admission in 76% of cases and was recorded as positive (Troponin-T  $\geq$  0.10) in 73% of these cases. Neither sex was found to have a higher rate of either measurement of Troponin-T, or an increased frequency of positive Troponin-T results, where the test had been performed.

### **Prior Contacts with Secondary Care Services**

The majority of patients in the cohort (62%) had been admitted at least once to one of the acute hospitals in ESHT in the two years prior to the index admission for a reason other than the management of heart failure. Of these 551 patients, 42% had been admitted only once, 27% twice, 13% three times and 18% had four or more previous admissions.

Only 21.5% of patients in the cohort had outpatient contact with a cardiologist in the period 2 years prior to the index admission and, of those that had, only 27% had more than one contact per year.

31% of patients had contact with either a cardiologist or a specialist heart failure geriatrician and, again, only 27% of these had more than one contact per year.

Only 12% of patients had contact with a heart failure specialist nurse and 71% of these had, on average, only one or fewer contacts per year.

Prior rates of contact with generalist services were similarly low in the cohort. Only 20% of the cohort had any out-patient appointment with a geriatrician in the two years prior to their index admission and only 13.5% had contact with a general medical clinic.

Rates of contact with non-medical specialists, which might be predicted to be high in an elderly cohort regardless of underlying heart failure, showed similar patterns.

29% of patients in this cohort had been seen at least once in ophthalmology out-patients in the 2 years prior to admission, 19% of the cohort had at least one out-patient contact with an orthopaedic surgeon, and 33% had been seen at least once in a general surgery clinic.

### **Speciality of in-patient care**

For the cohort as a whole, the majority of patients received care from a geriatrician (71%), with the remaining members of the cohort split equally between care by a cardiologist (14%) and a physician with another specialist interest (15%).



## **Event Rates**

The median length of follow-up was 730 days (minimum 0 days [died on day of admission], maximum 2037 days [5.6 years]). Patients were censored on the date of the closure of the study database if there was no record of their death before this time. The total number of deaths in the cohort over the entire period of follow-up was 558 (63% of patients). Mortality at 30 days from the date of the index admission was 17% and at 1 year was 38%.

### **7.III. COMPARISON OF THOSE SURVIVING TO DISCHARGE WITH THOSE NOT SURVIVING**

#### **THE INDEX ADMISSION.**

Of the total cohort of 883 patients, 160 (18%) died during the index admission. Table 14 compares the characteristics of patients not surviving to discharge with the remainder of the cohort.

Patients not surviving to discharge were older (85.2 years vs. 82.0 years;  $p < 0.001$ ) and had higher rates of renal dysfunction (eGFR < 60: 52.5% vs 32.6%;  $p < 0.001$ ), hyponatraemia ( $\text{Na}^+ < 130$ : 13.9% vs 7.8%;  $p = 0.014$ ), anaemia (86.9% vs. 79.4%;  $p = 0.03$ ) and myocardial ischaemia, evidenced by elevated troponins on admission (46.7% vs. 22.6%;  $p < 0.001$ ).

#### **7.IV. CHARACTERISTICS OF THE COHORT SURVIVING TO DISCHARGE**

Analysis of the cohort of patients surviving to discharge from the index admission (n=723) was performed to investigate for evidence of inequality. The median age in this cohort was 82 years (range 32.3 – 100.5) and, again, 51.3% of the cohort were female. The majority of patients were cared for by a geriatrician (69%) with an even split of the remaining patients being cared for by a cardiologist or a general physician.

Numbers of patients in the least deprived quintile were low (7.7% of the cohort), but there was a fairly even spread of patients between the other 4 quintiles (see table 14).

Overall rates of comorbidity were high, with 55% of patients having AF, and half of patients having had a documented history of hypertension, with similar numbers having a recorded history of ischaemic heart disease (49%). Almost a quarter of all patients had a diagnosis of chronic lung disease (24%) or diabetes (23%).

Hyponatraemia ( $\text{Na}^+ < 130$ ) was uncommon in the cohort surviving to discharge (7.8% of cases) but rates of anaemia were high (79%).

## **7.V. SES IN THE COHORT SURVIVING TO DISCHARGE AND ITS AFFECT ON OUTCOME**

Characteristics of this cohort are presented in table 16, according to quintile of deprivation. The pre-specified method of assigning quintile of deprivation was based on national ranking of IMD2007 scores, rather than internal ranking, and there were thus different proportions of the cohort in each quintile of deprivation (Q1 19%, Q2 28%, Q3 24%, Q4 21%, Q5 8%).

A significant trend was observed for a younger age at the time of the first admission for those in more deprived quintiles. Mean age at time of first admission was 77.9 years (S.D. 11.6 years) in the most deprived quintile and 82.3 years (S.D. 8.9 years) in the least deprived quintile ( $p$  for trend across the five groups = 0.036 – see table 16).

Rates of recorded chronic lung disease appeared to be higher in those in the most deprived two quintiles (30%) when compared with the least deprived quintile (16%). Rates of recorded ischaemic heart disease also appeared significantly higher in the most deprived group (60% vs. 46%) but without any significant observable trend across hierarchical levels of deprivation. Rates of prior outpatient contact with a cardiology clinic, however, were not significantly different between quintiles (32% overall and 35% in the most deprived quintile vs. 36% in the least deprived).

Overall mortality rates did not differ between quintiles of deprivation – 1 year mortality 23% in the most deprived group vs. 25% in the least deprived (28% overall with no observable trend across levels of deprivation).

A relationship was observed between deprivation and 30-day readmission rates. Overall rates of readmission at 30 days were 21% in the cohort surviving to discharge as a whole but 25% in the most deprived quintile, compared with 13% in the least deprived. When considering 30-day readmission rates across all 5 quintiles, statistically significant differential rates of readmission were evident across the five groups with a trend for lower rates as level of deprivation decreased ( $p=0.01$ ).

Survival analysis did not demonstrate any survival advantage associated with lower levels of deprivation (see table 20), nor any association between quintile of deprivation and the combined end-point of death or readmission with heart failure (figure 7).

## **7.VI. THE EFFECT OF AGE ON OUTCOMES IN THE COHORT SURVIVING TO DISCHARGE**

Overall survival differed significantly between the three subgroups of age. There was a clear survival advantage associated with those under 76 years old at first presentation compared with those in the older two groups, and there was an equally significant survival advantage associated with those 76-85 years when compared with those 85 and older ( $p < 0.0001$  across the three groups). However, no significant difference in 30-day readmission rates between subgroups of age was identified (21% in those under 85 and 22% in those over 85 years).

Clearly advancing age is always likely to be associated with higher mortality rates. Therefore, excess mortality throughout the life-course associated with admission with heart failure was estimated by standardised mortality ratios calculated for 5-year age groups within the cohort. The life tables for England published for the mid-point of the study period were used as the reference population (table 23). By this method, a significantly increased mortality rate in the study population was demonstrated even in patients well above 80 years of age. Indeed, patients aged 80 – 84 years in this cohort had an 8 to 9 times higher rate of death than the reference population, and death rates in even patients aged 90 – 94 were 3.5 – 4 times greater.

Given this excess mortality, candidate variables associated with increased mortality were examined using Cox Proportional Hazards modelling and the univariate analysis of pertinent candidate variables is shown in table 20. Advancing age continued to

confer a significant increased risk of death, but neither gender nor quintile of deprivation were associated with any significantly increased mortality. Only anaemia and significant renal impairment were associated with a significantly increased risk of death.

The prescription of medications known to be of benefit in improving prognosis in heart failure was also examined with respect to age. Treatment with an ACEi/ARB on discharge was associated with a decreased risk of death (HR 0.78 [95% C.I. 0.63 – 0.97];  $p=0.028$ ) but significance was lost when age was added to the model (HR 0.82 [95% C.I. 0.66 – 1.02];  $p=0.073$ ).

The prescription of a  $\beta$ -blocker was associated with a more marked reduction in the risk of death (HR 0.58 [95% C.I. 0.44 – 0.77];  $p<0.0001$ ) and the effect remained significant when age was added to the model (HR 0.72 [95% C.I. 0.54 – 0.96];  $p=0.024$ ).

Prescription of aldosterone antagonists on discharge did not appear to be associated with any significant change in the mortality rate (HR 1.11 [95% C.I. 0.90 – 1.38];  $p=0.33$ ). Where age was added to a model examining the effect of prescription of aldosterone antagonists an apparent increased risk of death was demonstrated where these agents were prescribed (HR 1.29 [95% C.I. 1.03 – 1.60];  $p=0.025$ ).

## **7.VII. CARE QUALITY**

### **7.VII.i. OVERALL QUALITY OF CARE AND THE EFFECT OF GENDER**

#### **7.VII.i.a. ECHOCARDIOGRAPHY**

For the cohort surviving to discharge, echocardiography was found to have been performed in 77% of cases. The majority of those who underwent echocardiography did so at some time in the follow-up period of the study following their discharge from the index admission (34% of the cohort as a whole / 44% of those who underwent echocardiography). Where echocardiography was performed other than during follow-up from the index admission, this was mostly done during the index admission itself (28% of the cohort / 36% of those who had an echo), with a small proportion of the cohort having an echocardiogram in the two years prior to the index admission without this being repeated at any other time (16% of the cohort / 20% of those who had an echo). The pre-specified marker of care quality – echocardiography during the index admission or within 6 weeks of discharge – was achieved in 37.5% of cases.

Left ventricular ejection fraction (LVEF) was recorded in 59% of the cohort as a whole, corresponding to 70% of those who had undergone echocardiography. However, subjective assessment of the left ventricular function was reported by the echocardiographer in a much higher proportion of cases where an echocardiogram



was performed (95%). A similarly high level of reporting of left ventricular end diastolic diameter (LVEDD) was observed (93%).

Mean LVEF was 45.7% for those where data were available and mean LVEDD 5.6cm. The distribution of the subjective measures of left ventricular systolic function are illustrated in figure 4. Note that 70% of cases were subjectively assessed as having some degree of systolic impairment and 51% were felt to have more than mild impairment alone.

Men were significantly more likely to have had an echocardiogram performed at any time during the period of interest for the study (94% vs. 87%;  $p=0.02$ ), and particularly during the primary admission (32% vs. 26%;  $p<0.001$ ). For the prespecified marker of care quality – echo during the index admission or within six weeks of discharge – the difference in rates of provision of echocardiography was less pronounced, though still reached statistical significance (39% of men vs. 33% of women;  $p=0.04$ ). Male gender was also significantly associated with the documentation of LVEF (69% vs. 56%;  $p<0.001$ ).

#### **7.VII.i.b. PRESCRIPTION OF MEDICATIONS**

##### **Diuretics**

Orally administered loop diuretics, either furosemide or bumetanide were commonly prescribed on discharge from the index admission, with overall rates of 92.5%. Of all those who received diuretics, the most common total daily dosages,

expressed in furosemide equivalents, were 40mg and 80mg (each 40% of cases).

Doses above 100mg per day were uncommon (11% of cases) and table 15

demonstrates the number of patients in each dosing schedule.

### **Inhibitors of the renin-angiotensin-aldosterone system**

ACE inhibitors were prescribed widely in the cohort, with 64% of those surviving the index admission discharged on this class of medication. Prescription of an ARB was

less common with 11.5% of patients discharged on these. Only 2 patients were discharged with instructions to take both agents, giving an overall prescription rate

of inhibitors of the renin-angiotensin system in those surviving to discharge of 75%.

Rates of aldosterone antagonist prescription were low, with 27% of patients surviving to discharge from the index admission prescribed either spironolactone or epleronone. Rates of aldosterone antagonist prescription were significantly lower in women than men (21.3% vs. 33.2%;  $p < 0.001$ ), though no gender inequality was observed in the prescription of ACEi/ARB (74% of women vs. 76% of men;  $p = 0.59$ ).

### **Beta-blockers**

Overall rates of prescription of these disease modifying therapies were low in this cohort, with only 19% of those surviving to discharge receiving a  $\beta$ -blocker licensed for the treatment of heart failure. 21% of men received an indicated agent compared with 18% of women, although this differential in prescribing rates was not statistically significant ( $p = 0.27$ ). A very small number of patients (3%) were discharged on  $\beta$ -blocker preparations not licensed for use in heart failure.

## **Digoxin**

Prescription of this cardiac glycoside was more common in the cohort as a whole than prescription of  $\beta$ -blockade, with an overall rate of 28%. Rates of prescription in women were found to be significantly higher than in men (36% vs. 24% $p=0.03$ ).

## **Combination therapy**

Intention to treat with a combination of an inhibitor of the renin-angiotensin system, a  $\beta$ -blocker and an aldosterone antagonist was evident in very few members of the cohort according to the drugs prescribed on discharge from the index admission.

Only 6% of cases received all 3 classes of drugs as part of their discharge medication.

18% of cases received none of these disease-modifying therapies on discharge and

49% received only one class of agent. 16.5% of cases were prescribed the

combination of ACEi/ARB and  $\beta$ -blocker (18% of men vs. 15% of women;  $p=0.224$ ).

Of those receiving no disease modifying therapy, all were taking diuretics on

discharge from the index admission.

## **Anti-platelet agents and anticoagulants**

Of those who received an anti-platelet agent, the majority were prescribed aspirin

alone (38%). Roughly equal numbers of patients received either clopidogrel alone

(9%) or the combination of aspirin and clopidogrel (10%). Of those who were

prescribed any anti-platelet agent, 57% were found to have a documented history of

IHD.

67% of those with a history of IHD were prescribed an anti-platelet agent but 43% of those with no such history were prescribed either aspirin or clopidogrel ( $p=0.01$ ). Prescription of clopidogrel, especially in combination with aspirin was strongly associated with a diagnosis of IHD ( $p=0.002$ ). Examination of those with a history of either IHD or stroke revealed a similar pattern to that seen in those with IHD alone, with 63% of those taking any anti-platelet therapy having at least one of these diagnoses.

Over three quarters of patients surviving to discharge (78%) had a history of at least one of either IHD or AF. No relationship was observed between the prescription of anti-platelet therapy and a diagnosis of AF with 50% of patients with AF receiving either aspirin or clopidogrel. A history of AF did appear to predict prescription of warfarin (82% of patients taking warfarin having AF) but rates of prescription of warfarin to those with AF were only 40%. Most patients with AF, however, were prescribed either warfarin or an anti-platelet agent (85%), with a small number of these receiving both therapies (4.5%).

### **Others**

Low rates of the prescription of calcium channel antagonists were observed in those surviving to discharge from the index admission (10%) and similar rates of prescription were observed for dihydropyridine and non-dihydropyridine agents (5.5% and 4.6% respectively). There were no observed differences in prescribing between men and women.

Rates of NSAID prescription were low at 2.5%. No further analysis was attempted on these data given the very low numbers involved.

## **7.VII.ii. THE EFFECT OF SOCIOECONOMIC STATUS ON CARE QUALITY**

Table 17 shows differences in care quality by quintile of deprivation. No trend was observed for differential rates of prescribing of ACEi/ARB, B-blockers or aldosterone antagonists according to quintile of deprivation. Nor was there any apparent deprivation related bias in the performance of echocardiography during the index admission or within 6 weeks of discharge, or the recording of LVEF at the time of echocardiography.

Rates of follow-up with a specialist doctor showed no clear relationship with quintile of deprivation, but rates of follow-up by a specialist nurse were significantly lower in those in the most deprived quintile (9%) when compared with the least deprived (16%). However, a convincing trend across the levels of deprivation was not demonstrated, with those in the middle quintile receiving the highest rates of follow-up (19%).

### **7.VII.iii. THE EFFECT OF AGE ON CARE QUALITY**

Table 18 shows the characteristics of the cohort surviving to discharge according to the three subgroups of age (“young” - <76; “old” – 76-85; and “very old” - ≥85). A significant trend was observed for higher proportions of women with advancing age (33% of “young” vs. 49% of “old” vs. 77% of “very old”;  $p < 0.001$ ).

Median LVEF showed a significant trend for higher ejection fractions with increasing age ( $p < 0.05$  for difference across 3 groups), being highest in the most elderly subgroup (51% [29-73%]), lower in the those aged 76-85 (45% [IQR 21-69%]), and lowest in the youngest subgroup (40% [IQR 21-59%]).

A significant trend was also observed for lower rates of documented ischaemic heart disease with advancing age (58% vs. 48% vs. 42%;  $p$  for trend  $< 0.001$ ) but this trend was reversed for rates of documented atrial fibrillation (47% vs. 56% vs. 64%;  $p$  for trend  $< 0.001$ ).

Older patients tended to have lower eGFR on average and lower mean hemoglobin concentrations but no significant differences were demonstrated between these variables in the old and very old.

Rates of prescription of ACEi/ARB were not significantly different between subgroups of age, although an apparent trend for lower rates in the more elderly was seen (80.6% vs. 74.3% vs. 71.4%;  $p = 0.076$ ).

A striking trend was observed, however, for reduced rates of prescription of both  $\beta$ -blockers and aldosterone antagonists with advancing age (see table 19). Indicated  $\beta$ -blockers were prescribed in 36% of young patients but only 15% of those age 76-85 years and 11% of very old patients ( $p$  for trend $<0.001$ ). Although rates of prescription of aldosterone antagonists were higher than those for  $\beta$ -blockers in the elderly, a significant difference in rates of prescribing across the subgroups of age was still evident. 36% of patients under 75 years old received an aldosterone antagonist (similar to the rate of prescription of  $\beta$ -blockade), whilst 26% of those aged 76-85 and 21% of those over 85 were prescribed these agents ( $p$  for trend = 0.002).

Provision of echocardiography within 6 weeks of the date of admission was also seen to be significantly reduced when moving through the age strata (51% vs 36% vs. 29%;  $p$  for trend $<0.001$ ) and, where echocardiography was performed, there was a significant trend for lower rates of reporting of LVEF (73% vs. 66% vs. 50%;  $p$  for trend $<0.001$ ) associated with advancing age (table 19).



#### **7.VII.iv. CONSIDERING THOSE WITH LV IMPAIRMENT**

In those where LV systolic function was described as anything other than normal or mildly impaired (71% of those who underwent echocardiography), prescribing rates were higher, but remained low for both  $\beta$ -blocker and aldosterone antagonist prescription (81% prescribed ACEi/ARB; 23.6% prescribed  $\beta$ -blocker; 33.1% prescribed aldosterone antagonist). Again no observable pattern was identified for differential prescribing rates between quintiles of deprivation. The significant trend for reduced prescribing of aldosterone antagonists in those in the more elderly subgroups was not evident when only those with LV impairment, described in this way, were included in the analysis but differential rates of  $\beta$ -blocker prescription between groups remained significant. Such results need to be interpreted with caution given the lower rates of echocardiography and documentation of LV function in the elderly.

### **7.VII.v. OVERALL DETERMINANTS OF CARE QUALITY**

The interaction between between patient characteristics, specialist follow-up, and the prescription of beneficial medications was explored in the univariate analysis presented in table 21.

This analysis confirmed the effect of age on the likelihood of prescription of medication with a crude odds ratio of 0.98 (95% C.I. 0.96-0.99) for the prescription of ACEi/ARB per year of advancing age. The most powerful age effect seemed to be in determining the likelihood of  $\beta$ -blockade prescription (OR 0.95 per year [0.94-0.97]), with age also influencing the chances of receiving an aldosterone antagonist (OR 0.97 per year [0.95-0.98]).

Gender did not appear to influence the prescription of either ACEi/ARB ( $p=0.59$ ) or  $\beta$ -blockers ( $p=0.27$ ). Aldosterone antagonists, however, were 84% more likely to be prescribed in men than in women (OR for male sex 1.84 [95% C.I. 1.32-2.57];  $p<0.001$ ).

Deprivation demonstrated no clear effect on the prescription of any class of medication but specialist follow-up was associated with a markedly increased likelihood of prescription of all 3 classes of prognostically beneficial medications. This effect was most marked for the prescription of  $\beta$ -blockers (OR 2.66 [95% C.I. 1.82-3.88]) but was evident for both ACEi/ARB (OR 2.40 [1.66-3.49]) and aldosterone antagonists (OR 1.88 [1.35-2.62]).

Comorbid renal dysfunction and documented history of chronic lung disease respectively affected prescription of ACEi/ARB and  $\beta$ -blockers. Those with stage IV or V chronic kidney disease (eGFR < 30) were significantly less likely to receive an ACEi/ARB compared to those with normal renal function (OR for CKD stage IV 0.57 [0.32-0.99]). No significant differences in prescription rates according to renal function were observed for  $\beta$ -blockers or aldosterone antagonists.  $\beta$ -blocker prescription was, however, 52% less likely where there was a documented history of chronic lung disease (OR 0.48 [95% C.I. 0.29-0.81]).

Of the 723 patients surviving to discharge, 398 (55%) had a documented history of AF (table 22). There was a highly significant trend ( $p < 0.0001$ ) for lower rates of prescription of warfarin in more elderly patients (22% in those 85 and over vs. 60% in those under 76) and for more common prescription of aspirin (59% vs. 37%). Older patients were more likely to be female and have suffered a previous stroke but had generally lower rates of other comorbidities. CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were  $\geq 2$  in all patients and, therefore, warfarin prescription would have been indicated in all cases unless bleeding risk was deemed excessively high.

## **8. DISCUSSION**

### **8.1. OVERALL SUMMARY OF FINDINGS**

This study has demonstrated that heart failure patients admitted to a single acute hospital serving an elderly local population have an average age of over 80 years, and female patients are significantly older than male patients at the time of their first admission with heart failure.

The majority of patients were not cared for by a cardiologist and rates of specialist follow-up were low, though neither of these factors were influenced by socioeconomic status. Nor was prior contact with any specialist or hospital services seen to be associated with level of deprivation.

Heart failure did not commonly occur in isolation in this cohort and the majority of patients admitted had 3 or more comorbid conditions complicating their heart failure. Important comorbidities influencing outcome in terms of mortality were significant renal dysfunction and anaemia, and these were more common with advancing age. Chronic lung disease was also prevalent, particularly in more deprived patients, and was seen to be associated with reduced rates of prescription of prognostically beneficial  $\beta$ -blockade. Only the most severe renal dysfunction was associated with significantly reduced rates of ACEi/ARB prescription.

These data confirm findings from the National Heart Failure Audit that increased levels of deprivation are associated with a younger age at first admission with heart failure. In contrast to previous reports, SUSSEX-HF has not found any increased mortality associated with increased deprivation in heart failure. The study has, however, demonstrated increased rates of readmission at 30 days in patients with increasing levels of deprivation.

Other than an observation that rates of specialist nurse follow up were low in the most deprived admitted quintile of patients, SUSSEX-HF has found no evidence to support significant variation in quality of care according to socioeconomic status in the cohort examined.

What has been demonstrated is that this cohort had significantly increased mortality compared to the contemporaneous population of England and Wales when matched for age and gender, and I propose that this excess mortality could have been reduced to an extent if the quality of heart failure management had been more optimal in the cohort. Overall rates of ACEi/ARB use in this cohort were comparable to previous reports, but still far from universal, and  $\beta$ -blocker prescription rates were very low, despite robust evidence and national guidelines to support their use available at the time of the study. Use of aldosterone antagonists was limited and gender bias appeared to be operating in this cohort to lead to lower rates of prescription in women.

The striking finding in this cohort is the extent to which age appears to influence variations in care quality. Older patients were less likely to undergo echocardiography, less likely to have formal documentation of their ejection fraction, and less likely to receive all classes of prognostically beneficial medication (though differences in rates of ACEi/ARB prescription by age were not statistically significant). Such factors might well have determined to some extent the poorer outlook for older patients in the cohort.

## **8.II. DEMOGRAPHY**

This study has described a cohort of patients admitted for the first time with a diagnosis of heart failure, drawn from an elderly local population. The cohort is notable for its advanced age when compared with other published data. The most easily referenced comparative data come from the UK National Heart Failure Audit, from which results are available for each twelve month period since 2007. April 2008 – March 2009[182] and April 2009 – March 2010[183] are considered here as the most meaningful comparative and contemporaneous data. The median age of patients in these two audits was 78 years and 79 years for the two, consecutive twelve month periods. The study cohort considered here has a much higher median age – 82.4 years. Data are available from a two-centre study in 2003/4 enrolling patients from the same centre as the current study and Hillingdon, West London. This prospective study, with a more rigorous case definition of heart failure, showed a median age at heart failure diagnosis of 75 in a cohort of 396 patients[49]. Data from Leicestershire for the period 1993 – 2001 confirmed an increase in the median age at first presentation with heart failure between 1993/4 and 2000/01 from 74 years to 77 years for men but showed a static median age at first presentation of 80 years in women in the same period[154]. Medicare data from the USA, presented by Bueno et al in 2010 show an essentially unchanged mean age at first admission of around 80 years (79.5 in 1993/4 to 80.0 in 2005/6)[184]. The EuroHeart Failure survey reported data in 2003 pertaining to late 2000 and early 2001, showing an overall age at admission of 71 years in Europe and 75 years in the UK[185]. Data from a single UK centre in Hillingdon, West London, from 1995/6 quote a median age of first

presentation for incident heart failure of 76 (73 years in men and 78 in women)[186]. Other registries of heart failure admissions are available, from Europe and North America, published in the first half of the last decade. The reported mean age for patients hospitalized with heart failure in these series range from 70 – 77[70, 137]. These registry data contrast with results from the Framingham cohort showing a mean age at diagnosis of heart failure of 80 years in the period 1990 – 1999 – markedly older than the mean age of 62.7 years recorded between 1950 and 1969[187].

Why should it be that this cohort appears so much older than those previously described? Several possibilities present themselves:

1. There is evidence for a secular trend for increasing age at first presentation of heart failure from the available literature and projections based on the changing population structure of Scotland have theorized that admissions of elderly patients will increase as the population ages[51]. The available population data for the catchment area of the study site confirm that the proportion of those in the recognized “at risk” age for heart failure (>55 years old) is markedly higher than the UK average, and the relative excess of those above the age of 70 years is higher than the excess observed in those around retirement age (figure 8). Therefore, these data may reflect the fact that a generally more elderly population gives rise to increased incidence of first heart failure admission at an older age.



2. There is good evidence from previously published work that women present at an older age than men. This has been confirmed in the current study. Perhaps it is the case that there is an over-representation of women in this cohort when compared to other published series. Whilst it is certainly true that clinical trials have tended to enroll patients with low ejection fractions – and, therefore, recruit a younger, predominantly male study cohort – it would also appear to be the case that there is an apparent gender bias in the reporting of results from observational studies. Taking the 2010 UK National Heart Failure Audit (UK NHFA) as an example, it can be seen that the percentage of women in the sample overall is 43% - similar to EuroHeart Failure II (39%)[188]. Our data agree with the finding that around 67% of heart failure patients 75 and under are male. The authors make the point that in those over 75 years old the proportion of men and women is roughly equal, a stark contrast to the data presented here where this is the case in the age group 76 – 85 years but there is a marked reversal of male:female ratio of admissions in those of 85 years and older. The resulting figure for comparison with the national data is that 68% of those over 75 years old are women. It may well be the case, therefore, that the excess of women is responsible for the overall higher age of the cohort.
  
3. This begs the question, “Why should there be an excess of women in this cohort?” The UK NHFA reports 36.1% of patients studied being 75 years or younger. Data from SUSSEX-HF give a figure of 26.4% of the cohort in this age range. These data seem more consistent with statements that 24.6% of patients admitted with heart failure are  $\leq$  75 years old. It may, therefore, be the case that

there is selective under-reporting of elderly cases of heart failure in such national audit programs. The UK NHFA 2010 reports that cases submitted to the Audit represent 42% of patients admitted nationally with a primary diagnosis of heart failure. The participation of trusts in the Audit is one of several “Indicators for Quality Improvement” identified by the Department of Health (DoH). The intention was to record data initially for the first ten patients in each month discharged with a primary diagnosis of heart failure; rolling out to record data for all such admissions in due course. Despite this aim, clearly there are significant missing data and there is no readily identifiable method for ensuring that cases submitted to the Audit are consecutive and unselected. It is also worth noting that our cohort includes admissions where heart failure is coded in the first or second diagnostic position, in contrast to the UK NHFA. As such, it is difficult to make direct comparisons between the two cohorts.

### **8.III. COMORBIDITY**

Rates of comorbid conditions in this cohort seem to largely be in line with those observed in most large scale registries of heart failure patients conducted in developed countries (table 24). This lends weight to the premise that the methods used to capture comorbidity data in this study were reliable. However, rates of hypertension and ischaemic heart disease (IHD) appear to be lower than in other published series, and this may well be due to the fact that SUSSEX-HF relied on coded diagnoses rather than recorded physiological measurements or self reported history of hypertension / IHD, potentially reducing the apparent prevalence in the cohort. Rates of comorbidity appear lower in the group who died prior to discharge in our cohort, other than for prior stroke. Given that only data from secondary care were available in this analysis, it may be that those individuals not surviving the index admission were “hospital naïve” and so had no coded diagnoses made previously and recording of co-morbidity on death certificates and subsequent coding of this information was not robust. It is pertinent to note that one US author has published evidence that of a cohort of 122630 Medicare beneficiaries with known chronic heart failure only 4% had heart failure alone and the risk of hospitalization in their cohort was strongly correlated with the number of non-cardiac comorbidities present[189]. Such comorbidity would be recorded on discharge from the index admission but not necessarily in those who did not survive. Prior stroke is the one comorbidity recorded which is most likely to have necessitated hospital admission and rates were similar amongst those who survived

to discharge and those who did not. No significant differences were seen in the number of prior outpatient contacts of individuals who failed to survive the index admission, lending weight to the proposal that rates of comorbidity in those individuals was no higher than in those who survived.

Rates of AF are higher than those seen in most published series, yet similar to those seen in the octogenarian sub-cohort of EuroHeart II, supporting the premise that AF prevalence increases with age. Indeed, in terms of overall comorbidity, the study cohort seems to most closely resemble this elderly, European group, with high rates of non-cardiac chronic conditions. Such levels of comorbidity have previously been cited as important contributors to adverse clinical outcomes in heart failure in the elderly, particularly in relation to high rates of readmission[190].

Despite high levels of comorbidity, these data reveal low rates of prior hospital outpatient contact, both with specialist and generalist / geriatric services, within the cohort. This is likely to represent an increased focus towards managing chronic conditions in the community rather than in the hospital setting[191], certainly in the UK, and this study is limited by not having access to data regarding exposure to primary care. It is not possible to comment from these data on whether or not improved rates of prior contact might be a factor in preventing hospitalizations as only those eventually hospitalized are available to be studied.

#### **8.IV. MORTALITY**

Crude mortality rates in SUSSEX-HF appear to be reasonably consistent with previously published data for admitted heart failure patients. The Rotterdam Study reported a 1-year mortality for incident heart failure of 37%, with a 30-day mortality of 14%[64]. Most published data on incident heart failure give similar figures of between 10 – 20% for 30-day mortality. 1 year mortality in the Hillingdon study – a not exclusively hospitalized group – was 38%[179], although recent evidence has suggested that the secular trend is for improved survival – 26% at 6 months in the original Hillingdon cohort (1995-1996) vs. 14% at 6 months in the 2004-2005 cohort[49].

1-year mortality in the 2010 UK NHFA was 32%, though rates of death during the index admission were considerably lower in the National Audit than those observed in our study (10% vs. 18%). The explanation for such disparity may well lie in the fact that this was a generally older cohort, with high rates of admission to non-cardiology wards and high rates of AF – all factors cited in the Audit as being predictive of in-patient death[183].

## **8.V. READMISSION**

Best estimates are that around a third of patients are readmitted for the management of heart failure within a year of discharge[48]. Data presented here would suggest that this is still the case despite marked developments in the understanding and management of heart failure since this result was first reported. It is difficult to compare readmission rates internationally but figures from SUSSEX-HF for readmission at one year are similar to those reported in Japan[161]. Rates for readmission within a year are not generally reported in the USA, but readmission rates at 6 months have been reported as approaching 50%[116].

The finding that 30-day readmission rates were 6.6% for heart failure and 21.3% for any cause is of high clinical relevance as well as carrying significant health economic consequences. It is also interesting to note that the all cause 30-day readmission rate was similar across all three age groups studied, suggesting that age alone is not the primary determinant of readmission in this heart failure cohort.

All cause 30-day readmission rates did appear to be higher in the most deprived groups compared with the least deprived group. This finding is not easily explained by any factor considered in this analysis. Although rates of contact with specialist nurses were lower in the same groups, it seems unlikely that there is a causal link between these two facts as rates of follow-up by specialist nurses over the course of two years were generally too low to have a clinically significant impact on reducing 30 day readmission rates. One might theorize that lower levels of social support or,

as previously reported, reduced rates of contact with GP services in more deprived households contributes to higher rates of readmission in these groups[145].

## **8.VI. THE EFFECT OF DEPRIVATION**

Whilst overall the SUSSEX-HF cohort is elderly, there is some evidence to support presentation at an earlier age in more deprived individuals. This finding is not readily explained by any differences between individuals in each quintile of deprivation identified in this study, though similarly younger ages in more deprived groups have been seen in the UK National Audit at the time of an unscheduled admission for heart failure. It is also the case that previous studies reporting increased incidence of heart failure associated with lower SES generally recruited patients of a young age and so some of the increased incidence seen in those of lower SES might well be related to a tendency for earlier onset of heart failure in these individuals. Rates of co-morbidity were generally high in all quintiles of deprivation, although rates of documented ischaemic heart disease and chronic lung disease were noted to be higher in the most deprived group. We have found no evidence to suggest that more deprived members of the cohort were more or less unwell at the time of presentation or subsequently in terms of rates of inpatient death in each quintile of deprivation and subsequent mortality rates in those surviving to discharge, in contrast to previous reports.

Our data do show that, following an admission with heart failure, subsequent management and outcome are not dependent on level of deprivation. No differences in survival are demonstrated between members of the cohort surviving to discharge according to quintile of deprivation, and no significant differences are observed between quintiles in access to echocardiography, recording of LVEF,



prescription of beneficial medications or provision of specialist follow-up. There is, however, a suggestion from these data that contact with specialist nursing services was lower in the more deprived 2 quintiles and that 30 day readmission rates are also higher in this group.

Rates of death were not found to be robustly associated with IMD 2007 Quintile in this cohort and no differences were observed in survival time, or time to death or first admission with heart failure. This contrasts with several previous reports which have proposed a link between increased deprivation, or lower socioeconomic status, and decreased survival times in heart failure patients.

We have employed a method for identifying individual levels of deprivation by using a proxy measure based on postcode of residence, allowing comparison of individuals according to nationally available comparative data. It may be argued that such a tool provides an inappropriate measure of deprivation for elderly individuals, as it is a cross-sectional measure, purely based on residence at the time of sampling for the study. However, it seems reasonable to propose that an individual's postcode of residence in retirement is a meaningful proxy for status over the life-course of that individual, as their eventual position in a hierarchical measure of deprivation is likely to have been predicted by their overall lifetime experience.

Notwithstanding such argument, it is the case that previously reported data have employed similar methods for defining socioeconomic status in heart failure cohorts and have demonstrated an apparent association between deprivation and mortality

or readmission rates. I cannot identify such an association in this cohort and propose several possible explanations for these findings:

1. Available comparative data are based mainly on studies of cohorts assembled in 1998-2000. This period was a time of rapid advancement in heart failure therapies and management strategies. The application of such developments in clinical practice is known to lag behind the publication of important clinical trial data, not only because guidelines for clinical practice take time to be released, but also because these guidelines need time to become disseminated and acted upon at “the coal face”. Where interventions are novel, and have potential cost implications – especially in health economies not operating universal coverage – then there is the potential for inequity to operate. The reasons which underlie this phenomenon are legion, but are likely to include higher awareness and demand for timely investigation and novel therapies amongst those of higher socioeconomic status. These data may suggest that in a more contemporary cohort, such factors may be playing a less important role in determining access to beneficial therapies as these are now considered as “routine” elements of heart failure management. In support of this argument is the fact that deprivation appeared to have no predictable association with access to echocardiography, follow-up, or the prescription of any class of disease modifying therapy in this cohort. However, the argument that “routine” heart failure management is being universally applied is not well supported by these data, given the low overall rates of medication prescription –

particularly in the cases of  $\beta$ -blockers and aldosterone antagonists. Other factors than deprivation appear to be responsible for mediating these effects.

2. Health inequality has been a focus of political interest in the UK over the course of the last decade. It may be the case that awareness of this issue, in part as a consequence of the previously published data in this area, and as a result of national programmes to highlight inequality and encourage health inequality audit, has borne fruit in tackling inequity in heart failure management – effectively abolishing health inequality according to socioeconomic status in this cohort.
  
3. These data demonstrates indirect support for previous findings that incident heart failure occurs at an earlier age in more deprived individuals and confirm the findings of the NHFA that more deprived patients present on average at a younger age. Median age at first admission with heart failure in this cohort was significantly lower in the most deprived group than the least deprived, with an observable trend across the quintiles of deprivation. This finding raises the possibility that the lack of observable differences in survival in those in higher quintiles of deprivation is a consequence of “survivor selection” amongst those admitted. The multivariate analysis does not support an interaction between age and quintile of deprivation in determining survival, with age remaining the strongest predictor of outcome, regardless of quintile of IMD-2007. Once admitted with heart failure, therefore, these data suggest that deprivation does not affect outcome,

despite the fact that admission is likely to occur earlier in life. Therefore, factors which determine the development of heart failure are likely to be more influenced by the operation of health inequality than is subsequent management of the syndrome itself.

All cause readmission at 30 days did appear to be more frequent in members of the cohort from the more deprived quintiles. This fact is not easily explicable by any of the data that have been collected as part of this study. No assessment of the severity of heart failure on admission was made but it seems unlikely that the severity on discharge was markedly different between quintile of deprivation as no differences in average diuretic dose was observed between groups. Groups also showed no significant differences in any of the markers of care quality, which might have been predicted to avoid readmission, other than the observation that low rates of specialist nurse follow up was seen in the most deprived quintile. Comorbidity might be a potential explanation for these findings, particularly the higher rates of chronic lung disease and ischaemic heart disease recorded in the more deprived quintiles. A lack of data on community support and GP services, however, limits the ability to draw firm conclusions on this.

The finding that readmission rates were higher in those from more deprived groups is pertinent given evidence from the USA that survival in the very elderly is improving but admission rates remain high[192] and also given that assessments of quality include measures of readmission rates in the UK.

## **8.VII. AGE RELATED INEQUITY**

SUSSEX-HF provides novel data for the operation of age related inequity in the management of heart failure in the elderly. These data demonstrate that admission for a first presentation with heart failure in this cohort carries an increased hazard ratio for death compared to the general population regardless of the age at which this admission occurs. Given this finding, it should be considered iniquitous to observe differential care quality on the basis of age alone. However, we have observed considerable evidence for the operation of such inequity in this cohort.

The prescription rates of ACE inhibitors, or ARBs, in the cohort do not appear to be influenced by age when other important factors are taken into consideration. Initial analysis of the data does appear to show a trend for lower rates of prescription according to advancing age, and univariate analysis of prescription related to age reveals this non-significant trend observed across the three age groups to be a result of an apparent decreasing likelihood of prescription with increasing age. However, encouragingly, this association is not significant in a multivariate model which takes into account LVEF and renal function. The apparently strong association between specialist follow-up and ACEi/ARB prescription is also lost in the final model. This is most likely to be explained by the fact that age was the most powerful predictor of specialist follow-up.

Such findings are encouraging in that they suggest that the decision to prescribe ACEi/ARB is based mainly on appropriate clinical considerations, regardless of the age

of the patient. It also implies that “non-specialist” physicians are comfortable with the use of these agents for the management of heart failure in the elderly.

Given that ACE inhibition is the modern prognostically beneficial therapy for which there is the longest standing historical evidence, these results support the theory that inequity is less likely to operate where there is long-standing experience and general guidance regarding the use of a treatment.

Contrasting these findings with the results regarding the relationship between age and  $\beta$ -blocker or aldosterone antagonist prescription, there is evidence from this cohort that age related inequitous prescribing behaviour is operating.

Our results lend weight to the supposition that several factors conspire to determine the reluctance of physicians to prescribe  $\beta$ -blockers to patients admitted with heart failure.

Firstly, overall rates of  $\beta$ -blocker prescription were low and this may be explained by a reluctance to institute  $\beta$ -blockade in the setting of a recent acute decompensation or recent myocardial infarction (given the high numbers of patients in the cohort with recorded positive Troponin-I). The methods used in this study did not allow for any recommendation to start  $\beta$ -blockers post-hospital discharge to be recorded.

However, there is evidence from the post-MI setting that unless therapies are instituted at discharge, or in the immediate post-discharge period, then chances of long-term therapy are low[193]. Therefore, the generally low rates of  $\beta$ -blockade observed on discharge in this cohort are disappointing, especially when compared

with data on prescription rates provided by the contemporaneous UK NHFA and other, recent European and North American registries. Some explanation for these lower comparative rates may lie in the decision to include in the study patients with heart failure diagnosed in the secondary position, where the primary diagnosis, felt to be the ultimate reason for admission, might increase reluctance to institute  $\beta$ -blockade. However, patients with heart failure recorded in the second diagnostic position have as much requirement for prognostically beneficial  $\beta$ -blockade as those admitted with a primary diagnosis.

Despite evidence supporting the use of cardioselective  $\beta$ -blockers in heart failure with co-existing lung disease[93] clinicians are generally more reluctant to prescribe these agents in this setting[165]. These data appear to lend weight to this supposition, demonstrating a strong association between history of chronic lung disease and reduced chances of  $\beta$ -blocker prescription on univariate analysis.

However, adding other variables to investigate the relationship further demonstrates that this association is abolished when other factors are taken into account. Advancing age powerfully predicts likelihood of  $\beta$ -blocker prescription in this cohort along with LVEF. It is clear from the data that specialist follow-up is strongly associated with age and powerfully predicts  $\beta$ -blocker prescription.

Taken together, these results seem to show that those patients who receive specialist follow-up are more likely to be young and more likely to be started on a  $\beta$ -blocker on discharge. The fact that the effects of chronic lung disease are muted by these factors would imply that those patients who receive specialist input are less

likely to have a  $\beta$ -blocker withheld for reasons of perceived risk. Our data, therefore, suggest that ageism operates both directly and indirectly in this cohort to reduce  $\beta$ -blocker prescription rates in the elderly. Those patients who are treated by generalists (in this case geriatricians) are potentially less likely to receive  $\beta$ -blockers due to:

1. Less physician experience of  $\beta$ -blocker use in heart failure due to the fact that this therapy is more novel than ACE inhibition.
2. Increased perception of the risks of  $\beta$ -blockade, especially in the elderly.

The picture is similar for those patients receiving aldosterone antagonists on discharge. The SUSSEX-HF data have demonstrated a strong age effect on the prescription of these agents, with patients in each age group analysed being progressively less likely to receive treatment as age advances. Female gender also seemed to be predictive of lower rates of aldosterone antagonist prescription on univariate analysis but further exploration suggests that this is mainly mediated by the higher proportion of women present in the cohort as age advances. Interestingly, renal dysfunction appeared not to influence the prescription of aldosterone antagonists, despite data in this cohort demonstrating that increased mortality is associated with the prescription of these agents in the setting of renal dysfunction, especially with increasing age.

Evidence for the use of aldosterone antagonism in heart failure at the time of this study was based on data from the RALES trial (1999)[78] – performed in a generally



much younger cohort and in patients exclusively with severe left ventricular dysfunction – and to some extent on data from EPHESUS (2003)[194], using eplerenone in the post-MI setting. These data have been considered and formed the basis of recommendations made in North American, European and UK NICE guidance for the treatment of heart failure to use aldosterone antagonists as a third line agent. In the UK, at the time of this study, the published NICE guidance recommended addition of aldosterone antagonists to treatment with ACE inhibitor and  $\beta$ -blocker under the direction of a specialist.

Given these contemporary recommendations, our data regarding the prescription of aldosterone antagonists are interesting for several reasons:

1. Overall rates of prescription are higher than those for  $\beta$ -blockers, suggesting that physicians are in general happier to prescribe these agents in heart failure. This may be explained, in part, by perceptions regarding the diuretic effect of spironolactone and familiarity with its use in the treatment of chronic liver disease. Such perceptions may well lead physicians to be more comfortable with using aldosterone antagonists in the acute setting, with the primary aim of reducing congestion.
2. Higher subsequent rates of follow up with specialist services were associated with prescription of aldosterone antagonists at discharge on univariate analysis but, whereas this effect seems to be clearly age mediated in its association with  $\beta$ -blockade, the relationships are more difficult to identify regarding aldosterone antagonism.

3. Univariate analysis of the effect of gender on the prescription of aldosterone antagonists reveals a strong relationship, which persists with the addition of age to the model, suggesting that there is an inherent gender bias in prescribing in this area.

What seems to be suggested by these data is that patterns of aldosterone prescribing are less predictable than those observed for either ACEI/ARB or for  $\beta$ -blockade. This is most likely to be explained by the fact that the use of these agents in heart failure is less well understood by non-specialists and their use has not been as clearly mandated by robust evidence and national guidance. Where there is such potential for variation in practice then inequity is more likely to occur, and this appears to be demonstrated here.

Further support for this proposition comes from the finding that warfarin prescription rates are significantly lower in the more elderly AF patients in this cohort. Awareness of the importance of formal anticoagulation in high-risk patients, as determined by a validated risk assessment tool – the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, has increased with the publication of European guidelines on AF[99], since the initial work in developing the score was undertaken. In the period over which data for SUSSEX-HF were collected, such guidelines were not available and so the judgement of individual clinicians exclusively informed decisions regarding the prescription of formal anticoagulation. Clearly clinicians still exercise such judgement regarding these decisions, but robust risk assessment tools give more confidence in the decision to prescribe medications when personal experience may have previously

caused physicians to adopt a more cautious approach to anticoagulation due to perceived risks of bleeding in the elderly. Having said this, clearly data are not available from SUSSEX-HF regarding the potential bleeding and falls risk of the patients in the study, and this needs to be borne in mind when considering these data.

A significant trend has been observed for reduced provision of echocardiography in elderly patients in this cohort. This is associated with an overall effect of there being significantly fewer timely echocardiograms performed in women in this cohort than in men. At the very least, indirect gender based inequality in provision of echocardiography exists in this cohort, and there is evidence for age based inequitable access to echocardiography. It is also worth noting that similar inequitable patterns were observed in the recording of LVEF where echocardiography was performed.

The benefits of echocardiography and assessment of LVEF are likely to stem from the administration of beneficial therapies on the basis of the information gained. Indeed, when analysis was confined to the administration of drug therapy in those with documented LV impairment, prescription rates were improved and inequitable prescribing on the basis of age was diminished. This cohort is constructed primarily on the basis of coded diagnosis of heart failure with corroboration of this coding on the basis of clinical findings. Where echocardiography has been performed in the cohort it is clear that higher LVEF have been recorded in elderly patients, and yet fewer measurements of LVEF have been taken in this group. It may well be the case that those with reduced LVEF are not being identified and appropriately managed

due to iniquitous provision of echocardiography. To a certain extent this may be a result of the widely reported predominance of heart failure with normal ejection fraction in elderly women reported in the literature. Physicians may well be aware of these facts, either from such epidemiological reports, or from their own experience, and this may drive the reduced provision of echocardiography in elderly, female patients – especially where a limited resource may already be under pressure in terms of numbers of echocardiograms which can be performed. This finding is of particular relevance, given the fact that recently updated NICE guidance recommends that echocardiography be performed within two weeks in cases of new or suspected heart failure[40].

It is worth noting that these data do not consider the aetiology of heart failure in this cohort. Clearly echocardiography is a key investigation for defining this in the acute setting. Identification of valve disease or acute left ventricular regional wall motion abnormality will also have important consequences for determining treatment and eventual outcome.

## **9. LIMITATIONS OF THE CURRENT STUDY**

Clearly the study has several important limitations and the results and conclusions must be considered in the light of these.

Firstly, this is a single centre study. Examination has been made of the outcomes and management of an historical cohort presenting to a single hospital and therefore managed by a limited number of physicians. No attempt has been made in the analysis to examine individual physician behaviour, but it is possible that the results may be affected by the “rogue” behaviour of a single individual. Such a conclusion is unlikely, especially given the similarity of our data to contemporary national audits in terms of event rates and ACEi/ARB and aldosterone antagonist prescription rates. It is difficult to believe that the actions of a single individual, or indeed the influence of a prevailing practice within the centre, are responsible for the markedly low  $\beta$ -blocker prescription rate.

The lack of availability of GP data in this study significantly limits the generalizability of the conclusions. Both selection bias and spectrum bias are introduced due to the lack of availability of such data. Much of the treatment of long-term conditions, including heart failure, is carried out in the community and this study has been unable to provide a picture of the ongoing treatment of patients over time following their discharge from hospital, or indeed any information on those patients with heart failure who are exclusively managed in the community.

Patients may have been admitted to hospital with varying degrees of severity of heart failure depending both on their contact with primary care services and the ability of those services to manage heart failure. Such data may well be pertinent in determining overall quality of care in the population as differences in the quality of heart failure management provided by primary care services might well have an impact on the rates of acute admissions to hospital, both in terms of index admissions and readmissions.

The sample size calculation to investigate for a mortality effect of deprivation was based on limited information from previously published studies. Death rates in the cohort were higher than those initially predicted and it is unlikely that these analyses would not detect a clinically relevant effect if it were present. However, numbers of patients in the least deprived quintile were lower than predicted as the spread of patients was not even between quintiles (based on national ranking). This may have had consequences in detecting smaller numbers of event rates in the least deprived quintile. However, the lack of any discernable trend across quintiles of deprivation makes it unlikely that any important effect was missed in the analysis.

The retrospective nature of the study and the reliance of collection of data from health records limit the confidence with which any associations observed may be ascribed to causal relationships. The study design attempted to allow for as many potential confounding factors as possible in the analyses, but some data were not reliably available. Significantly, blood pressure, smoking status and NYHA status are not included in our analyses. Certainly there was no robust assessment of the

severity of heart failure on admission and this, leaves the study open to spectrum bias as the heart failure cohort considered might well be a very heterogeneous one in terms of severity.

The study is also limited by the fact that the case definition of heart failure used relies heavily on retrospective coding of hospital admissions. Attempts have been made to introduce some internal validity into this system by using available clinical data. It is possible that an element of selection bias has operated in so far as heart failure cases have been excluded or included inappropriately on this basis. By assembling a large cohort over the course of consecutive years an attempt has been made to limit the impact of such inappropriate selection bias.

## **10. CLINICAL RELEVANCE**

Inequalities in health according to socioeconomic status are well recognised within the UK, and life expectancies in those in the most deprived groups are up to ten years lower than those in the least deprived stratum[195]. Of even greater concern is the observation that disease free life expectancy shows an even more marked social gradient.

This study confirms that this health inequalities gap is evident in heart failure, with admission to hospital for the management of a first episode of heart failure occurring on average 4 years earlier in those in the most deprived quintile vs. those in the least deprived quintile. However, policies targeting health inequality based upon deprivation would do well to address factors occurring earlier in the life-course in order to derive maximal benefit.

This study has demonstrated no adverse social gradient in outcome following admission with heart failure in this cohort, other a tendency to higher rates of early readmission in the most deprived. Neither has any evidence been found that inequitous provision of services operates once admission has occurred. It is likely that earlier onset of ischaemic heart disease, less well managed hypertension, poorer nutrition and “status syndrome” itself all contribute to earlier onset of heart failure. However, it is encouraging that clinicians, on the basis of these findings, seem blind to deprivation factors when managing admitted heart failure. In a time of austerity,



and attention to maximizing the impact of health interventions, these data do not support investment in specific policies aimed to direct heart failure services into more deprived areas.

Despite such encouraging findings, these data have demonstrated evidence for disappointingly low rates of  $\beta$ -blocker use in this cohort, in stark contrast to nationally reported data. A broader definition of heart failure admissions and the generally older nature of this cohort may explain this observation. However, this cohort does appear to be representative, and the population from which it is drawn is similar to that predicted for the UK over the next decade. As such, these data serve as a clarion call against complacency in improving treatment of heart failure.

There is evidence of marked age related inequity in the management of heart failure in this cohort and if this were to be translated to a national scale then the consequences in terms of early heart failure deaths and potentially avoidable readmissions would be vast. Access to echocardiography and disease modifying therapy in the elderly heart failure population should be a key priority in the UK in the future.

These data support the proposition that more novel therapies are those which are most likely to be under-utilized according to iniquitous patterns. Data regarding the lower rates of use of aldosterone antagonists in women and the elderly are of particular concern given the strongly positive results of the recent EMPHASIS trial[95]. The indication for use of these agents now seems stronger than ever, but it

will take time for this message to reach general physicians, who, on the basis of these results, are commonly treating heart failure, especially in the elderly.

In order to minimize age related inequality in the treatment of heart failure this study has provided some evidence that specialist follow-up is important, and these findings are supported by other available data. A multi-disciplinary model of heart failure management in the elderly, involving cardiologists and specialist geriatricians is likely to be required to ensure optimal management of these patients over the course of the next ten years. Studies to explore the practicalities and impact of such a model would be welcome.

## **11. GENERAL CONCLUSIONS AND PRACTICAL RECOMMENDATIONS**

These data from the SUSSEX-HF study provide evidence for an increasingly elderly heart failure population in the UK. Management of heart failure in this cohort is not affected by socioeconomic factors but does appear to be strongly influenced by advancing age. The significantly higher proportion of women amongst the very elderly results in the indirect operation of gender inequality in the management of the syndrome.

Ongoing audit on a national scale continues to highlight these inequalities on a yearly basis and yet they persist. What, therefore, can be done to reduce iniquitous provision of services along lines of age and gender?

The UK National Institute for Health and Clinical Excellence has published quality standards for chronic heart failure explicitly setting out the aspects of care which should be provided for all patients presenting with the syndrome[196]. Of particular relevance when considering the data presented in this thesis are the standards for admitted patients with heart failure:

**“Quality statement 10: Management plans for people admitted to hospital. People admitted to hospital for heart failure have a personalised management plan that is shared with them, their carer(s) and their GP.”**

**“Quality statement 11: Contribution of multidisciplinary heart failure team to management plans.** People admitted to hospital because of heart failure receive input to their management plan from a multidisciplinary heart failure team.”

**“Quality statement 12: Hospital discharge and follow-up care.** People admitted to hospital for heart failure are discharged only when stable and receive a clinical assessment by a member of the multidisciplinary heart failure team within 2 weeks of discharge.”

These standards provide a framework against which high quality care may be assessed and provide a tool whereby local audit may be designed to assess the adherence to these standards. In order to facilitate continuous local audit, acute hospitals should develop pathways for the care of the admitted heart failure patient to ensure adherence with each of the standards by mandating echocardiography and necessitating review by the heart failure multi-disciplinary team within a specified period of admission. Checklists for recommended investigations could easily be included in such pathways and they should also include prompts for consideration of the introduction of ACEi/ARB,  $\beta$ -blockers and aldosterone antagonists with a section to record any variance from recommended management and the justification for this.

Providing a personalized management plan could easily be assessed by designing standardized electronic discharge summaries with relevant fields recording clinical

status, location of in-patient care, investigations performed, medications prescribed, and plans for follow-up.

A key point, demonstrated in both SUSSEX-HF and the UK NHFA, is that patients often present for admission with heart failure in the absence of a preceding diagnosis. My data also demonstrate that these patients are commonly admitted with heart failure in the second diagnostic position and with multiple comorbidities. Such patients are predominantly elderly and local systems exist to divert their care away from cardiologists due to admissions policies and ward based systems of care – common in acute hospitals in the NHS. The quality standards regarding diagnosis and initial management are designed to facilitate pathways for the management of heart failure patients in the community, but I would recommend a more robust guideline laying out the standards of management for patients presenting to hospital with acutely decompensated heart failure, and this is something that has been commissioned by NICE. Such a guideline would do well to include specific standards for the timing of echocardiography for de-novo admissions, the documentation of LV systolic function, and for the care of patients on cardiology units. Of paramount importance when drawing up such a guideline will be that it specifically recommends standards for patients of all ages.

With such standards in place, commissioning of acute heart failure services could be better informed and high quality care could be further incentivized by linking the achievement of these standards to the tariff paid for a heart failure admission.

Penalizing early readmission would not appear to be a reasonable strategy to improve care quality on the basis of the data presented in this thesis as higher rates observed in more deprived individuals seem independent of quality of care and no increased rates were observed in more elderly individuals despite the fact that markers of care quality were worse.

The SUSSEX-HF demographic data have important consequences for benchmarking when commissioning services. Attention should be paid to the high numbers of elderly female patients in the cohort presenting with heart failure. Epidemiological data used as the assumption for benchmark activity in localities may well be inaccurate where there are high numbers of the very elderly and women may be over-represented. Commissioners in such areas will need to be attuned to this fact to ensure adequate resources are made available to ensure high quality services in these populations.

Ongoing work in this area will need to concentrate on the reasons behind the presentation of patients from more deprived backgrounds at an early age, but this is likely to require an ambitious longitudinal population based study.

Examination of the interplay between primary and secondary care in the treatment of heart failure, alongside the development of integrated systems of care designed to improve outcomes for patients throughout their transit through the healthcare system, will require continuous and rigorous audit at both a local and national level. Highlighting good practice should be a key feature of the national audit programme

and this should be combined with high quality education as part of the continuing professional development of those involved in the care of heart failure patients. Evidence of involvement in such practice should be provided as a key part of the revalidation cycle for all those involved with such patients.

## 12. FIGURES AND TABLES

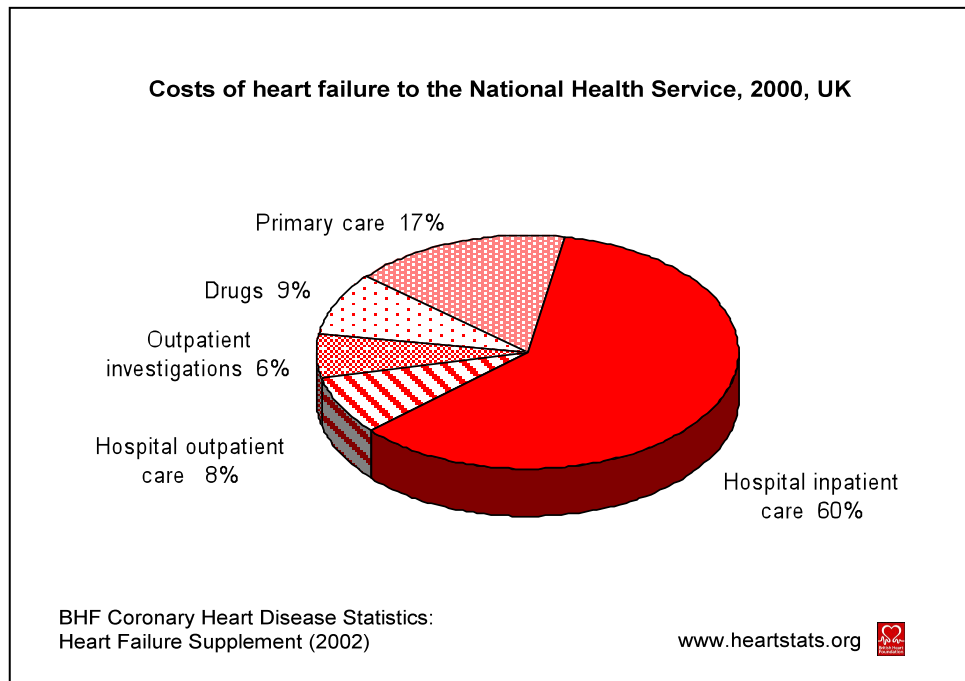


Figure 1: Breakdown of total spend of UK heart failure budget in NHS in 2000[57]



NYHA class	Description	Category
I	<b>No limitation:</b> ordinary physical activity does not cause fatigue, breathlessness or palpitations	<b>Asymptomatic</b>
II	<b>Slight limitation in physical activity:</b> comfortable at rest but ordinary activity results in fatigue, breathlessness or palpitations	<b>Mild</b>
III	<b>Marked limitation of physical activity:</b> comfortable at rest but less than ordinary activity results in fatigue, breathlessness or palpitations	<b>Moderate</b>
IV	<b>Unable to carry out any physical activity without discomfort:</b> symptoms of cardiac failure at rest with increased discomfort with any physical activity	<b>Severe</b>

Table 1. New York Heart Association (NYHA) classification of heart failure

severity by symptoms.

Drug	Initial dose (mg)	Maximum recommended daily dose (mg)
<b>Loop diuretics</b>		
Bumetanide	0.5-1.0	5-10
Furosemide	20-40	250-500
Torsemide	5-10	100-200
<b>Thiazides</b>		
Bendroflumethiazide	2.5	5
Metolazone	2.5	10
<b>Potassium-sparing diuretic</b>		
Amiloride	2.5-5	20-40
Triamterene	25-50	100-200

Table 2. Diuretics used in the treatment of heart failure (based on recommendations from UK National Institute for Health & Clinical Excellence [NICE]).

ACE inhibitor	Starting dose	Target dose
Captopril	6.25mg three times daily	50mg three times daily
Enalapril	2.5mg twice daily	10-20mg twice daily
Lisinopril	2.5-5mg once daily	20mg once daily
Ramipril	2.5mg once daily	5mg twice daily or 10mg once daily
Trandolapril	0.5mg once daily	4mg once daily

Table 3. ACE inhibitors used in the treatment of heart failure (based on recommendations from UK National Institute for Health & Clinical Excellence [NICE]).

<b>BB</b>	<b>Starting dose</b>	<b>Target dose</b>
Bisoprolol	1.25mg once daily	10mg once daily
Carvedilol	3.125mg twice daily	25-50mg twice daily
Nebivolol	1.25mg once daily	10mg once daily

Table 4. Beta-blockers used in the treatment of heart failure (based on recommendations from UK National Institute for Health & Clinical Excellence [NICE]).

CHA <sub>2</sub> DS <sub>2</sub> -VASc Risk Factor	Score
CHF / LVEF $\leq$ 40%	1
Hypertension	1
Age $\geq$ 75	2
Diabetes	1
Stroke/TIA/ Thromboembolism	2
Vascular Disease	1
Age 65 - 74	1
Female	1

Table 5: CHA<sub>2</sub>DS<sub>2</sub>-VASc score calculation[98].

CHF Grade	Definition
0	No dyspnoea, cardiac disease score = 0 & no treatment for CHF
1	Cardiac disease score > 0, no dyspnoea & no treatment for CHF
2	Cardiac disease score > 0 & either dyspnoea or treatment for CHF
3	Triad of cardiac disease score > 0, dyspnoea and treatment for CHF
4	Died with CHF during follow-up

Table 6: Congestive Heart Failure (CHF) Grade according to the criteria specified in the original 1987 European Heart Journal article by Eriksson et al. to validate a scoring test for cardiac and pulmonary causes of dyspnoea[142].

Hastings & Rother PCT	East Sussex Downs & Weald PCT
<p>Bexhill Hospital</p> <ul style="list-style-type: none"> <li>• Outpatient services</li> <li>• GP managed respite and rehabilitation in-patient beds</li> <li>• Day-surgery</li> <li>• Radiology (plain X-ray)</li> </ul>	<p>Lewes Victoria Hospital</p> <ul style="list-style-type: none"> <li>• Outpatient services</li> <li>• GP managed respite and rehabilitation in-patient beds</li> <li>• Day-surgery</li> <li>• Radiology (plain X-ray)</li> <li>• Minor Injuries Unit</li> </ul>
<p>Rye Memorial Hospital</p> <ul style="list-style-type: none"> <li>• Outpatient services</li> </ul>	<p>Uckfield Community Hospital</p> <ul style="list-style-type: none"> <li>• Outpatient services</li> <li>• Day-surgery</li> <li>• Minor Injuries Unit</li> </ul>

Table 7: Services provided by East Sussex Hospitals' NHS Trust at each location within the region.

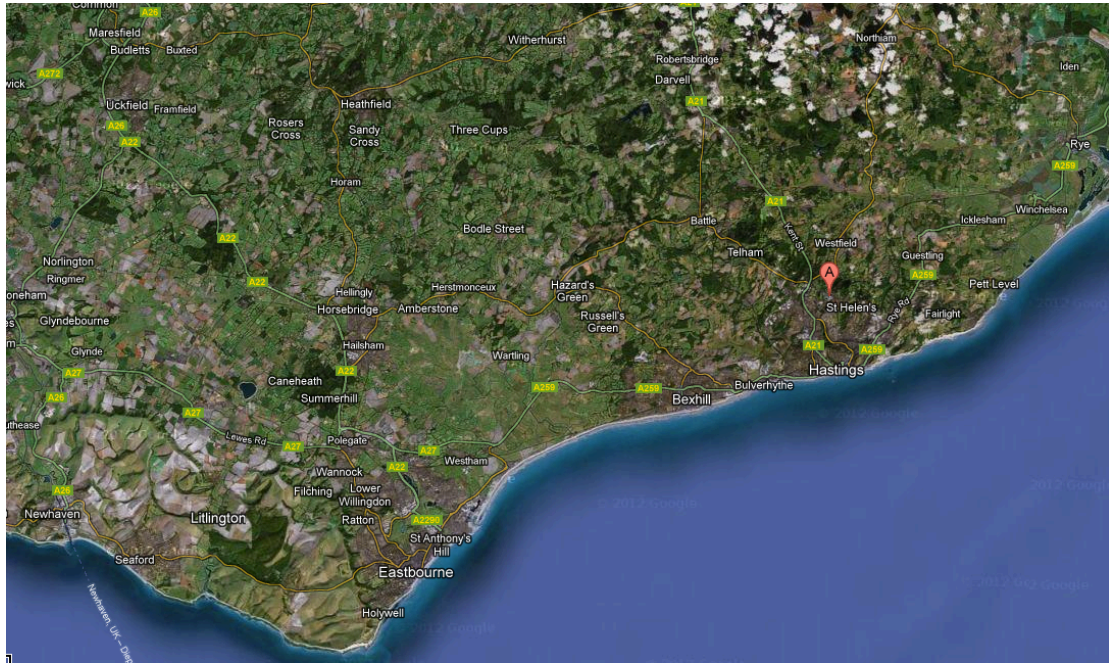


Figure 2: Map showing the road network and geographic setting of Conquest Hospital (A) within the region served by East Sussex Hospitals' NHS Trust. *Source Googlemaps – downloaded June 2010.*



ICD-10 Code	Definition
I50.0	Congestive Heart Failure
I50.1	Left Ventricular Failure
I50.9	Heart Failure, unspecified
I42.0	Dilated Cardiomyopathy
I42.9	Cardiomyopathy, unspecified
I25.5	Ischaemic Cardiomyopathy
I11.0	Hypertensive Heart Disease with (Congestive) Heart Failure

Table 8: ICD-10 codes used to identify a heart failure admission in the SUSSEX-HF study.

Criterion point	Value*
<i>Category I: history</i>	
Rest dyspnea	4
Orthopnea	4
Paroxysmal nocturnal dyspnea	3
Dyspnea on walking on level	2
Dyspnea on climbing	1
<i>Category II: physical examination</i>	
Heart rate abnormality (if 91-110 beats/min, 1 point; if >110 beats/min, 2 points)	1-2
Jugular-venous pressure elevation (if >6 cm H <sub>2</sub> O, 2 points; if >6 cm H <sub>2</sub> O plus hepatomegaly or edema, 3 points)	2-3
Lung crackles (if basilar, 1 point; if more than basilar, 2 points)	1-2
Wheezing	3
Third heart sound	3
<i>Category III: chest radiography</i>	
Alveolar pulmonary edema	4
Interstitial pulmonary edema	3
Bilateral pleural effusions	3
Cardiothoracic ratio $\geq 0.50$ (posteroanterior projection)	3
Upper-zone flow redistribution	2

\*No more than 4 points are allowed from each of the 3 categories; hence, the composite score, the sum of the subtotal from each category, has a maximum possible score of 12 points. The diagnosis of heart failure is classified "definite" for a score of 8 to 12 points, "possible" for a score of 5 to 7 points, and "unlikely" for a score of 4 points or less.

Table 9: Boston Criteria for Congestive Heart Failure[44].

<b>Domain</b>	<b>Weight given to domain in determining overall IMD 2007 (%)</b>
Income Deprivation	22.5
Employment Deprivation	22.5
Health Deprivation and Disability	13.5
Education, Skills & Training Deprivation	13.5
Barriers to Housing & Services	9.3
Crime	9.3
Living Environment Deprivation	9.3

Table 10: Domains used in the calculation of the IMD 2007 score, including the weighting given to each domain in determining the overall score[172].

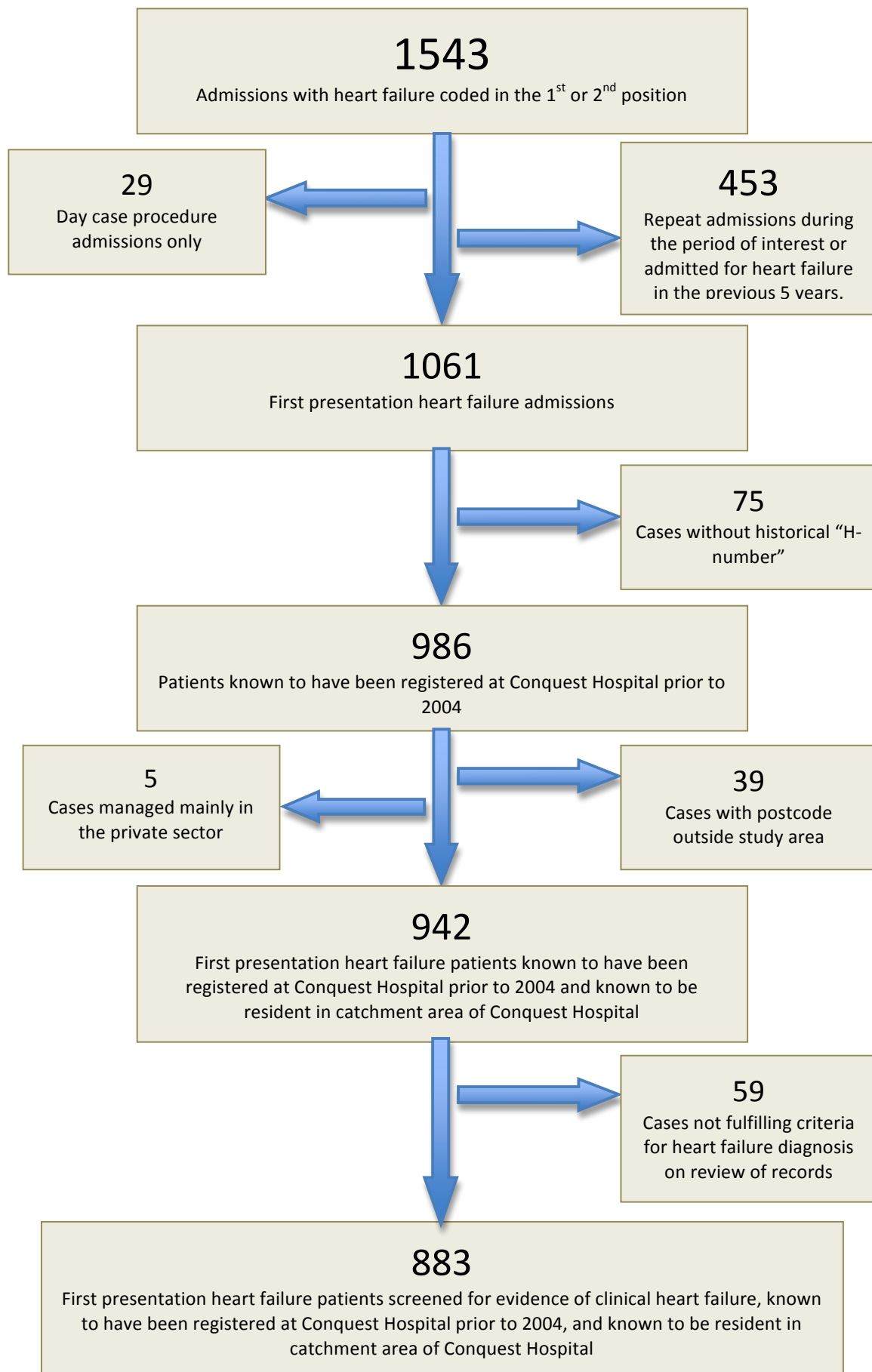
IMD 2007 Rank for England	Quintile of Deprivation
1 – 6, 496	1 (Most Deprived)
6, 497 – 12, 993	2
12, 994 – 19, 489	3
19, 499 – 25, 986	4
25, 987 – 32, 482	5 (Least Deprived)

Table 11: Determining quintile of deprivation from IMD 2007 rank.

CKD Stage	eGFR (mls/min/1.73m <sup>2</sup> )	Estimation of renal impairment used in SUSSEX-HF
1	≥90	No significant renal impairment
2	60 – 89	
3a	45 – 49	Significant renal impairment
3b	30 – 44	
4	15 – 29	
5	<15	

Table 12: The association between Chronic Kidney Disease (CKD) Stage, estimated glomerular filtration rate (eGFR), and degree of renal impairment.

Figure 3: Flowchart describing the exclusion of potential members of the cohort at each stage of the construction of the final cohort.



Number of Comorbidities	Females (%)	Males (%)
0 - 1	16	12
2	24	22
3	24	24
4	17	21
≥5	18	21

Table 13. Percentage of male and female patients with multiple comorbid conditions.

	<b>Died prior to discharge n = 160 (18.1%)</b>	<b>Survived to discharge n = 723 (81.9%)</b>	
Age [median (IQR)]	85.2 (10.2)	82.0 (12.0)	P<0.001
Male [n (%)]	78 (48.8)	352 (48.7)	P=0.98
Comorbidity [n (%)]			
Atrial Fibrillation	45 (28.1)	398 (55.0)	
Hypertension	43 (26.9)	362 (50.1)	
IHD	45 (28.1)	352 (48.7)	
Diabetes	21 (13.1)	165 (22.8)	
Lung disease	21 (13.1)	173 (23.9)	
Stroke	23 (14.4)	106 (14.7)	
IMD Quintile			
1 (18.9%)	22 (13.8)	145 (20.1)	
2 (28%)	49 (30.6)	198 (27.4)	
3 (24.1%)	40 (25)	173 (23.9)	
4 (21.4%)	38 (23.8)	151 (20.9)	
5 (7.6%)	11 (6.9)	56 (7.7)	
eGFR			
≥60	72 (45)	483 (66.8)	
<60	84 (52.5)	236 (32.6)	
Admission Serum Sodium [mean (S.D.)]	137.1 (4.84)	135.6 (6.73)	P=0.002
Sodium < 130 [n(%)]	22 (13.9)	56 (7.8)	P=0.014
Anaemia	139 (86.9)	571 (79.4)	P=0.03
Troponin +ve [n(%)]	55 (46.7)	125 (22.6)	P<0.001
LVEF			
Recorded [n(%)]	52 (32.5)	425 (58.8)	
Mean (S.D.)	45.3 (15.1)	45.7 (15.2)	
LVEDd			
Recorded [n(%)]	63 (39.4)	571 (79.0)	
Mean (S.D.)	5.43 (0.97)	5.58 (1.00)	
Patients ≥ 76 years old [n(%)]	133 (83.1)	532 (73.6)	P=0.011
Speciality of care [n(%)]			
Cardiology	15 (9.4)	111 (15.4)	
Gen. Medicine	19 (11.9)	112 (15.5)	
Geriatrician	126 (78.8)	500 (69.2)	
Prior Outpatient Contacts [median (IQR)]	1 (4)	2 (5)	P=0.142

Table 14: Characteristics of those patients surviving to discharge from the index admission compared with those who did not.



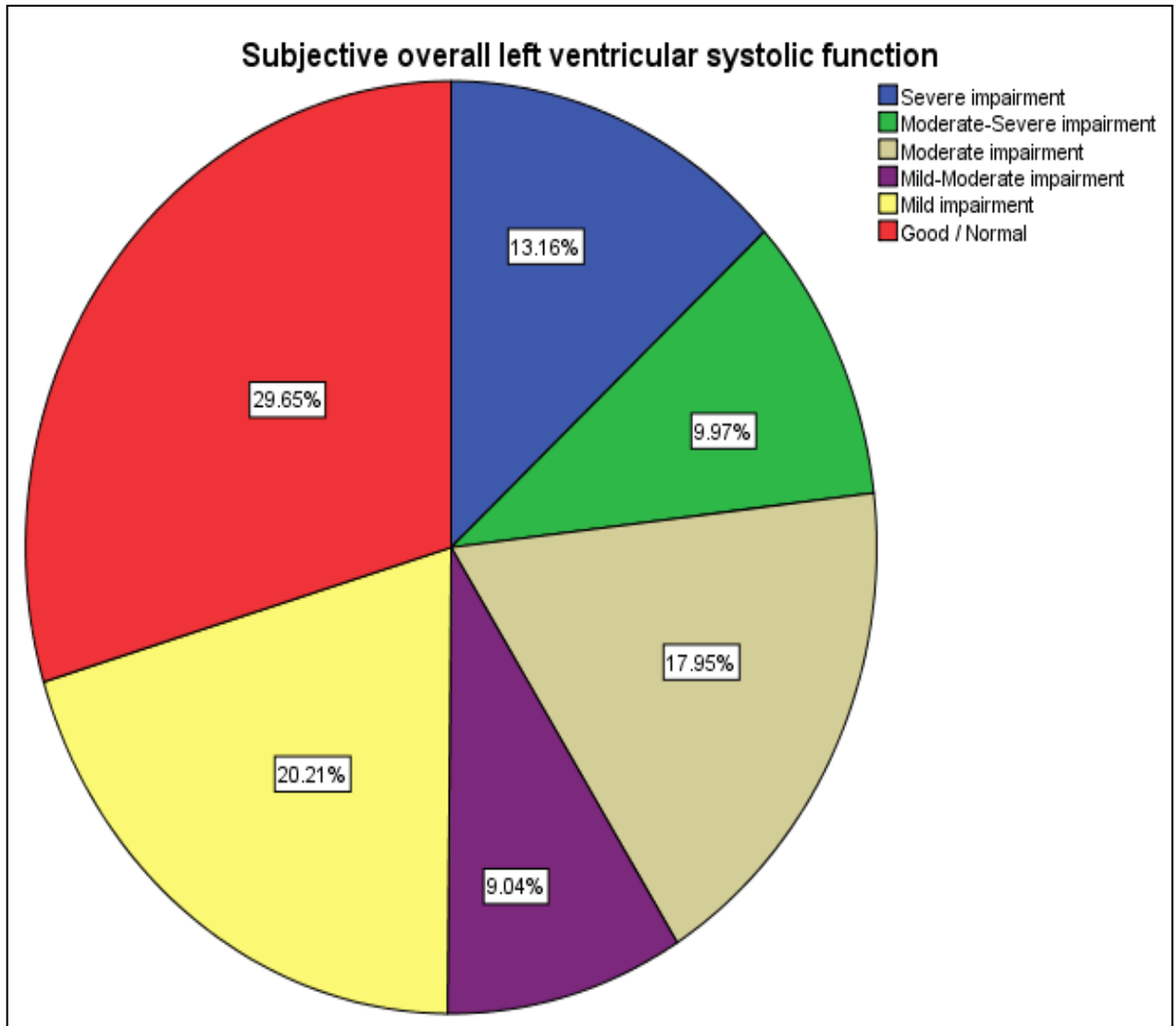


Figure 4: Subjective assessment of LV function.

Daily diuretic dose (furosemide equivalents in mg)	Frequency (%)
0	54 (7.5)
1 – 39	15 (2)
40 – 79	288 (39.8)
80 – 119	286 (39.6)
≥120	80 (11.1)
<b>Total</b>	<b>723 (100)</b>

Table 15: Frequency of different diuretic dosing schedules in the cohort surviving to discharge.

Quintile of Deprivation	1	2	3	4	5	
Age Mean (S.D.)	77.9 (11.55)	80.3 (11.05)	80.2 (10.50)	81.1 (9.39)	82.3 (8.91)	P=0.036
Male 352 (48.7)	71 (49.0)	100 (50.5)	76 (43.9)	81 (53.6)	24 (42.9)	NS
Coded Position of HF						
1	76 (52.4)	127 (64.1)	105 (60.7)	91 (60.3)	34 (60.7)	NS
2	69 (47.6)	71 (35.9)	68 (34.3)	60 (39.7)	22 (39.3)	
Comorbidity						
AF	78 (53.8)	107 (54.0)	93 (43.8)	86 (57.0)	34 (60.7)	
HTN	73 (50.3)	103 (52.0)	86 (49.7)	72 (47.7)	28 (50.0)	
IHD	88 (60.7)	91 (46.0)	71 (41.0)	76 (50.3)	26 (46.4)	
DM	41 (28.3)	43 (21.7)	37 (21.4)	36 (23.8)	16 (28.6)	
Stroke	18 (12.4)	40 (20.2)	16 (9.2)	24 (5.9)	8 (14.3)	
CLD	43 (29.7)	60 (30.3)	30 (17.3)	23 (15.2)	9 (16.1)	
LVEF Recorded [n(%)]	84 (57.9)	115 (58.1)	101 (58.4)	92 (60.9)	33 (58.9)	NS
Mean (S.D.)	45.1 (13.83)	46.4 (17.45)	45.5 (14.85)	46.8 (15.19)	42.8 (10.93)	
Prior contact with general medical services 360 (49.8)	83 (57.2)	87 (43.9)	82 (47.4)	84 (55.6)	24 (42.9)	NS
Prior contact with Cardiology services 234 (32.4)	50 (34.5)	59 (29.8)	54 (31.2)	51 (33.8)	20 (35.7)	NS
1 Year Mortality 201 (27.8)	34 (23.4)	60 (30.3)	53 (19.1)	40 (26.5)	14 (25.0)	NS
30 day readmission 154 (21.3)	36 (24.8)	53 (26.8)	26 (15.0)	32 (21.2)	7 (12.5)	P=0.01

Table 16: Characteristics of the cohort surviving to discharge according to quintile of deprivation.

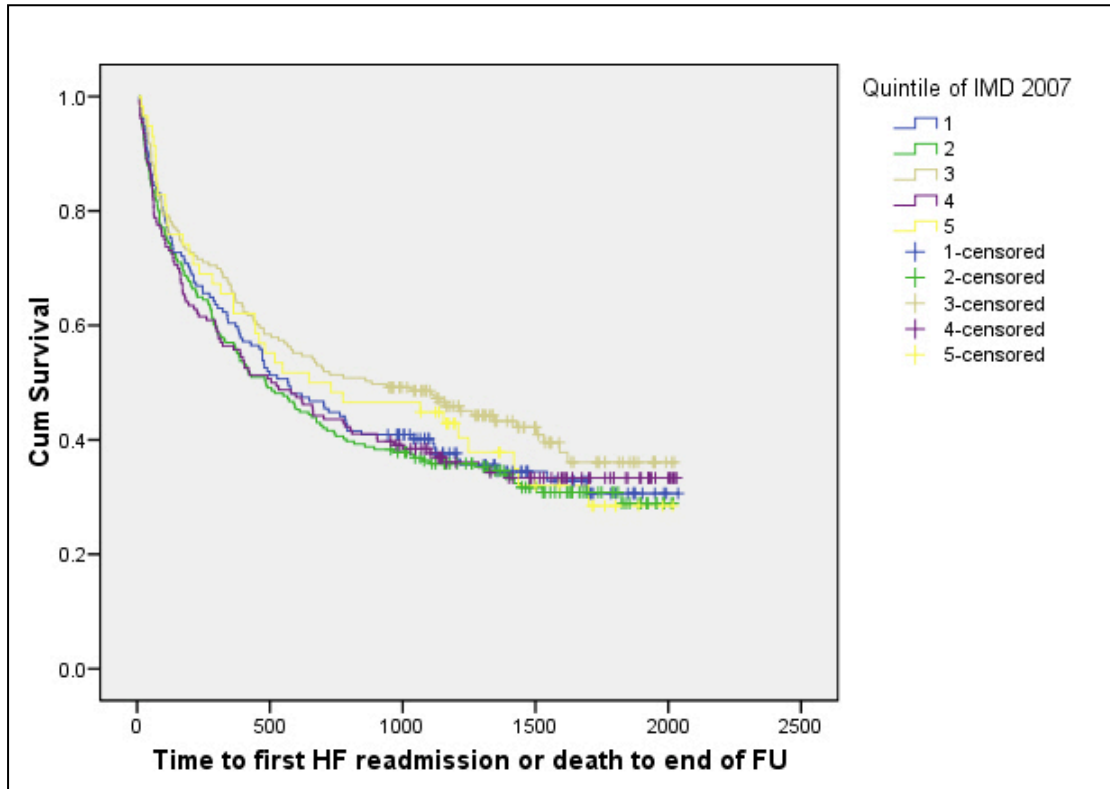


Figure 7: Kaplan Meir analysis of time to death or first readmission with heart failure according to quintile of deprivation.

Quintile of Deprivation	1	2	3	4	5
Echo performed within 6/52 271 (37.5%)	62 (42.8)	77 (38.9)	59 (34.1)	52 (34.4)	21 (37.5)
LVEF recorded where echo performed 425 (70.1%)	84 (70.0)	115 (66.9)	101 (70.1)	92 (75.4)	33 (68.8)
ACE/ARB prescribed 542 (75%)	120 (82.8)	129 (65.2)	136 (78.6)	114 (75.5)	43 (76.8)
B-blocker prescribed 138 (19.1%)	31 (21.4)	34 (17.2)	33 (19.1)	31 (20.5)	9 (16.1)
Aldosterone antagonist prescribed 196 (27.1%)	47 (32.4)	48 (24.2)	48 (27.7)	39 (25.8)	14 (25.0)
Cardiology / HF physician follow-up 295 (40.8%)	53 (36.6)	71 (35.9)	84 (48.6)	67 (44.4)	20 (35.7)
Specialist Nurse follow-up 105 (14.5%)	13 (9.0)	25 (12.6)	33 (19.1)	25 (16.6)	9 (16.1)

Table 17: Quality of care according to quintile of deprivation.

Age Group	Under 76 N=191	76 – 85 n=280	85 and over n=252	
Male [n (%)]	128 (67.02)	142 (50.71)	82 (32.54)	P<0.001
LVEF mean	41	46	51	P<0.05 for differences across 3 groups
Daily furosemide dose mean	63	66	62	NS
Hb mean (SD)	12.9	12.2	12.1	P<0.05 for difference between youngest and oldest 2 groups
Na+ mean (SD)	138	137	137	NS
eGFR mean (SD)	64.3	56.9	53.3	P<0.05 for difference between youngest and oldest 2 groups
IHD [n (%)]	111 (58.12)	135 (48.21)	106 (42.06)	P<0.001
AF [n (%)]	82 (42.93)	156 (55.71)	160 (63.49)	P<0.001

Table 18: Characteristics of the cohort surviving to discharge according to age group.

Age Group	Under 76	76 – 85	85 and over	
Readmission within 30d N (%)	40 (20.94)	58 (20.71)	56 (22.22)	NS
ACEi or ARB prescribed N (%)	154 (80.6)	208 (74.3)	180 (71.4)	NS
B-blocker prescribed N (%)	68 (35.6)	43 (15.4)	27 (10.7)	P<0.001
Aldosterone antagonist prescribed N (%)	69 (36.1)	74 (26.4)	53 (21.0)	P=0.002
Echo performed within 6 weeks N (%)	98 (51.3)	101 (36.1)	72 (28.6)	P<0.001
LVEF recorded N (%)	140 (73.3)	185 (66.1)	127 (50.4)	P<0.001

Table 19: Quality of care according to age group.

Variable	Crude Hazard Ratio (95% C.I.)
Age (per year of advancing age))	1.04 (1.03 – 1.05)
Male gender	1.04 (0.88 – 1.23)
IMD 2007	
Q1	1.0
Q2	1.17 (0.90 – 1.53)
Q3	1.31 (0.87 – 1.48)
Q4	0.98 (0.75 – 1.29)
Q5	1.17 (0.89 – 1.52)
Chronic Kidney Disease	
Stage I	1.0
Stage II	1.08 (0.86 – 1.35)
Stage III	1.66 (1.32 – 2.07)
Stage IV-V	2.10 (1.64 – 2.67)
LVEF < 50%	1.14 (0.91 – 1.42)
Anaemia	1.28 (1.02 – 1.59)

Table 20: Univariate analysis of candidate variables affecting the risk of death.



	Crude OR for prescription of ACEi/ARB	Crude OR for prescription of B-blocker	Crude OR for prescription of Aldosterone antagonist
Age (per year)	0.98 (0.96-0.99)	0.95 (0.94-0.97)	0.97 (0.95-0.98)
Male Gender	1.10 (0.78-1.54)	1.23 (0.85-1.79)	1.84 (1.32-2.57)
IMD 2007			
Q1	1.0	1.0	1.0
Q2	0.39 (0.23-0.66)	0.76 (0.44-1.31)	0.67 (0.41-1.07)
Q3	0.77 (0.44-1.35)	0.87 (0.50-1.50)	0.80 (0.49-1.30)
Q4	0.64 (0.36-1.13)	0.95 (0.54-1.66)	0.73 (0.44-1.20)
Q5	0.69 (0.32-1.47)	0.70 (.031-1.59)	0.70 (0.35-1.40)
CKD			
Stage I	1.0	1.0	1.0
Stage II	0.89 (0.57-1.37)	0.64 (0.39-1.04)	1.45 (0.97-2.18)
Stage III	0.74 (0.47-1.18)	0.73 (0.44-1.22)	1.05 (0.67-1.66)
Stage IV	0.57 (0.32-0.99)	1.07 (0.59-1.95)	1.27 (0.73-2.20)
Stage V	0.06 (0.01-0.28)	-	0.30 (0.38-2.40)
Specialist follow-up	2.40 (1.66-3.49)	2.66 (1.82-3.88)	1.88 (1.35-2.62)
Documented chronic lung disease	-	0.48 (0.29-0.81)	-
LVEF (per 1%, n=450)	0.97 (0.96-0.99)	0.98 (0.96-0.99)	0.96 (0.95-0.98)

Table 21: Univariate analysis of candidate variables affecting the likelihood of prescription of prognostically beneficial medications.

<b>Age Group (years)</b>	<b>&lt;76 (n=82)</b>	<b>76 – 85 (n= 156)</b>	<b>≥85 (n= 160)</b>
Female (%)	28	49	68
Hypertension (%)	51	58	45
Diabetes (%)	35	28	16
Ischaemic heart disease (%)	51	52	39
Prior stroke (%)	11	15	24
Median CHA2DS2VASc (range)	4 (2 – 7)	5 (3 – 8)	5 (3 – 8)
Aspirin alone (%)	37	48	59
VKA (%)	60	45	22

Table 22: Patient characteristics and Vitamin K Antagonist (VKA) prescription by age group.

Age Group	Gender	Expected Mortality Rate	Observed Number of Deaths	SMR	Standard Error of SMR
30-34	M	0.00198	0	0	0
35-39	M	0	0		
40-44	M	0.0036	1	277.7778	277.7778
45-49	M	0.01375	1	72.72727	72.72727
50-54	M	0.03087	3	97.18173	56.1079
55-59	M	0.07513	2	26.62052	18.82355
60-64	M	0.23604	10	42.3657	13.39721
65-69	M	0.64908	14	21.56899	5.764555
70-74	M	1.41984	24	16.90331	3.450374
75-79	M	4.13019	50	12.10598	1.712044
80-84	M	8.63674	69	7.989126	0.9617777
85-89	M	11.26777	66	5.857415	0.7209979
90-94	M	7.16224	27	3.76977	0.7254927
95-99	M	2.89128	8	2.766941	0.9782612
100+	M	0.91448	1	1.093518	1.093518
<b>Overall (Male)</b>		<b>37.43299</b>	<b>276</b>	<b>7.373175</b>	<b>0.443813</b>
30-34	F	0	0		
35-39	F	0.0007	1	1428.572	1428.572
40-44	F	0	0		
45-49	F	0.00362	1	276.2431	276.2431
50-54	F	0.0058	0	0	0
55-59	F	0.03942	3	76.1035	43.93837
60-64	F	0.07656	2	26.1233	18.47196
65-69	F	0.12364	3	24.26399	14.00882
70-74	F	0.60224	19	31.54888	7.23781
75-79	F	2.08193	33	15.85068	2.759249
80-84	F	6.6798	59	8.8326	1.149907
85-89	F	11.95294	86	7.194882	0.7758442
90-94	F	15.484	55	3.552054	0.4789588
95-99	F	8.22146	18	2.189392	0.5160447
100+	F	0.793	2	2.522068	1.783371
<b>Overall (Female)</b>		<b>46.06511</b>	<b>282</b>	<b>6.12177</b>	<b>0.3645461</b>
<b>Population Total</b>		<b>83.4981</b>	<b>558</b>	<b>6.682787</b>	<b>0.2829049</b>

Table 23: Standardized Mortality Ratio (SMR) by 5 year age band for men and women in the cohort.

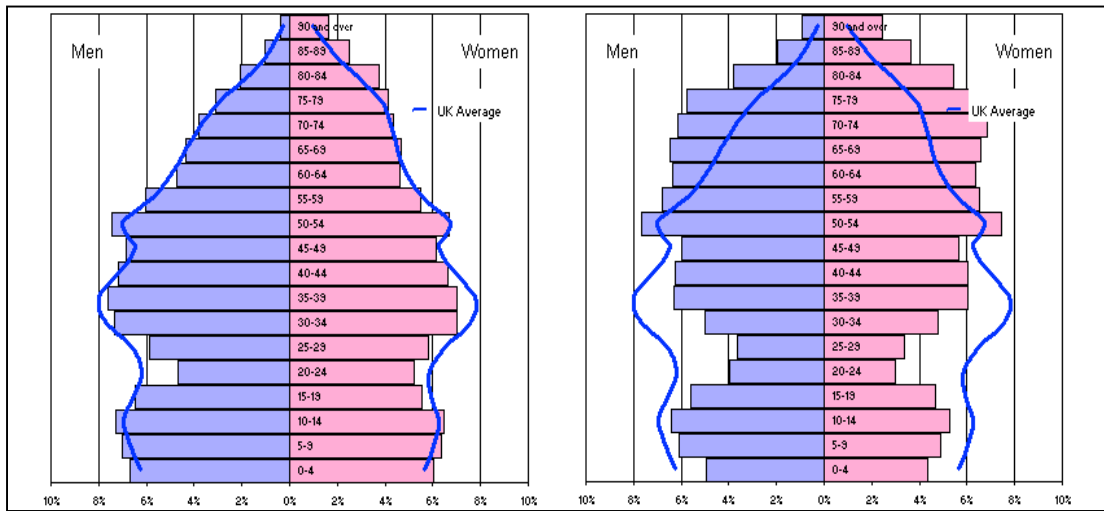


Figure 8: Population pyramids for the districts of Hastings (A) and Rother (B) compared with UK average. Crown Copyright 2008. Source National Statistics Website. [www.statistics.gov.uk](http://www.statistics.gov.uk).

	Aggregate (CHARM, 3-CPO, EuroHeart I) [%]	SUSSEX-HF [n=883] [%]	Euroheart II (Cohort ≥ 80) [n=741] [%]	EuroHeart II (Cohort < 80) [n=2836] [%]	ADHERE [n=105338] [%]	OPTIMIZE-HF [n=48612] [%]
CAD	62	45	51	54	57	49.5
HTN	55	46	67	61	73	70.9
DM	28	22	29	34	44	41.5
AF	35	50	48	36	31	30.8
COPD / CLD	26	21	22	19	30	27.6
Stroke	15	15	20	12		15.5
Anaemia		51	47	37		17.6

Table 24: Data comparing comorbidity in the SUSSEX-HF cohort with rates observed in other published studies.

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