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The Diagnosis and Management of Heart Failure across Primary and Secondary Care

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The Diagnosis and Management of Heart Failure across Primary and Secondary Care

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For Karen, Ayşe and Tamer

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Abstract

NAME: Dr Ahmet Fuat

TITLE OF THESIS: The Diagnosis and Management of Heart Failure across Primary and Secondary Care

HIGHER DEGREE FOR WHICH SUBMITTED: Doctor of Philosophy (PhD)

YEAR OF SUBMISSION: 2006

This thesis is centred on the complex arena of heart failure diagnosis and management across the primary-secondary care interface, including service delivery models and the utility of natriuretic peptides in triage of patients. The thesis combines qualitative and quantitative methodologies to identify barriers to heart failure care and to test strategies for overcoming these.

The findings were:

1. GPs found heart failure difficult to diagnose and treat due to clinical uncertainty, lack of awareness of the relevant research evidence and organisational issues including lack of access to diagnostics.
2. With regard to specialists variable opinions and practice in diagnosis and management of heart failure in hospitals and across primary-secondary care were confirmed, these centred on diagnostic difficulties, treatment issues and service delivery problems.
3. A GP-specialist led one-stop diagnostic clinic facilitated expedient, accurate diagnosis of left ventricular systolic dysfunction.
4. An integrated heart failure service across primary and secondary care delivered evidence based therapy, patient and carer education and access to social and palliative care for patients with heart failure.
5. Natriuretic peptide measurement had high negative predictive value for excluding heart failure in a consecutive GP referred cohort.
6. Electrocardiography was not as accurate at excluding heart failure as suggested by national guidelines.

7. Use of N-terminal pro B-type natriuretic peptide as a pre-screening test for secondary care referral may have reduced potential referrals, but the low specificity of the test and high prevalence of confounding factors in the screened population increased demand on diagnostic services and did not lead to cost savings.

Conclusions

The diagnostic and treatment difficulties identified by GPs and hospital specialists are dependent on a complex interplay of patient, clinician and organisational factors. Barriers need to be overcome in locality specific and multi-faceted implementation strategies across primary-secondary care. This thesis described an integrated heart failure diagnosis and management system that overcame these barriers and delivered accurate diagnosis and modern evidence based treatment.

The relatively poor positive predictive value and low specificity of natriuretic peptides in real life practice meant that large numbers of patients with raised BNP/NT proBNP did not have heart failure due to left ventricular systolic dysfunction.

This thesis demonstrated that the prognostic power of BNP/NT proBNP extended beyond LVSD to most cardiac conditions. Ideally, all patients with raised natriuretic peptides deserve a full cardiac assessment including echocardiography, followed by optimal use of evidenced based pharmacotherapy and health professional support. We need to find ways of providing expedient diagnostic and treatment services to these patients especially in rationed health care systems such as the NHS. Until this issue is addressed widespread natriuretic peptide use is unlikely within the UK.

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Publications

The work presented in this thesis has been published in the following peer reviewed journals:

Fuat A, Hungin APS, Murphy JJ. Identifying barriers to evidence based practice in the diagnosis and management of heart failure in primary care. *Heart* 2001 1985 (Supplement I): 845

Fuat A, Hungin APS, Murphy JJ. Barriers to effective diagnosis and management of heart failure in primary care. *British Medical Journal* 2003; 326: 196-200

Fuat A, Hungin APS, Murphy JJ. Designing Heart Failure Services; a Primary Care Perspective. *Heart* 2003; 89: Supplement 1 (A7-8)

Fuat A, Murphy JJ, Hungin APS, Curry J, Mehrzad A, Hetherington A, Johnston JI, Smellie WSA, Duffy V, Cawley P. A comparison of the two commercially available assays for B-type natriuretic peptide when selecting patients with suspected heart failure in primary care. Which should we use? *Heart* 2003: 89; Supplement 1 (A38)

Fuat A: GPs look set to tackle heart failure. *Health and Ageing* May 2003; 20-21

Fuat A, Murphy JJ, Hungin APS: Designing Heart Failure Services: a Primary Care Perspective. *European Journal of Heart Failure* 2003; 2(1):163-164

Fuat A: Heart Failure: How should it be treated? *New Generalist* 2004; 2(1): 15-21

Fuat A, Murphy JJ. The ECG in diagnosis of heart failure (HF) due to left ventricular systolic dysfunction (LVSD) – is advice from guidelines flawed? *The European Heart Failure Journal* 2004; 3(Suppl I): 84

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Fuat A, Murphy JJ. Natriuretic peptide testing in primary care. *Circulation.* 2006; 113(9): 35-6

Fuat A. Improving diagnosis and management of heart failure across the primary-secondary care interface – a review of the evidence base and the Darlington service delivery model. *Clinical Focus Primary Care* 2005; 1(2):43-48

Fuat A, Murphy J, Mehrzad A. Service delivery and diagnostics for suspected heart failure: which model do general practitioners prefer? *Heart* 2006; 92(Suppl II):A118

Murphy J, Chakraborty R, Brennan G, **Fuat A**, Cleland J, Davies M. How do Primary Care Trusts provide heart failure care in England? *Heart* 2006; 92(Suppl II):A118-9

Lokare A, Johnston J, Smellie W, **Fuat A**, Murphy J, Mani S. Impact of introducing natriuretic peptide assay for patients presenting acutely to secondary care. *Heart* 2006; 92(Suppl II): A59-60.

Mani S, Lokare A, **Fuat A**, Johnston JI, Smellie WSA, Murphy JJ. Impact of introducing natriuretic peptide assay for patients presenting acutely to secondary care with suspected heart failure. European Heart Failure Journal 2006; 5(1)(Suppl): A105.

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Authorship notes

The contribution of a number of individuals in this thesis is formally acknowledged.

In chapters 2, 3, 6 and 7, Professor Pali Hungin and Dr Jerry Murphy contributed to study design, analysis of data and reviewed written materials.

For chapter 6 Dr Ali Mehrzad, Dr Andrew Hetherington, Mrs Victoria Duffy and Mrs Patsy Cawley contributed with participant selection and consent, data collection and reviewed the final paper. Miss Jane Curry provided echocardiography measurement and reporting. Miss Jenny Johnston and Dr Stewart Smellie provided support and advice on measurement of natriuretic peptide assays and reviewed the final paper.

For chapter 7 Dr Ali Mehrzad contributed to patient selection, data collection, ECG analysis and reviewed the final report. Mrs Gillian Brennan contributed to data collection. Miss Jenny Johnston and Dr Stewart Smellie provided support and advice on measurement of natriuretic peptide assays and reviewed the final paper. Professor James Mason contributed to exploratory cost analysis and review of written material.

Declaration

The research contained in this thesis was carried out by the author between 1999 and 2006 while a part-time postgraduate student in the Centre for Integrated Health Care Research. None of the work contained in this thesis has been submitted in candidature for any other degree.

Statement of Copyright

Abbreviations

GP = general practitioner

HF = heart failure

CHF = chronic heart failure

ECG = electrocardiogram

CXR = Chest X-ray

LVSD = left ventricular systolic dysfunction

LVDD = left ventricular diastolic dysfunction

LVD = left ventricular dysfunction

DD = diastolic dysfunction

Echo = echocardiogram

BNP = B-type natriuretic peptide

ANP = atrial natriuretic peptide

NT proBNP = N terminal proB-type natriuretic peptide

DMH = Darlington Memorial Hospital

BAGH = Bishop Auckland General Hospital

AF = atrial fibrillation

COPD = chronic obstructive pulmonary disease

CHD = coronary heart disease

IHD = ischaemic heart disease

HT = hypertension

VHD = valvular heart disease

AR = aortic regurgitation

AS = aortic stenosis

MR = mitral regurgitation

MS = mitral stenosis

ACEi = angiotensin converting enzyme inhibitor

ARB = angiotensin receptor blocker

AIIA = angiotensin 2 antagonist

BB = Beta blocker

CAPO = central appointments patient office

GPwSi = general practitioner with a specialist interest

GMS = general medical services

NHS = National Health Service

QMAS = quality management and audit system

AMI = acute myocardial infarction

MI = myocardial infarction

MINAP = myocardial infarction national audit programme

PE = pulmonary embolism

NPV = negative predictive value

PPV = positive predictive value

CI = confidence interval

ROC = receiver operating curve

AUC = area under the curve

ETT = Exercise treadmill test

NSF = National service framework

NICE = National Institute for Clinical Excellence

ESC = European Society of Cardiology

BCS = British Cardiac Society

RCGP = Royal College of general practitioners

RCP = Royal College of physicians

ACC = American College of Cardiology

AHA = American Heart Association

PCCS = Primary Care Cardiovascular Society

LVEF = Left ventricular ejection fraction

PLVEF = Preserved left ventricular ejection fraction

NYHA = New York Heart Association

Chapter 1.

A resume of the literature

This literature review has been, by necessity, an iterative process over a six year period, with several additions made during that time. This has been necessary in order to keep up to date, both clinically and as a researcher, with the rapidly changing and expansive arena that heart failure research has become worldwide.

"Heart failure fulfils the three simple criteria for identifying diseases that should have a high priority and be the focus of healthcare programmes; it is common, it can be detected, and treatment is effective"[1].

1.1 The definition of heart failure and descriptive terms

Before general practitioners can accurately diagnose and optimally treat heart failure they need to be clear about how it is defined. Research and clinical management of heart failure (HF) has been handicapped by the absence of a generally accepted practical definition[2-4]. Dargie (1998) argues that we need an acceptable definition not only for diagnosis but also for "budgeting within health services, for regulatory reasons and for research purposes"[5]. The much quoted textbook definition of heart failure; "a state in which an abnormality of cardiac function is responsible for failure of the heart to pump blood at a rate commensurate with the requirements of the metabolising tissues or, to do so, only from an elevated filling pressure"[6], gives useful pathophysiological insight but does not address the practical definition required by clinicians.

The difficulty in clinically defining heart failure stems from the fact that it is not a clear-cut diagnosis or disease per se, but a complex clinical syndrome[7]. Unlike renal or pulmonary failure there is no easily measured organ function parameter (e.g. serum creatinine or pulmonary function tests) to help us in diagnosis. Although left ventricular ejection fraction (LVEF) is often used as a descriptor of left ventricular function, different methods of measurement give different results in the same patient. One problem clinicians face in

establishing a diagnosis of heart failure is that there is no clearly defined LVEF below which HF or LVSD is confirmed[5]. The European Society of Cardiology (1995)[8] and American College of Cardiology/American Heart Association guidelines[9,10] suggest that LVSD should be diagnosed if LVEF is less than 40%; in some studies 35% was used as the cut off, and in significant mitral regurgitation an ejection fraction of less than 60% is considered abnormal. Furthermore it is not always possible to measure LVEF especially in patients who are obese or have significant chronic obstructive pulmonary disease (COPD), mainly due to the inability to identify an adequate echocardiographic window for trans-thoracic assessment. These difficulties are compounded by the fact that major clinical trials use different LVEF cut-points for patient enrolment and "definition" of HF or LVSD. (See table 1.1 below)

Table 1.1 LVEF cut-points in major HF clinical trials

Major HF clinical trial	LVEF cut-point for LVSD diagnosis
SOLVD T[11]	≤ 35%
CAPRICORN[12]	≤ 40%
CHARM[13]	≤ 40%
CIBIS II[14]	≤ 35%
COMET[15]	≤ 35%
DIG[16]	≤ 45%
ELITE II[17]	≤ 40%
MERIT HF[18]	≤ 40%
RALES[19]	≤ 35%
SAVE[20]	≤ 40%
Val-HeFT[21]	≤ 45%

Historically, matters have been confounded by a multitude of descriptive terms such as; acute and chronic, right and left, high and low-output, forward and backward, overt, treated, congestive and undulating heart failure.

The Task Force on Heart Failure of the European Society of Cardiology did address this in their "Guidelines for the diagnosis of heart failure"[8] by suggesting that heart failure could be described in acute or chronic terms. They suggested the terms of acute (cardiogenic) pulmonary oedema and cardiogenic shock (a syndrome characterised by a low arterial pressure, oliguria and a cool periphery). Chronic heart failure can be classified as either systolic or diastolic left ventricular dysfunction. These do seem to be acceptable, practical descriptive terms, which also point to the correct management strategy, which differs for each entity[22].

The clinical definition of heart failure agreed by the Task Force (1995)[8] guides diagnosis and encapsulates subjective, objective and retrospective criteria[4];

<u>Definition of Heart Failure</u>.

(Criteria 1 and 2 should be fulfilled in all cases).

1. Symptoms of heart failure (at rest or during exercise) and
2. Objective evidence of cardiac dysfunction (at rest) and
3. Response to treatment directed towards heart failure (in cases where the diagnosis is in doubt).

Symptoms of heart failure are typically breathlessness or fatigue, either at rest or during exertion, or ankle swelling. A clinical response to treatment directed at heart failure alone is not sufficient for diagnosis.

Tan and colleagues reviewed hitherto proposed representative definitions of heart failure. It would seem reasonable to have the practical definition proposed by the Task Force and preface this with a statement that reflects the recent developments in our understanding of the pathophysiological basis of heart failure. Professor Philip Poole-Wilson proposed the definition "a syndrome which develops as a consequence of cardiac disease, and is recognised clinically by a constellation of symptoms and signs produced by complex circulatory and neurohormonal responses to cardiac dysfunction"[23].

1.2 Epidemiology of heart failure

1.2.1 Introduction - Heart failure, a problem that will not go away.

Despite growing public awareness of the risk factors for heart failure, chronic heart failure (CHF) as a result of coronary heart disease continues to inflict a terrible toll on the people of this country. The current estimate that 900,000 people in the UK have CHF is predicted to increase by about 10% each year[24].

The resulting cost to society is impossible to assess fully. Approximately, 6,000 deaths occur annually in the UK due to CHF – nearly 40% of patients will die within 1 year of CHF diagnosis[25]. However, the pain and suffering caused by the symptoms of CHF affect even more people and their families. The shortness of breath associated with CHF can severely restrict mobility in all but those experiencing mild CHF[6], and the effects on quality of life are far reaching with emotional worries and social limitations a frequent occurrence [56, 57]. Many of these symptoms result in hospitalisation of patients; an estimated 5% of all emergency medical admissions to hospital are for CHF and up to 50% of severe cases require readmission within 3 months[24,26]. Inevitably, such a health burden is associated with an economic burden and CHF is thought to cost the NHS around £625 million per year[27].

The risk of CHF increases with age – around 1 in 35 people aged 65-74 years has heart failure, increasing to about 1 in 15 of those aged between 75 and 84, and to >1 in 7 in those aged 85 years and older – and as the average age of the UK population is increasing, this alone points towards an increasing number of people at risk[24]. There is a clear association between the risk of CHF and the presence of other cardiovascular defects such as previous myocardial infarction (MI), hypertension, atrial fibrillation, cardiomyopathy and cerebrovascular disease (e.g. strokes) [23]. Other conditions that are known to contribute to cardiovascular disease (CVD) in general increase the risk of CHF. For example, patients with CHF are four-times more likely than the general population to have diabetes (1 in 5 patients with CHF have diabetes compared with 1 in 20 of the general population).

There have been comprehensive reviews of epidemiology and the associated burden of heart failure published by McMurray and colleagues[28,29], and Cowie et al[30,31]. These describe prevalence and incidence data as well as addressing aetiology, prognosis, quality of life (QOL) and health economic issues.

1.2.2 How are epidemiological data obtained?

Data relating to the epidemiology of heart failure are available from five types of studies[29]:

1. Cross sectional and longitudinal follow up of well defined populations. These tend to focus on individuals with clinical signs and symptoms indicative of heart failure. Examples include the American Framingham Heart Study and the Swedish Study of Men born in 1913[32,33].

2. Cross sectional surveys of individuals who have been medically treated for signs and symptoms of heart failure within a well defined region. An example is prevalence data based on prescription data from the county of Nottinghamshire[34]

3. Echocardiographic surveys of individuals within a well defined population to determine the presence of LVSD. The first population based study was provided by McDonagh and colleagues from Glasgow[35]. Subsequently studies from Southampton and the Midlands have followed[36,37].

4. Nationwide studies of annual trends in heart failure related hospitalisations. The British Heart Foundation collates such data from National Statistics[24].

5. Comprehensive clinical registries collected in conjunction with major clinical trials.

1.2.3 Prevalence of heart failure

There are many studies from across the western world that are outlined in the above mentioned reviews, but I propose only to mention those studies that are particularly relevant to primary and secondary care in the UK.

1.2.3.1 Surveys from general practice

Parameshwar and colleagues[38] surveyed the clinical records of diuretic-treated patients in three general practices in northwest London in 1992 to identify possible cases of heart failure. From a total of 30,204 patients, 117 cases (71 female and 46 male) of heart failure were identified, giving an overall prevalence of 3.9 cases per 1000. The prevalence of heart failure increased significantly with increasing age – from 0.6 cases/1000 in those under 65 to 28 cases/1000 in those aged 65 or over. A methodological weakness of this study was that objective investigation of left ventricular function was only undertaken in about a third of cases.

Wheeldon and colleagues[39] reviewed the GP notes of 12012 patients in Carnoustie, Scotland. The estimated prevalence of LVSD was 0.84%, whereas 1.6% of the population received loop diuretics for this indication. However, just under a half of patients invited did not attend for echocardiography and this non-responder bias suggests that the calculated prevalence figure is probably too low.

In 1996 Mair et al[40] used similar methodology to identify 266 cases of heart failure from 17,400 patients within two general practices in Liverpool. The overall prevalence was 15 cases/1000 in individuals aged under 65, rising to 80 cases/1000 in those aged 65 or over. Both the above studies could be subject to selection and location bias which may limit generalisabilty of results to a wider population.

Clarke and colleagues[41] conducted a larger survey based on similar methods by analysing loop diuretic prescriptions for all residents in Nottinghamshire. It was estimated that between 13,017 and 26,214 patients had been prescribed frusemide. Random case record review found that 56% were being treated for heart failure. Overall prevalence was estimated at 8-16 cases/1000 for those less than 70 years of age. Prevalence increased to 40-60/1000 among those aged 70 years and over.

UK national data from RCGP surveys of research practices[42,43] shows an increase in overall prevalence from 3/1000 in 1985 to 9/1000 in 1995 (patients aged 25 to 74). There was no data for older patients from 1985 but a

prevalence of 74/1000 was recorded for those aged 65-74 years of age in 1995.

Toal and Walker[44] audited the notes of 3 north Cumbria general practices with a total population of 23210. Prevalence rate for HF was 1.1% (n = 258)

A limitation of all retrospective analyses of notes is that they are open to bias and error due to variable legibility and completeness of medical records and difficulty of data interpretation by a detached clinician not present at the moment of the doctor-patient consultation. Computerisation of data may reduce some of these errors but analyses are still dependent on accuracy and completeness of data entry.

1.2.3.2 Cross sectional surveys using echocardiography

McDonagh and colleagues[35] studies a representative cohort of 2000 people aged 25-74 years living in North Glasgow. Of these 1640 (83%) underwent echocardiographic assessment of cardiac function. LVSD was defined as LVEF ≤ 30%. The overall prevalence of LVSD was 2.9%. Interestingly only 1.5% had symptoms of heart failure with the other 1.4% being asymptomatic. Prevalence was both greater in men and increased with age. The use of a strict criterion (LVEF ≤ 30%) was designed to identify those with significant LVSD but may have excluded those with mild or moderate LVSD who are also at risk of early death, poor morbidity and hospitalisation. This suggests that the prevalence data may be an underestimate especially in an area with recognised high CHD rates.

Morgan and colleagues[36] carried out a cross sectional survey in four general practices in Poole, Dorset. 870 elderly patients aged 70 to 84 had left ventricular function assessed by echocardiography. Measurement of ejection fraction was possible in 82% of patients. The overall prevalence for LVSD was 7.5% (95% CI 5.8% to 9.5%). At all ages prevalence is much higher in men than in woman (odds ratio 5.1, 95% CI 2.6 to 10.1). 52% of patients with left ventricular dysfunction had not previously been diagnosed. A conclusion from this is that unrecognized left ventricular dysfunction is a common problem in elderly patients in a general practice setting and diagnosis should not be based on clinical history and examination alone. Whilst this raises the

feasibility and desirability of screening patients in general practice, it should not be implemented until the optimum method of identifying left ventricular dysfunction is clarified and the cost effectiveness of screening has been shown.

Davies and colleagues[37] randomly selected 6286 patients aged over 45 years from 16 practices in the West Midlands. 3960 (63%) were assessed clinically, and by ECG and echocardiography. LVSD (LVEF < 40%) was diagnosed in 72 (1.8%; 95% CI 1.4-2.3) with a mean age of 69 years and 54 subjects (1.4%) had definite HF (by ESC diagnostic criteria) from other causes apart from LVSD, with a mean age of 73 years. Half of the LVSD group were asymptomatic. The overall prevalence of significant cardiac dysfunction was 3.2%. These results are lower than the North Glasgow despite the use of a lower LVEF (≤35%) in the Glasgow study[35] and may be related to a high frequency of IHD in that population, a major precursor for LVSD. The prevalence rate was also lower than the Poole study[36] which used different diagnostic methods in an elderly select population.

1.2.3.3 Why such variation in prevalence of heart failure?

Different epidemiological surveys show considerable variations in the prevalence of chronic heart failure. Whilst some of this may be accounted for by true differences in populations including social, demographic and risk factor profiles of study cohorts in contrasting geographical locations, the greatest cause of variability is most likely to be related to differing definitions, research methodologies, methods of measuring and assessing heart failure. Most data show progressive increase of prevalence of CHF with age and a significant co-relation with CHD, hypertension and diabetes. Furthermore prevalence seems to have increased over the past few decades. Until there is a consensus in terms of definition of heart failure for epidemiological studies, they are unlikely to achieve a homogeneous figure collection and allow a true data comparison.

1.2.4 Incidence of Heart Failure

There appears to be much less known about the incidence of heart failure[29], with only two studies relating to British populations. Cowie and colleagues[45] in

a population-based study determined the incidence of heart failure in a UK population through the surveillance of 151,000 patients registered with 52 primary care practices in Hillingdon, south London. Using the ESC criteria for the diagnosis of heart failure, the overall incidence was found to be 1.3 cases per 1000 population per year. The incidence rate was age related and increased steadily from 0.02 cases per 1000 population per year in those aged 25 to 34, to 11.6 cases per 1000 population per year in those aged over 85. The incidence of heart failure was greater in men than in women with an age standardised incidence ratio of 1.75 (p < 0.0001). That was maintained across all age groups. The median age of onset of heart failure was 76 years, considerably higher than the median age of patients involved in clinical trials evaluating pharmacological therapy of the disease.

Johansson and colleagues[46] conducted a survey of UK GPs who had diagnosed patients with heart failure as part of the general practice research database covering three million patients. This revealed an overall incidence of 4.4 per thousand population per year in men and 3.9 per thousand population per year in woman. Whilst this study suggests a significant incidence of heart failure in the UK population, it should be noted that the diagnosis criteria may not have been as stringent as in other population based studies.

Studies from Sweden, Finland and the USA give broadly similar incidence rates to that estimated by Cowie and colleagues:

Table 1.2. Heart Failure Incidence

Study and year	Location	Incidence rate (total population)	Incidence rate in older age groups
Eriksson et al 1989[33]	Sweden	-	10/1000 (61-67 years)
Remes et al 1992[47]	Finland	1-4/1000 (45-74 years)	8/1000 (> 65 years)
Rodeheffer et al 1993[48]	Rochester USA	1/1000 (<75 years)	16/1000 (> 65 years)
Ho et al 1993[32]	Framingham USA	1/1000	12/1000 (>85 years)

As with prevalence data there is an obvious increased incidence in older individuals.

1.2.5 A summary of prevalence and incidence of heart failure

Heart failure is a major public health problem in industrialised countries with ageing populations. Prevalence rates vary between 3 to 35 per 1000 under the age of 65, rising to between 28 to 130 per 1000 over 65[30]. These estimates probably vary widely due to differences in methodology and timing[30] and diagnostic heterogeneity in clinical studies[49], rather than reflecting true differences between populations. Incidence rates average between 1 to 5 per 1000, but can rise up to 40 per 1000 in over 75 years of age in some studies[30].

1.2.6 Prognosis and quality of life

Annual mortality exceeds 60% in severe heart failure and 5 year mortality approaches 50% even in mild cases[32,50-52]. This is worse than many forms of cancer[53]. The commonest cause is now ischaemic heart disease, followed by hypertension[54]. As populations age, and the management of ischaemic heart disease, myocardial infarction and hypertension continues to improve, the prevalence and incidence will continue to escalate[55]. In terms of morbidity it impairs quality of life more than any other common chronic condition (including hypertension, diabetes, arthritis, chronic lung disease and angina)[56,57]. There are several disease specific quality of life (QOL) measures for HF which are reliable, valid and responsive in measuring changes of health, including the left ventricular dysfunction questionnaire (LVD-36) and the Minnesota living with HF questionnaire[58,59]. Unfortunately most studies tend to focus on mortality endpoints rather than QOL. In elderly patients in particular QOL may be equally or more important than prolongation of life, although I could find no studies that addressed this difficult ethical issue. Whilst QOL measures are useful research tools they are rarely used in clinical practice, largely due to time and workload pressures faced by secondary and primary care clinicians and health professionals.

1.2.7 Health service workload and health economic issues.

Heart failure not only imposes a huge burden on the patient and their carers, but also is a great drain on NHS resources. The majority of these patients are cared for in general practice[39]. A GP with a list size of 2000 would expect to see 20 patients with heart failure per year (10 of these being new cases). These patients will generate 45 consultations, 8 outpatient visits and 4 inpatient episodes per year. Heart failure accounts for 1.68 million GP consultations per annum[39].

Hospital care accounts for 59% of the total direct economic costs of NHS heart failure expenditure per annum (compared to only 1% for drug costs). This total amounted to £359 million in 1990/1991, and represented just over 1% of the total NHS budget[60]. This is similar to the total expenditure on asthma and stroke care. More contemporary UK data from coronary heart disease statistics shows a sharp rise in NHS costs to around £625 million in 2000[27]:

Costs of HF to the UK NHS (2000)

Cost element	£ million
Primary care	103.8
Hospital inpatient care	378.6
Hospital day case care	0.45
Hospital outpatient care	51.25
Outpatient investigations	37.44
Drugs	54.08
Total	625.62

Pie chart: Primary care 16.5%, Drugs 9%, Outpatient investigations 6%, Hospital outpatient care 8%, Hospital inpatient care 60.5%
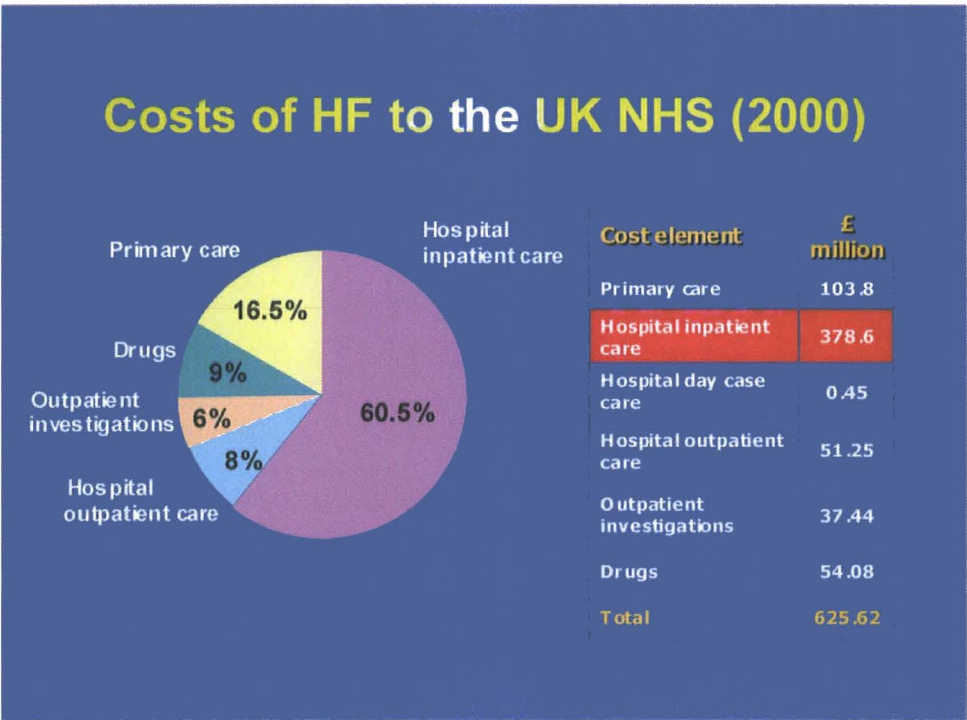
Figure 1.1 Costs of heart failure to the UK (2000)

The biggest cost is hospital inpatient care and hospitalisations are increasing in the western world,[55,61,62] with heart failure now accounting for 5% of all general medical and geriatric admissions to hospital in the UK. Average length of inpatient stay is 14-16.5 days[61,62] and readmission rates are high[62]. Age-adjusted readmission rates for HF represented 23% of all hospitalisations for CHF in Scotland during 1996[63]. Scottish data from McMurray and colleagues[62] documents a mean length of stay for a heart failure related admission in 1990 at 11.4 days on acute medical wards and 28.5 days on acute elderly care wards. About one third of patients in this study were readmitted within 12 months of discharge[62]. The trajectory of HF includes episodes of relative stability interspersed by episodes of decompensation that can lead to readmission to hospital. Identifying factors that lead to repeated hospitalisation could help target those patients for intensive follow up in an attempt to reduce admissions[64,65].

Khand and colleagues[66] analysed a large Scottish database (n = 12640; mean age 74 years) who had had a first admission in 1992. 23% of these died on their first admission and the remaining 9718 patients had 22747 readmissions and 4877 deaths over the subsequent 3 year period. The reasons for first readmission were primarily HF (first listed diagnosis) without any obvious precipitating event in 37% of cases, renal failure or respiratory infection in 12%, acute ischaemic events (including MI) in 19%, MI alone in 8% and AF in 11%.

Opasich and colleagues[67] identified concomitant factors contributing to decompensation in 161 out of 304 HF patients (mean age 59) followed up over a 2 year period. These included arrhythmia in 24%, infection (23%), poor treatment compliance (15%), episodic chest pain (14%) and iatrogenic causes mostly relating to inadequate treatment in 10%. Along with the above study, this study confirms that concomitant factors not directly related to cardiac pathology were an important determinant in frequency of decompensation and hospital admission.

These studies suggest that systematic structured review in the community with emphasis on holistic care that also focuses on co-morbidities, social support and treatment compliance is necessary to prevent costly

readmissions to hospital. Multidisciplinary models of care will be discussed in detail later in this review.

1.3 Aetiology and pathophysiology of heart failure

1.3.1 Aetiology of heart failure

Heart Failure is the common end-result of many different conditions and processes that impair cardiac function, both systolic and diastolic[54]. In the westernised world coronary artery disease and hypertension are the commonest causes of heart failure[29]. However, it is often impossible to determine the primary aetiology as patients may have multiple co-morbidities that contribute to the development of heart failure, including coronary artery disease, hypertension, diabetes mellitus, atrial fibrillation and valvular heart disease.

Aetiology of heart failure can be inferred from population based studies, cohorts attending clinics or from clinical trial databases and registers. Whilst earlier Framingham data reported by Kannel and colleagues[68] in 1972 reported hypertension as the sole or contributory cause of heart failure in over 70% of patients[68], more recent data confirms that coronary artery disease is now the commonest cause[30]. One has to remember that the earlier Framingham data[68] was based on clinical assessment only and more recent increases in invasive coronary investigations have undoubtedly increased the importance of coronary artery disease. Furthermore, the decline of rheumatic fever has also reduced the number of cases with valvular disease in the Framingham cohort and the western world in general. Treatment advances in anti-hypertensive drugs and more aggressive treatment thresholds have also reduced the degree of heart and renal damage that may contribute to the development of cardiac impairment.

McMurray and colleagues[29] studied seven large clinical trial registers (number of patients from 1663 to 9580 in these studies) between 1991 and 1999. Ischaemic heart disease was documented as the main cause of heart failure in 54% to 71% of patients. Whilst hypertension was a co-morbidity in 27% to

46%, it was only considered a cause of heart failure in between 4% to 20% of these studies[29].

In UK hospital or GP studies ischaemic heart disease appears to be the commonest cause. Parameshwar and colleagues[28] found 32% of 117 patients with heart failure in primary care had IHD, 6% hypertension, 19% VHD and 4% cor pulmonale. Mair and colleagues[40] found that in 266 GP patients, 45% had IHD, 18% hypertension, 9% VHD, 2.3% cardiomyopathy and 6.8% cor pulmonale. Lip and colleagues[69] in a survey in 3 West Birmingham general practices found that of 118 heart failure patients 53% had IHD, 36% hypertension, 7% VHD, 15% cardiomyopathy, 29% atrial fibrillation and 23% diabetes. In a more recent study McCallum and colleagues[70] in a Scottish primary care setting found in 100 patients with LVSD, 66% had IHD, 11% hypertension and 13% VHD.

In practice one of the most important aspects of the investigation of patients with heart failure is the identification of a cause that may need specific treatment or optimisation of therapy e.g. revascularisation in CAD, rate or rhythm control in AF and aggressive treatment of hypertension, especially if associated with LVH. This is a further argument for thorough investigation including ECG, CXR and echocardiography.

1.3.2 Pathophysiology of heart failure

Heart failure was formerly known as a mainly a haemodynamic problem of pump dysfunction but is know considered to be a highly complex clinical syndrome encompassing many extra-cardiac features including neurohormonal alterations (renin-angiotensin-aldosterone system and the sympathetic nervous system), skeletal muscle disturbance and cytokine release.

Cardiac damage and remodelling (e.g. after MI) leads to reduced cardiac output, which in turn activates the sympathetic nervous system [23]. The cardiac endocrine system tries to compensate by releasing natriuretic peptides that increase diuresis, natriuresis and increased vascular dilatation. However, increased heart rate and vasoconstriction often ensues and by reducing renal perfusion activates the renin-angiotensin-aldosterone system. Production of

angiotensin II leads to sodium retention (via aldosterone production), fluid retention (via posterior pituitary vasopressin production) and further vasoconstriction that causes structural arteriolar changes with stiffness of blood vessels via increased vascular total peripheral resistance. These arteriolar changes contribute to the symptoms of HF by affecting skeletal muscle (fatigue) and reducing respiratory function by increased physiological dead space and airways obstruction (breathlessness). All of these changes may cause further cardiac dilation and remodelling creating a cycle of deteriorating symptoms unless therapies directed at reducing sympathetic over activation (beta blockers), blocking the renin-angiotensin-aldosterone system axis (ACE inhibitors or ARBs), reducing fluid overload (diuretics) and/or blocking aldosterone action (spironolactone or eplerenone) are initiated. In some instances further reduction in cardiac output can lead to electrical instability and thrombus formation which can lead to sudden death by inducing fatal arrhythmias or progressive pump failure.

1.4 The diagnosis of heart failure

1.4.1 Introduction

The key to reduction of mortality, morbidity and cost of heart failure is accurate and early diagnosis of LVSD. Unfortunately, heart failure is difficult to diagnose accurately on clinical grounds[71,72]. This is mainly due to the non-specificity of the clinical symptoms and the non-sensitivity of the clinical signs[73,74], especially in elderly patients who often have multiple co-morbidities and are on polypharmacy. This would suggest that to establish positively a diagnosis of heart failure in primary care, patients must be referred for cardiac imaging.

1.4.2 Past medical history and the diagnosis of heart failure

The past medical history may provide useful clues in assessing patients with suspected HF. A patient who has IHD and in particular previous MI is more likely to have objective evidence of LVSD than a patient who does not[35,73,75].

Hypertension, atrial fibrillation and diabetes mellitus also raise suspicions that a patient presenting with breathlessness or oedema may have HF[35,40,76].

Skaner and colleagues[77] report an interesting study on GPs' clinical diagnosis of HF. They used a clinical judgement analysis using 45 case vignettes based on actual patients. Participants were 27 GPs from 9 health centres in Stockholm. The GPs utilisation of clinical information in their judgement strategies was measured using clinical variables as independent variables. The variation between the GPs' assessments of the probability of HF was considerable. An important source of this variation was the difference in how they made use of clinical information, with the most important variables being lung and heart X-rays and a history of MI. This shows the need for a better understanding of the relationship between cues provided by clinical information and a diagnosis of HF by GPs, and is at least one important reason behind difficulties GPs face in achieving accurate diagnosis.

1.4.3 Symptoms in the diagnosis of heart failure

HF can present with very few symptoms in its early stages or a lot of symptoms once well established. Typical symptoms include breathlessness (at rest or on exercise), fatigue, reduced exercise tolerance and ankle oedema. In elderly patients unexplained confusion and altered mental state may also be present. Orthopnoea and paroxysmal nocturnal dyspnoea are less common in the general population and may be useful and specific, but less sensitive for suggesting the presence of HF due to LVSD[78].

However, breathlessness is a very common symptom in primary and secondary care with estimated prevalence of up to 25% in a community cohort[78]. Major medical textbooks document more than 30 possible causes for breathlessness[79].

Interpretation of symptoms such as breathlessness, ankle oedema and fatigue can be very difficult in elderly patients, the obese, women and those with pre-existing pulmonary disease[8]. Indeed in elderly patients presenting with dyspnoea it is particularly problematic to differentiate between pulmonary and cardiac aetiologies[80]. Other factors including physical deconditioning or lack of fitness can cause dyspnoea on exertion. Extra-cardiac causes of

peripheral oedema not related to HF are common and include, venous insufficiency causing dependent oedema, hypoproteinaemia, renal failure and iatrogenic oedema caused by various commonly used drugs (e.g. calcium channel blockers, corticosteroids and non-steroidal anti-inflammatory agents).

Inter-observer reproducibility of eliciting presence or absence of symptoms in the diagnosis of HF is low[81,82]. There have been several studies that have examined the sensitivity, specificity, and positive and negative predictive value of symptoms for the diagnosis of HF. These studies have concentrated on dyspnoea on exertion, orthopnoea, paroxysmal nocturnal dyspnoea (PND) and ankle oedema. See Table 1.3 below.

There is considerable variation between results and it is difficult for the clinician to draw any conclusion from these studies, except that none of the symptoms studied are consistently useful in the diagnosis of HF[74]. Furthermore, reliance on symptoms and signs alone may lead to under or over-diagnosis of HF and inappropriate care[80,84].

1.4.4 Clinical signs in the diagnosis of heart failure

The clinical signs of HF reflect the consequences more than the causes of HF[74]. Cardiomegaly caused by ventricular dilatation may be detected by a displaced apex beat, increased area of cardiac dullness and a third heart sound; fluid retention is reflected in signs of congestion including ankle oedema, a raised jugular venous pressure and pulmonary crepitations or crackles; neuroendocrine activation causing increased sympathetic tone leads to a resting tachycardia; and low cardiac output causes decreased proportional pulse pressure due to poor perfusion.

Several studies and systematic reviews have determined the value of clinical signs and clinical examination in diagnosis of HF by examining sensitivity, specificity and predictive values. See Table 1.4 below.

Table 1.3: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of symptoms for diagnosis of HF (%)

	Harlan[83]	Chakko[84]	Stevenson[85]	Echeverria[86]	Davie[75]
Dyspnoea on exertion					
Sensitivity	66			97	100
Specificity	52			15	17
PPV	23			63	18
NPV				75	100
Orthopnoea					
Sensitivity	21	66	91	73	22
Specificity	81	47	100	40	74
PPV	2	61	100	65	14
NPV		37	64	50	83
Paroxysmal nocturnal dyspnoea					
Sensitivity	33			50	39
Specificity	76			45	80
PPV	26			58	27
NPV				38	37
Ankle oedema					
Sensitivity	23	46	23	23	49
Specificity	80	73	100	70	47
PPV	22	79	100	54	15
NPV		37	18	38	83

Table 1.4: Sensitivity, specificity, PPV and NPV of signs for the diagnosis of HF (%)

	Harlan[83]	Heckerling[87]	O'Neill[88]	Chakko[84]	Butman[89]	Stevenson[85]	Echeverria[86]	Davie[75]
Resting tachycardia								
Sensitivity	7							22
Specificity	99							92
PPV	6							33
NPV								86
Pulmonary crackles								
Sensitivity	13			66	24	19	70	29
Specificity	91			84	100	100	35	77
PPV	27			87	100	100	62	19
NPV				61	35	17	44	85
Ankle Oedema								
Sensitivity	10			46		23	40	20
Specificity	93			73		100	70	86
PPV	3			79		100	67	21
NPV				46		18	44	85
Third heart sound								
Sensitivity	31			73	68	98	63	24
Specificity	95			42	73	14	55	99
PPV	62			66	86	88	68	77
NPV				85	48	50	50	87
Jugular venous distension								
Sensitivity	10			70	57	58	47	17
Specificity	97			79	93	100	65	98
PPV	2			85	95	100	67	64
NPV				62	47	28	45	86
Increased percussion								

	Harlan[83]	Heckerling[87]	O'Neill[88]	Chakko[84]	Butman[89]	Stevenson[85]	Echeverria[86]	Davie[75]
distance								
Sensitivity		94						
Specificity		67						
PPV								
NPV								
Displaced apex beat								
Sensitivity			59				60	66
Specificity			76				50	96
PPV			59				64	75
NPV			77				45	94
Proportional pulse pressure								
Sensitivity						91		0
Specificity						8		100
PPV						91		0
NPV						87		84
Wheeze								
Sensitivity								12
Specificity								82
PPV								11
NPV								83

Similar to symptoms suggestive of HF, utility of clinical signs show variation between studies in terms of specificity, sensitivity, PPV and NPV for detecting HF. Systematic reviews[78,90] also came up with differing utility of certain signs. Mulrow and colleagues[78] concluded that the initial assessment was approximately 70% accurate in determining cause in patients presenting with dyspnoea. Badgett and colleagues[90] concluded that abnormal apical impulse and a third heart sound were the best clinical indicators of systolic dysfunction. Davie and colleagues[75] also found in a study of hospitalised patients that a displaced apex beat was the best predictor of LVSD with a sensitivity of 66% and specificity of 96%. However, patients with HF may not have signs such as displaced apex beat, raised JVP[85] or a third heart sound[91].

Furthermore, there is wide variability in the precision and reliability of eliciting clinical signs between clinicians[92,93]. It would appear that the most useful signs are probably the most subtle: third heart sound, increased width of cardiac dullness and displaced apex beat[74] but are likely to be difficult signs for GPs to be able to elicit with confidence.

In summary, whilst symptoms and signs are important as they alert a clinician to the possibility that HF exists, the clinical suspicion must be confirmed by more objective tests particularly aimed at assessing cardiac function.

1.4.5 Clinical scoring systems in the diagnosis of heart failure

The combinations of symptoms and signs suggestive of HF have been used to devise several scoring systems for the diagnosis of HF[50,94-98]. Mosterd and colleagues[99] compared the usefulness of six HF scores in non-hospitalised subjects. They demonstrated that five of the six scores were broadly similar in the detection of manifest HF, but felt that there was generally low sensitivity for detecting possible HF. The authors concluded that given the atypical presentation and low sensitivity in suspected HF clinical scoring systems were unlikely to be useful in clinical practice and suggested that all such patients need objective assessment of cardiac function by echocardiography.

In summary, clinical scoring systems are interesting but of limited use in practice[99]. Clinical evaluation must be combined with objective assessment in confirming LVSD[8].

1.4.6 Symptoms and severity of heart failure

Once a diagnosis of HF has been established, symptoms can be used to classify severity and may be used to monitor progress and the effects of therapy. The New York Heart Association (NYHA) classification[100], initially developed for patients with angina, is widely used in practice and in clinical trials. See Table 1.5 below.

Table 1.5: New York Heart Association classification of heart failure[100]	
Class I	No limitation: ordinary physical exercise does not cause undue fatigue, dyspnoea, or palpitations
Class II	Slight limitation of physical activity: Comfortable at rest but ordinary activity results in fatigue, palpitations, or dyspnoea
Class III	Marked limitation of physical activity: Comfortable at rest but less than ordinary activity results in symptoms
Class IV	Unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with any physical activity

However, symptoms are often very subjective and may not correlate particularly well with degree of cardiac impairment[71,82]. In practice it is not always easy to apply an NYHA class to all patients, and clinicians often simply label patients as having mild (NYHA II), moderate (NYHA III) or severe (NYHA IV) HF. Guidelines[101] suggest the use of walking distance or number of stairs climbed in a given time as an objective measure of functional capacity and hence HF severity. Most GPs are unlikely to be aware of or routinely use such measures, although no formal assessment of their knowledge has been made.

A simpler and more practical method of classifying and staging HF has been proposed by American College of Cardiology/American Heart Association guidelines[10]. However, it remains to be seen whether this will be used in

everyday clinical practice or indeed in future clinical trial staging and assessment of HF (See table 1.6 below).

Table 1.6 American College of Cardiology/American Heart Association Staging System for Heart Failure 2001

	Stage	Patient Description
A	**High risk for developing heart failure (HF)**	• Coronary artery disease • Hypertension • Diabetes mellitus • Family history of cardiomyopathy
B	**Asymptomatic HF**	• Previous myocardial infarction • Left ventricular dysfunction • Asymptomatic valvular disease
C	**Symptomatic HF**	• Known structural heart disease • Shortness of breath and fatigue • Reduced exercise tolerance
D	**Refractory end–stage HF**	• Marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from hospital without specialized interventions)

1.4.7 The electrocardiogram in the diagnosis of heart failure

All guidelines[8,22,101-104] and NICE guidance[105] for the diagnosis and management of heart failure due to LVSD suggest that if a 12 lead ECG is normal then LVSD is very unlikely. This has led to suggestions that a normal ECG be used to screen out patients with suspected HF prior to referral for echocardiography. This advice appears to be largely based on a trial by Davie and colleagues[106] suggesting that LVSD is unlikely to be present if an ECG is normal, with a sensitivity of 94% and NPV 98%. However, these claims have been contradicted by other studies. The following Table 1.7 summarises the available studies where ECG has been assessed against an echocardiographic diagnosis of LVSD.

Table 1.7: Sensitivity and specificity of ECG studies in identifying HF

Study author/year	Sensitivity	95% CI	Specificity	95% CI
Davie 1996[106]	0.94	0.86-0.97	0.61	0.57-0.66
Khandekar 1996[107]	0.78	0.64-0.88	0.20	0.12-0.30
Gillespie 1997[108]	0.98	0.88-1.00	0.69	0.48-0.86
Houghton 1997[109]	0.89	0.85-0.94	0.46	0.31-0.66
Lindsay 2000[110]	0.91	0.82-0.95	0.65	0.60-0.70
Sandler 2000[111]	0.73	0.61-0.83	0.53	0.45-0.60
Nielsen 2000[112]	0.87	0.60-0.98	0.56	0.46-0.65
Landray 2000[113]	0.42	0.26-0.58	0.87	0.78-0.93
Hutcheon 2002[114]	0.96	0.83-1.00	0.50	0.44-0.56
Ng 2003[115]	0.88	0.64-0.99	0.61	0.58-0.64

It is obvious from this table that there is considerable variation between sensitivity and specificity of studies. Relying on an abnormal ECG as a screen for echocardiography would have failed to detect between 2% to 58% of individuals with LVSD in the various study cohorts. In a further study in patients randomly selected from those attending a heart failure clinic, Talwar and colleagues[116] found that using the ECG as a screening tool would have led to failure to diagnose significant systolic impairment (left WMI < 1.2) in 33% (n= 12) of patients with a normal ECG (n = 36), and a further 17% (n =6) with mild to moderate systolic impairment (left WMI between 1.3 and 1.9).

Only four of these studies[106,107,110,111] were broadly representative of patients seen by GPs with suspected HF as they were all based on studies of OAE services, in a UK setting. Others studies were either patient referred to secondary care clinics, acute admissions with dyspnoea or cohorts enrolled in research projects in secondary care. Even within these 4 studies there was considerable heterogeneity between studies in NPV and PPV, where NPV could be used to estimate the utility of ECG in excluding HF. The results were Davie et al[106], PPV 35%, NPV 98%; Lindsay et al[110], PPV 43%, NPV 96%;

Khandekar et al[107], PPV 36%, NPV 61%, and Sandler et al[111], PPV 39%, NPV 82%. One possible explanation of this variation was that in the first two studies displaying high NPV both the ECG and echocardiograms were reported by cardiologists, who are more likely to have expertise in this area.

The variation in studies may be explained by several other factors. Dependence on case selection (consecutive patients studied in an attempt to reduce potential selection bias) and the prevalence of LVSD in the population studied; differences in referral criteria; differences in echocardiographic reporting criteria (LVEF, WMI or semi-quantitative measures) and ECG classification (i.e. what constitutes an abnormal ECG?) and the experience of the person reporting these tests. Most studies used very similar ECG criteria[117] but only the Khandekar et al study[107] reported that consecutive patients were studied. Very recently Khunti and colleagues[118] evaluated the accuracy of a 12-lead ECG in screening patients with suspected HF for OAE by means of a systematic review and meta-analysis. They concluded that a 12 lead ECG is an inadequate screening tool for identifying patients with suspected HF who require echocardiography[118].

Furthermore, GPs and hospital doctors may not have sufficient skills and express lack of confidence in interpretation of ECG changes[119,120]. Clinicians are also doubtful as to the accuracy of interpretive ECG machines[121]. This has led to calls for courses on interpreting ECGs to improve GPs' skills[122].

In summary these findings would suggest that use of a normal ECG to rule out HF due to LVSD may miss a significant number of patients with this condition. It is likely that previous studies may not have been representative of patients referred by GPs with suspected HF. More research is needed to investigate the role of the ECG in triage of patients with suspected HF by GPs. Furthermore, studies of GP confidence of interpreting ECGs and educational initiatives to improve skills in this area are needed. With developments in natriuretic peptides to rule out HF, studies comparing the ECG with natriuretic peptides and the incremental value of using both tests are also needed.

1.4.8 The chest X-ray in the diagnosis of heart failure

Patients are often referred by their GP to diagnostic clinics due to cardiomegaly (defined as a cardio thoracic ratio of over 50%). However, there is considerable doubt as to the usefulness of the chest X-ray as a diagnostic tool or as a means of selecting which patients to refer for echocardiography. Research shows that there is a poor relationship between heart size on a chest X-ray and left ventricular systolic dysfunction[123] and conversely significant LVSD may occur in the absence of cardiomegaly[124]. Furthermore, there are significant differences between GPs use of clinical information provided by the chest X-ray in their judgement of heart failure diagnosis[77].

Whilst pulmonary oedema with classical bats wing appearance, upper lobe venous diversion or redistribution, fluid in the horizontal fissures, Kerley B lines in the costophrenic angles with or without effusions, may be helpful signs in diagnosing left ventricular failure, this does not always mean the patient has LVSD. Furthermore, inter-observer agreement in interpretation of pulmonary oedema is only modest[125].

The cardiac silhouette in valvular calcification may point to aetiology, e.g. left atrial enlargement in rheumatic mitral disease or a calcified aortic stenotic valve[126].

Badgett and colleagues conducted a review of the evidence for the diagnostic utility of the chest X-ray for left ventricular dysfunction[90]. Two independent readers reviewed 29 studies. They found that upper lobe venous redistribution best diagnosed increased preload with a sensitivity of 65% (95% CI 55 to 75%) and specificity 67% (95% CI, 53 to 79%). Cardiomegaly best diagnosed decreased left ventricular ejection fraction with a sensitivity of 51% (95% CI, 43 to 60%) and specificity of 79% (95% CI, 71 to 85%). Inter-rater reliability was fair to moderate for redistribution and moderate for cardiomegaly. They concluded that whilst redistribution and cardiomegaly are the best chest radiographic findings for diagnosing increased preload and reduced left ventricular ejection fraction, unfortunately neither finding alone could adequately exclude or confirm left ventricular dysfunction in a usual

clinical setting. Furthermore redistribution was not always reliably interpreted[90].

In general practice the chest X-ray is useful in excluding pulmonary disease as a cause of symptoms and if there is evidence of cardiomegaly or vascular redistribution with symptoms suggestive of heart failure, the patient should be referred for further investigation. The chest X-ray should not be considered as a substitute for echocardiogram or radionuclide ventriculography[127].

1.4.9 Haematology and biochemistry in the diagnosis of heart failure

Guidelines[8,22,104,105] suggest the measurement of urea and electrolytes, creatinine, full blood count, thyroid function tests, serum glucose, urinalysis and lipids in assessment of patients with suspected or established HF.

Anaemia may exacerbate HF and is associated with increased risk of morbidity and mortality[128]. Hyperthyroidism and hypothyroidism need to be excluded as a cause of HF. HF and renal dysfunction may co-exist especially in diabetes or hypertension. Electrolyte balance needs to be assessed and reviewed especially once treatment with diuretics and ACE inhibitors or ARBs has been started.

1.4.10 Natriuretic peptides in the diagnosis of heart failure

NICE[105] and ESC guidelines[104] suggest the use of natriuretic peptides in the diagnostic triage of patients with suspected HF. They recommend that in clinical practice BNP or NT proBNP is used as a rule out test to exclude significant cardiac disease in primary care and in certain aspects of secondary care (e.g. the emergency room and clinics). The role of natriuretic peptides will be reviewed in detail in Chapter 5.

1.4.11 Echocardiography and heart failure

Echocardiography is the preferred method for the documentation of cardiac dysfunction at rest and is encouraged by all guidelines for the diagnosis of HF. Transthoracic echocardiography (TOE) is rapid, safe and widely available in secondary care. The process of making this test available to primary care

physicians has stimulated considerable debate and research and will be discussed in detail later in this review.

TOE is a non-invasive technique that can be used to assess chamber dimensions, wall thicknesses and geometry, indices of regional and global systolic and diastolic function. It also provides semi-quantitative assessment of valvular function[104,129].

The most important measurement of ventricular function is the LVEF for distinguishing patients with cardiac systolic function from those with preserved systolic function. Patients with an ejection fraction less than 40% are generally considered to have systolic dysfunction[9,10]. Diastolic dysfunction is deemed to be present if the following three conditions are simultaneously satisfied: (1) presence of signs or symptoms of CHF, (2) presence of normal or only mildly abnormal left ventricular systolic function (LVEF ≥ 45-50%), and (3) evidence of abnormal left ventricular relaxation, diastolic distensibility, or diastolic stiffness[130]. This may be particularly difficult to assess in atrial fibrillation. However, reproducibility of LVEF among different observers is poor, even when the same techniques are used[8,104].

Willenheimer and colleagues[131] proposed a rapid, simplified semi-quantitative echocardiography method that was reliable and accurate for assessing systolic function and may be used as a screening tool in place of standard echocardiography.

If heart failure is suspected, echocardiography is essential to clarify whether the patient has LVSD, to help establish aetiology and identify other cardiac abnormalities. Guidelines[8,104], NICE guidance[105] and the NSF for CHD[132] suggest echocardiography for all patients with suspected heart failure. However, echocardiography provision is limited by lack of trained technicians, cardiologists, equipment and potentially overwhelming numbers of patients in need of assessment.

1.4.12 Other non-invasive tests in HF diagnosis and assessment

Other investigations such as radionuclide ventriculography (RNVG), stress echocardiography, and cardiac magnetic resonance imaging (CMRI) may be

used in specialist centres if echocardiography at rest has not provided enough information and in selected patients with CAD or diagnostic uncertainty.

RVNG has been used in some studies of HF and reproducibility of LVEF may be better than with echocardiography[104]. Stress echocardiography may be useful for detecting ischaemia as a cause of reversible or persistent cardiac dysfunction and in determining the viability of akinetic myocardium[104]. CMRI is currently largely an experimental research tool for delineation of cardiac anatomy[104].

1.4.13 Systolic versus diastolic heart failure

In recent years, various studies have suggested that diastolic HF may account for more than 50% of the hospitalisations for HF in elderly patients[133-135]. The ESC has produced guidance[130] on how to diagnose diastolic dysfunction (see under echocardiography section 1.4.11). Despite this others remain sceptical[136,137] and deny the fact that diastolic abnormalities may play such an important role in HF or even exist, and suggest that the diagnosis of diastolic HF is overestimated in a large number of cases.

It is important to clarify terminology in this area. HF with preserved left ventricular ejection fraction (PLVEF) and HF because of left ventricular diastolic dysfunction (LVDD) are not synonymous[130]. The former diagnosis implies the evidence of preserved LVEF and not the demonstration of left ventricular diastolic dysfunction. The diagnosis of LVDD requires echocardiographic evidence of abnormal diastolic dysfunction (see 1.4.11)[130].

In a review of the topic Cohen-Solal[138] felt it was definitely possible to have a history of chronic or, more often, intermittent HF, despite relatively preserved systolic function and that this accounted for a large number of hospitalisations. The concept of HF with preserved systolic function is probably heterogeneous and comprises cases of clearly altered diastolic dysfunction (hypertrophic cardiomyopathy, diabetes, hypertension, diabetes) as well as cases of transient HF where the combination of moderate diastolic dysfunction, mild systolic dysfunction, reduced compensatory mechanisms and precipitating factors (e.g., respiratory infection in an elderly person) operate altogether. For many patients with a diagnosis of heart failure but

preserved left ventricular function there is an alternative explanation for their symptoms – for example, obesity, lung disease, and myocardial ischaemia. These alternative diagnoses should be rigorously sought and managed accordingly[137].

Despite the guidelines it is clear that specialists disagree and diagnosis is difficult. It is no surprise then that GPs are not familiar with the concept of systolic/diastolic dysfunction. In the Improvement-HF survey, nearly 40% of GPs were unaware of it. As GPs are not familiar with the concept of diastolic dysfunction we cannot tell them to apply the results of 'evidence-based medicine' to the general population of HF as the diastolic dysfunction group are not represented in large clinical trials that enrol patients with LVSD. Therefore, we do not as yet have a clear effective therapy for diastolic dysfunction based on robust trial outcomes[138].

1.5 What is the reality in investigation and management of HF in primary and secondary care?

1.5.1 The use of diagnostic tests for suspected heart failure

Symptoms and clinical signs often do not allow one to accurately differentiate between cardiac and non-cardiac causes of breathlessness (especially in the early stages of GP presentation and in women, elderly and obese). All patients with suspected heart failure should have further investigation including baseline blood tests, chest X-ray, ECG and echocardiography.

Several studies in the USA, Finland and the UK have shown that a high percentage are falsely diagnosed in primary care when diagnosis is re-evaluated by cardiac imaging or specialist review, with only around 40% to 56% having LVSD or HF:

Framingham:	40%	(McKee1971)[50]
Boston:	42%	(Carlson1985)[96]
Kuopio:	50%	(Remes 1991)[71]
Dundee:	53%	(Wheeldon 1993)[39]
Nottingham:	56%	(Clarke 1994)[41]

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Furthermore when patients with suspected HF in primary care are referred for open access echocardiography most do not have LVSD confirmed:

Edinburgh: 26% had LVSD (Francis 1995)[139]

Darlington: 20% significant LVSD (Murphy 1996)[140]

Edinburgh: 16% had LVSD (Davie 1997)[75]

Those patients with LVSD would benefit from the introduction of evidence based pharmacotherapy. Although most patients investigated for suspected heart failure receive chest X-ray and electrocardiography only about a third undergoes echocardiography[38,40,41,69], for which routine use has been advocated for optimal diagnosis[8,101,141]. (See Table 1.8)

Table 1.8: Use of ECG, CXR and echocardiography in the UK

Author	Year	Setting	Patients with HF	ECG	CXR	Echo
Parameshwar[38]	1992	London GP	117	89%	87%	28%
Mair[40]	1996	Liverpool GP	266	80%	89%	30%
Lip[69]	1997	Birmingham GP	90	68%	64%	36%
Clarke[41]	1994	Nottingham GP/Hospital	281	80%	75%	31%
Lip[142]	1997	Birmingham GP/Hospital	260	100%	82%	34%
Parameshwar[143]	1992	London Hospital	140	98%	97%	58%
Hillis[144]	1996 (1992 data)	Aberdeen Hospital	325	-	-	37%
Hillis[145]	1996	Aberdeen Hospital	265	-	-	72%

A likely reason for lower use of echocardiography in primary care is that open access echocardiography is not uniformly available to GPs across the UK. One survey confirmed only 30% of hospitals offered the service to GPs[146].

1.5.2 Surveys of primary and secondary care diagnosis and management of heart failure across Europe

There have been several large pan-European surveys in primary care and hospital practice that have reviewed the use of diagnostics for suspected HF and treatment for those with confirmed HF[147-150].

Hobbs and colleagues[147] conducted a postal questionnaire based survey on a random sample of 200 primary care physicians in each of 5 European countries (France, Germany, Italy, Netherlands and Spain) and of 250 UK primary care physicians. The adjusted response rate varied from 17% (France) to 56% (Britain). Primary care physicians generally underestimated the prevalence of heart failure. Most patients were diagnosed with symptoms and signs alone with only 32% having further investigations or referral for echocardiography. Although most primary care physicians stated they prescribed ACE inhibitors in heart failure, this was for only 47 to 62% of patients and at doses below those identified as effective in trials. There were obviously limitations of data including the general problem of questionnaires whether responses accord with actual clinical practice, and specific to these data, the low response rate in some countries[147].

A further Euro heart survey[148,149] was conducted in 115 hospitals from 24 European and Mediterranean countries. A total of 46,788 consecutive hospital admissions were screened yielding a total of 11,327 patients with suspected or confirmed heart failure. The treatment received by these patients over a 6 week period was analysed in 11,304 patients. Overall, ACE inhibitors were prescribed in 61.8% of patients and beta blockers in 36.9%. There was however marked variations in prescribing practice between countries. The proportion of patients receiving ACE inhibitors ranged from 40 to 85%, while the proportion given beta blockers ranged from 10% to 65.8%. Age under 70 and the presence of co-morbidities such as diabetes, ischaemic

heart disease or stroke were strong predictors of the likelihood of receiving ACE inhibitor therapy.

Cleland and colleagues[150] carried out a survey which included data from 11,062 patients treated by 1,363 physicians in 15 European countries. In the IMPROVEMENT survey, while most physicians (approximately 60 – 90%) were aware of the beneficial of ACE inhibitors and beta blockers on prognosis, only 60% of patients overall were receiving ACE inhibitor therapy and only 34% were receiving beta blockers with considerable variations between countries. In the UK cohort 60% were receiving ACE inhibitors, 12% ARBs and only 26% beta blockers. Only 20% were receiving both an ACE inhibitor and a beta blocker across Europe. More over, even when treatment was given the doses used were often suboptimal. Overall, the doses prescribed were about 50% of those recommended in the European Guidelines: the proportion of patients receiving ACE inhibitors or beta blockers at target doses or higher ranged from 32 to 91% and 38 to 61% respectively. In patients with LVSD, ACE inhibitors were more likely to be prescribed and beta blockers less likely than in patients without evidence of systolic dysfunction[150].

Review of these large surveys suggest that there is a temporal increase in ACE inhibitor use and to a lesser extent beta blocker use, but there is great variability between different countries and continuing failure to prescribe evidence based therapies for HF. Furthermore, even when ACE inhibitors and beta blockers were used these were often at sub optimal doses in relation to doses shown to be effective in mortality studies.

1.5.3 Questionnaire studies of heart failure in UK primary care settings

There have also been smaller surveys in two separate locations in England that have addressed GP knowledge about HF, the use of diagnostic tests and use of ACE inhibitors for confirmed HF.

Mair and Bundred[151] conducted a postal questionnaire in the Liverpool area. 298 GPs were contacted and 148 replied (50% response rate). Around 40% of GPs were aware of the findings of major HF studies. Encouragingly 98% of GPs used ACE inhibitors in the management of HF, with 89% stating they

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would initiate patients in practice. However, 38% said they only occasionally used ACE inhibitors. This was not in line with guidelines. Some of those reluctant to initiate therapy held the opinion that they wanted the patient fully assessed before starting treatment. This supports the view that that in order to optimise the treatment of HF, it will be necessary to improve access to diagnostic tests such as echocardiography. 70% of GPs wanted an OAE service but 26% did not and wanted further education on echocardiography use and interpretation of results. While GPs in this survey were using ACE inhibitors to some degree and were aware that echocardiography is a valuable tool the full benefits of early diagnosis and treatment of LVSD were not wholeheartedly perceived. The authors suggested that more emphasis be given to increasing awareness of recent changes in approach to management and encouraging a higher profile for HF in the GP setting. The low response rate of this survey in one locality limited the generalisability of results.

Houghton and Cowley[152] surveyed 515 GPs in the Nottingham Health District, with a 60.2% response rate. They found that although 39% of respondents underestimated the poor prognosis associated with HF, 98% were aware of the prognostic benefits conferred by ACE inhibitors. However, 43% expressed concerns about potential adverse effects associated with ACE inhibitors, the main fears being hypotension and renal impairment. GPs who were concerned about adverse effects were significantly less likely to have initiated an ACE inhibitor for HF than those who were not ($p < 0.01$). This study suggests that concerns about adverse events are a major factor in the failure of GPs to make widespread use of ACE inhibitors in the treatment of HF, despite that fact that symptomatic hypotension was seen in only 2% of patients started on enalapril 2.5 mgs twice daily in the SOLVD study[11]. The authors suggested that further research is needed to identify which patients are particularly at risk of adverse events when ACE inhibitors are commenced in the community and called for effective and practical guidelines for primary care use of ACE inhibitors.

1.5.4 Qualitative studies of heart failure in primary care

Whilst quantitative surveys are useful in telling us about self reported GP behaviour in diagnosis and management of heart failure they do not generally provide information as to why they are behaving in that manner. Qualitative approaches often provide a better understanding of physician behaviour and decision making processes and may also provide reasons behind the evidence-treatment mismatch or gap in CHF diagnosis and management.

Khunti and colleagues[153] undertook a qualitative study of heart failure management using semi-structured interviews with 38 GPs in 18 general practices in the Leicester area. Analysis was based on open coding using a constant comparative approach. Many GPs reported that they would diagnose HF on respiratory examination and a positive finding of basal crepitations. Many would arrange a chest X-ray to establish diagnosis and some arranged an ECG. A few GPs mentioned that they diagnosed HF with a trial of diuretics. Obstacles to diagnosis included lack of facilities for appropriate investigation (especially echocardiography) and lack of time and expertise. Many GPs were unaware of the impact ACE inhibitors can have on morbidity and mortality. Some stated that they would be reluctant to initiate ACE inhibitors in patients symptomatically stable on a diuretic already. Obstacles to management of HF included lack of time, inconvenience of monitoring patients on ACE inhibitors, high costs of drugs, difficulty with diagnosis, selection bias towards younger patients and not having the confidence to initiate ACE inhibitors. It would appear from this study that although symptoms and signs are not sufficiently specific for diagnosing HF, many GPs treat patients on the basis of a clinical examination alone. Such findings suggest that there is a need for education of physicians about the benefits of newer therapies in heart failure. The authors recommended that further qualitative work is needed to identify barriers to the diagnosis and management of heart failure and methods of overcoming them and that specific implementation strategies need to be tailored to overcome obstacles.

Hickling and colleagues[154] used a novel practice based approach combining the presentation of data on current management of heart failure with the nominal group technique to elicit and rank relevant barriers to effective

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management of heart failure in general practice. There was a degree of selection and non-responder bias in that only ten of forty five eligible practices approached agreed to participate and all were part of the Medical Research Council General Practice framework practices in the North Thames region. This raises questions about generalisability to non-research practices in other areas of the UK. Of the 674 patients requiring investigation, only 34% were referred for echocardiography and only 47% with probable heart failure were prescribed ACE inhibitors. The barriers for the effective management of heart failure in general practice were thought to be complex. The main barrier to the use of echocardiograms in diagnosis of heart failure was lack of open access. The main barrier to the use of ACE inhibitors in treating heart failure was GPs concerns about the possible adverse effects. This study used a different approach to Horne and colleagues who used structured qualitative interviews and Houghton and colleagues who used a quantitative questionnaire methodology. Identification of barriers to the application of research evidence using qualitative methods are essential if practice is to be improved and the authors felt that further research in this area was necessary[154].

Horne et al[155] used structured face to face interviews to elicit the views of a stratified representative sample of 100 GPs working in England and Wales about the diagnosis and treatment of heart failure. Questionnaire items were based on previous open interviews with 11 GPs and 4 hospital physicians and formulated by qualitative content analysis techniques. Responses to three heart failure case vignettes provided an indication of the degree to which GPs' knowledge of HF and trial results might be applied to diagnosis and treatment intentions. Participants were generally aware of clinical trials that showed prognosis could be improved by treatment, but trial results appeared to have little influence on treatment intentions in the three case scenarios. The major barriers to optimum management were the difficulties in securing a confident diagnosis of HF and the perceived properties of ACE inhibitors relative to diuretics. In the case scenarios, less than 30% reported that they would undertake basic investigations, such as a CXR, ECG or haemoglobin. Over 70% relied on the patient's response to diuretics to confirm diagnosis. The

most frequent reasons for not prescribing ACE inhibitors were the perceived inconvenience in monitoring patients; the risk of adverse events (41%) and the view that most patients can be managed successfully on diuretics alone (27%). 83% of the sample was dissatisfied with the quality of information accompanying HF patients discharged from hospital. The results of this study strengthen the case for development of a collaborative model of care that delivers diagnostic tests and improves communication. Further support for GPs in the form of additional training in the diagnosis of HF and the optimum use of both ACE inhibitors and diuretics are needed.

1.5.5 Summary of studies

A number of patient or physician related factors may contribute to the under utilisation of heart failure therapies. Physician's perceptions of the risks and benefits of different therapies may influence the extent to which guidelines are adopted. Physicians may be reluctant to adopt new treatment approaches for a variety of reasons including lack of education, conservative attitudes to therapy, concerns about potential side effects of treatments, the complexity of therapy, avoidance of polypharmacy as well as lack of access to facilities to confirm the diagnosis of heart failure and a continuing emphasis on symptomatic treatment rather than using therapies with proven effects on prognosis.

1.6 Availability and use of Echocardiography and diagnostic services for heart failure

1.6.1 Introduction

The NSF for CHD[132] details alternative models of care which will be dependent on local circumstances and may include specialist one stop HF clinics, mobile echocardiography units, or intermediate care facilities provided by suitably trained and accredited GPs. Above all equity of access to all patients in a locality should be ensured. The following sections outline models that have been developed in selected UK locations and attempts to expand upon the relative merits of each.

1.6.2 Open access echocardiography

1.6.2.1 Definition of open access echocardiography (OAE)

Chambers et al defined OAE as echocardiography requested by a GP without prior assessment by a cardiologist, and produced guidelines for referral to an OAE service[156]. A non-invasive test that has the power to bridge the divide between community and hospital may open up the possibility of more varied patterns of care for patients, especially as diagnosis of heart failure in the early stages of disease may be difficult for GPs[157].

1.6.2.2 Open access echocardiography studies in the UK

Five observational cohort studies from the UK have been published, and Khunti has recently conducted a systematic review[158].

Francis and colleagues[139] report their experience of an OAE service in Edinburgh where GPs referred patients with HF or suspected HF using a clinical pro-forma. In a 5 month period 259 consecutive patients were seen. 119 had already been treated for HF, 99 were untreated with symptoms and signs of HF and 9 asymptomatic with risk factors for LVD.

In this study echocardiography was combined with a cardiology registrar-based clinical assessment including further investigations performed by attendant medical staff. Advice on treatment was recommended. Strictly speaking this paper does not truly reflect an OAE service with echocardiogram performed and reported by a technician or clinician.

Furthermore the conclusion that echocardiography led to advice about a change in treatment in 70% of patients with established or suspected HF as diagnosed by GPs is misleading. Their 70% represented 82 of 119 patients receiving treatment when referred. However, this figure should include those 14 in the suspected HF group (n = 99) for whom the cardiologist advised a change in management. This would have made the true proportion of echocardiograms resulting in advice 44% (96/218). Generalisability of results was further limited by the poor uptake rate by GPs (17% [93/550]).

Murphy and colleagues[140] introduced an OAE service that was piloted to 24 GPs in 5 practices in Darlington. The service was audited after 250 cases

(mean age 71; range 16-92) referred over 22 months. The impact on clinical management was assessed by reviewing GP notes two months after the echocardiogram. Significant impairment of left ventricular function was found in 49 patients (20%) and significant valve disease in 20 (8%). 38 (78%) of the 49 LVSD patients identified by OAE had been started on ACE inhibitors by their GP and 14 (70%) of the 20 valve lesion patients had been referred for cardiology assessment. The provision of an OAE service with simple guidelines for use was popular with GPs and the information resulted in appropriate management decisions being made. Following this pilot study the service was extended to all GPs in the locality.

Sandler and colleagues[111] reported on the first 18 months of an OAE service for GPs in the Chesterfield area. A difference in this study from the Darlington and Edinburgh services was that apart from referral indications of suspected HF and unexplained breathlessness (68%), patients with atrial fibrillation and a heart murmur were accepted. 486 patients (mean age 68; range 13-94) were seen over 18 months within a mean time of 49 days (range 3 to 97 days). LVSD was noted in about 40% of cases referred with suspected heart failure. Those with AF or heart murmurs were more likely to have abnormalities (74% and 46% abnormal respectively). Interestingly of the patients with suspected HF or breathlessness 27% with a normal ECG were found to have LVSD; a finding that contradicts guidelines that suggest that patients with a normal ECG are very unlikely to have LVSD. Uptake of the service was variable with individual GPs requesting between 1 to 27 studies in the 18 months.

Lindsay and colleagues[110] reported an OAE service for suspected HF or dyspnoea in Glasgow. 416 patients (265 females) were referred over a 3 year period from 1995-1997. Overall 23% (n = 95) had impaired left ventricular function and 3% (n = 12) had a significant valve lesion. An important finding was that 60% were being treated for presumed HF with an ACE inhibitor, diuretic or both. However, the study showed that 73% were probably receiving inappropriate therapy; although it is possible they needed treatment for co-morbidity such as hypertension. This study and others (Sandler) found differences between sexes in prior treatment and referral patterns. Women

accounted for the majority of referrals, most of who had normal left ventricular function and yet were on treatment. It is not entirely clear what the explanation for this is, although it may be related to the increased presence of non-cardiac oedema and obesity in women. A further finding of this study was the high NPV (96%) of a normal ECG in excluding HF. The combination of a normal ECG and no history of MI increased the NPV to 99% and Lindsay and colleagues suggest that this could have utility in reducing the number of unnecessary echocardiograms if used by GPs to screen patients with suspected HF.

Sim and Davies[159] reported an OAE service in Newport, Wales. Data was presented on the first 200 patients referred within 13 months. As with the Darlington service this service was introduced through educational meetings and the presentation of a referral guideline. Guidelines were followed in 94% of referrals and 90% were seen within 14 days. LVSD was found in 12% (n = 22) and significant valvular lesions in 14% (n = 24). Uniquely the authors then showed high levels of patient and GP satisfaction with the service by way of a questionnaire. GPs indicated that they would have referred 87% of the patients to the hospital if OAE was not available compared to the 11% who were actually referred to hospital. Crude cost analysis based on this showed the service to be cost effective.

1.6.2.3 Discussion of open access echocardiography services

There has been considerable debate around the various strategies to deliver essential echocardiographic diagnosis of HF and subsequent treatment for those with LVSD[157,160-166]. In particular secondary care has expressed concerns about over referral to already "strained systems"[167]. Despite these worries the above mentioned studies have demonstrated that GPs use open access services appropriately[111,139,140,159].

Review of these OAE services suggests that benefits include the potential to deliver early, accurate diagnosis of HF and identify important valvular lesions; initiate appropriate evidence based treatment[139,140]; and withdraw inappropriate medications[111,139,159]. Furthermore, this may reduce the burden on secondary care outpatient services and is likely to be cost

effective[156,159,168,169]. Senni and colleagues[170] demonstrated that the under use of echocardiography appears to be associated with poorer survival and under use of ACE inhibitor therapy in a US population. In a Cumbrian cohort Toal et al[44] also demonstrated that patients who had an echocardiogram were much more likely to be on an ACE inhibitor. It should be remembered that negative results can be reassuring and management of the patients' problems may well have been made easier for GPs[163].

Despite these potential benefits there have been some cautionary comments. Saltissi and Chambers[171] felt that echocardiography in the community needed quality control and felt that expansion of services may be limited by lack of adequately trained technicians. Chambers[156] warned that whilst OAE may improve the management of more patients than can be accommodated within the current system, at worst it could deprive some patients of a specialist cardiological opinion. Furthermore Khunti[158] called for rigorous cost effectiveness evaluation of OAE services within other models of care including primary care HF nurse clinics or consultant led direct access HF clinics, before widespread establishment of OAE could be recommended. Where OAE is deemed the most appropriate local system, standardization of referral forms, and clinician generated reports incorporating treatment suggestions needs to be provided.

It has been suggested that the correct interpretation of echocardiographic information in a clinical context can only come from history, examination and other investigations. Furthermore, the introduction of newer therapies such as beta blockers, and new indications for older therapies such as spironolactone has made HF a therapeutically complex area to treat and is likely to be out with the expertise or comfort zone of most GPs. Partly because of this specialist heart failure clinics have been proposed as a benchmark of optimal diagnosis and care[172].

1.6.3 Specialist heart failure clinics

1.6.3.1 An introduction

Specialist clinics caring for patients with other common chronic disorders such as asthma, hypertension and diabetes are common in both primary and

secondary care, but few patients with HF are cared for in such clinics. There is observational data which suggests that patients managed in a specialist heart failure clinic may have improved outcomes in terms of accuracy of diagnosis, initiation of evidence based therapies and possibly reduced mortality, morbidity and hospitalisations[172-175].

There appear to be many differing models reported in the literature. These include rapid access diagnostic clinics situated in secondary care and run by clinicians; secondary care medical clinics for ongoing management in patients with previously confirmed HF (invariably diagnosed during hospital admission); clinics set up in secondary care (and one report of a research clinic in primary care) as part of research projects to assess a particular aspect of HF management; nurse-led clinics in secondary care to optimise HF therapies and bridge the gap between secondary care and the community; and recently protocol-driven HF clinics staffed by nurses and pharmacist specialists.

1.6.3.2 Secondary care heart failure clinic models

Fox and colleagues[172] reported the success of a rapid access secondary care heart failure clinic in South East London serving a 290,000 population. Over a 15 month period patients were seen usually within 24 hours of referral by a GP. There were 0.4 referrals per 100,000 per weekday in which 178/383 (46%) were felt to have definite or possible HF at initial assessment and 101/383 (21%) were found to have LVSD. 98% of these patients were started on an ACE inhibitor. High uptake of ACE inhibitors (80%) was also seen in a similar clinic in Nottingham, with Houghton and colleagues[174] also stressing the importance of the clinic in stopping inappropriately started medications including ACE inhibitors. The strength of this model lies in the fact that it focuses on suspected first presentation of HF rather than known HF in the belief that the maximum benefit for individual patients was in correctly making a diagnosis, defining aetiology and starting appropriate therapy, rather than making adjustments to existing therapies. A weakness was the fact that no patient education was delivered and no mention of structured follow up of patients after initiation of therapy was made. Referral back to the GP cannot be assumed to deliver evidence based therapy at target doses.

Galatius and colleagues[176] reported a diagnostic and therapeutic HF clinic in Copenhagen. Over a 21 month period 460 patients were referred, with 320 (70%) having clinical HF and of this group 88% (n = 283) had LVSD (defined as LVEF ≤ 45%). The majority of patients were started on ACE inhibitors and beta-blockers but importantly there was a 23% decline in HF related hospital admissions during the first year of the operation of the clinic. It is not possible to determine whether there were any confounding factors that contributed to the fall in hospitalisation and it cannot be assumed that this was purely due to the introduction of a HF clinic model locally.

Gates and colleagues[173] conducted a retrospective audit of 100 patients with confirmed LVSD attending a heart failure clinic in secondary care. Median age was 72 with a range of 50 to 87 years. They found that 74% were on an ACE inhibitor and 15 % on an ARB or vasodilator. Average length of survival from the first clinic attendance was 5.3 years for females and 2.97 years for males. Hospitalisation rates were 0.7 +/- 0.1 admissions per patient per year with a length of stay in hospital of 11.8 +/- 2 days for women and 10.5 +/- 2.2 days for men. This data suggest that attendance at a specialist heart failure clinic ensures optimisation of evidence based medication, reduces patient admission rates and duration of hospital stay. Strength of this approach was the emphasis placed on patient education, including a reinforcement of the need for strict adherence to treatment regimens.

Introduction of evidence based therapies have been shown to be increased by attendance at a specialist clinic. McMullan and Silke[177] compared the rate of low-dose spironolactone among patients with HF in a general medical inpatient setting and in a specialist left ventricular dysfunction clinic in Belfast. 38% of general medical patients and 72% of those attending the LVD clinic had been prescribed spironolactone. When contraindications were considered, more patients in the LVD clinic were treated with spironolactone (77% vs. 54%).

1.6.3.3 Primary care heart failure clinics

There are no reports of ongoing formal heart failure clinics in primary care although McCallum and colleagues[70] set up a research funded clinic to

investigate whether SIGN guidelines on heart failure could be implemented in general practice. Of 67 patients referred for an echocardiogram 41% (n = 28) had LVSD. Only 58.3% of these were initially on an ACE inhibitor or ARB but after one year this had risen to 90.5%. Although only 22.7% were taking a beta-blocker at presentation, the study did not report any alteration to this figure after a year.

1.6.3.4 Nurse-led heart failure clinics

Sweden seems to be the leading nation in terms of introduction of nurse-led heart failure clinics, with 148 heart failure nurses in 69% of 86 hospitals. Within the Swedish system nurses integrate care between hospitals and the community and are able to titrate and alter medication based on standard protocols[175,178,179].

Whilst the large majority of clinics have been observational studies Stromberg et al[180] report a small prospective, randomised trial in Linkoping, Sweden to evaluate the effect of follow up at a nurse-led HF clinic on mortality, morbidity and self-behaviour for patients hospitalised due to HF for 12 months after discharge. A total of 106 patients were randomly assigned to either nurse-led HF clinic follow up or to usual care. There were fewer patients with events (death or admission) after 12 months in the intervention group compared to the usual care group (29 vs. 40, p = 0.03). The intervention group had fewer admissions (33 vs. 56, p = 0.045) during the first 3 months, and after 12 months a 55% decrease in admissions per patient per month (0.18 vs. 0.40, p = 0.06) and fewer days in hospital/patient/month (1.4 vs. 3.9, p = 0.02). The intervention group had significantly higher self care scores at 3 and 12 months compared to the control group. Hence follow up after hospitalisation at a nurse led HF clinic can improve survival and self-care behaviour in patients with HF as well as reduce number of events, readmissions and days in hospital. This small trial needs repeating in a geographically different and larger cohort of patients before results can be considered to be generalisable to all HF populations.

A small Scottish study studied the role of the nurse specialist. Smith and Irving[181] assessed the effectiveness of a nurse specialist in managing HF

patients in the community by conducting a before and after study. They compared out patient attendances and hospital re-admissions to hospital for the two years (April 1995-97) before the service started compared with the two years afterwards (April 1997-99). 61 patients with severe HF were enrolled. 28 died within the study period. Of those surviving total re-admissions (bed days used) were reduced from 605 to 270 days and outpatient clinic attendances fell from 168 to 60. There was not a control group and it is therefore impossible to conclude that these results were not due to other confounding factors e.g. increased uptake of evidence based therapies that have been shown to reduce hospitalisations over the time period studied.

Initiation of beta blockers in patients with LVSD is likely to need specialist support or attendance at protocol driven clinics. In another Swedish study in Goteborg, Andersson and colleagues[182] evaluated the outcome of drug titration in 418 patients referred to a nurse-run clinic from 1995 to 2001. Throughout that period most patients were discharged on ACE inhibitors and beta blockers. In particular beta blocker use increased during the observation period from 43% to 88%. Furthermore patients started on ACE inhibitor therapy continued taking therapy in 89% and in 95% when started on beta-blockers. Three year mortality was reduced from 27% to 10% and in multivariable analysis survival was associated with higher ejection fraction, better renal function, beta blocker and ACE inhibitor use and negatively with digoxin therapy. As well as showing that nurse-directed titration succeeded in introducing more patients on beta blockers than ACE inhibitors, mortality was reduced during the study period. These findings suggest the observed benefits of beta blockers and ACE inhibitors in randomised clinical trials can be reproduced in everyday clinical practice through efficient medical treatment.

1.6.4 Multidisciplinary heart failure management programs

1.6.4.1 An introduction

Whilst such clinics may improve outcomes for patients with heart failure they are likely to be part of a multidisciplinary heart failure management program.

There have been many such studies reported over the past decade and several meta-analyses and systematic reviews published summarising the available data[183-186]. Stewart and Blue edited the first textbook[187] to cover this area and is unique in that it goes beyond the usual consideration of diagnosis and management by standard textbooks, to focus on the way to organise care the patient receives from an international perspective. The contributors to this book represent the multidisciplinary collaboration that is the hallmark of effective care in a HF population.

1.6.4.2 Some examples of multidisciplinary programs for heart failure

Rich and colleagues[188] contributed the first and also one of the larger and better designed case-control studies of the impact of bridging hospital and community care with cardiac nurse practitioners. This prospective trial involved 282 patients randomised to either a broad multidisciplinary intervention (n = 142, mean age 80 years) or usual care (n = 140, mean age 78 years). The intervention included patient education about CHF, dietary assessment, counselling, social service involvement and intensive targeted cardiology follow up including treatment optimisation. The primary outcome measure was survival for 90 days without hospital readmission. This was achieved in 91 patients in the intervention group and 75 patients in the control group, a result that did not achieve statistical significance (p = 0.09), However, there were 94 readmissions for any reason in the control group with 53 in the treatment group (p = 0.02), and 54 readmissions for HF in the control group compared with 24 in the intervention group (p = 0.04). Patients in the intervention group had a higher quality of life and used fewer hospital resources leading to cost savings. Whilst this may be considered a modest impact it was suggested that wider use of such an intervention could substantially reduce healthcare costs for CHF patients.

Blue and colleagues[189] conducted the only UK randomised controlled trial of specialist nurse intervention to date in Glasgow. 165 patients admitted with HF due to LVSD were randomised prior to discharge to an intervention group (n = 84) or usual care group (n = 81). The intervention included a number of planned home visits of decreasing frequency, supplemented by telephone contact as needed for up to one year. The main outcome measure was time

to first analysis of death from all causes or readmission to hospital with worsening heart failure. 31 patients (37%) in the intervention group died or were readmitted with HF compared with 45 (53%) in the usual care group (hazard ratio = 0.61, 95% CI 0.38-0.96). Patients in the intervention group had fewer readmissions for any reason (86 vs. 114, p = 0.018), fewer admissions for HF (19 vs. 45, p < 0.001) and spent fewer days in hospital for HF (mean 3.43 vs. 7.46 days, p = 0.0051). Home visiting seems to be pivotal to reducing admissions, perhaps by ensuring regular and effective patient contact. This study conducted in a city with high cardiovascular prevalence suggests that home based interventions from trained nurses reduce readmissions and should be considered as part of any effective HF service.

1.6.4.3 Systematic reviews of multidisciplinary programs for heart failure

The first two reviews by Rich[183] and McAlister and colleagues[184] concluded that disease management programs for the care of patients with heart failure that involved specialised follow up by a multidisciplinary team reduce hospitalisations and appear to be cost saving. McAlister et al [184] included 11 trials involving 2,067 patients in their review. However, they felt that trials were too short (maximum follow-up 12 months) to show clear effects on mortality (RR = 0.94, 95% CI 0.75 to 1.19). Both reviews called for further studies to establish the incremental benefits of the different elements of these programs.

Phillips and colleagues[185] revisited this area and included 18 studies from 8 countries randomising 3304 older inpatients with CHF to comprehensive discharge planning plus post discharge support or usual care. Fewer intervention patients were readmitted compared with controls (555/1590 vs. 741/1714, NNT = 12, RR 0.75, 95% CI 0.64-0.88). Analysis of studies (n = 14) reporting secondary outcomes found a trend toward lower all cause mortality for patients in intervention groups compared with usual care (RR 0.87, 95% CI 0.73 -1.03). Furthermore quality of life measures improved in the intervention group compared to baseline scores and there were similar or lower costs for medical care. The authors concluded that reduction in risk of readmission, trend towards improved survival, improvement in QOL, and potential cost savings had important implications for system change, health outcomes, and

resource utilisation for older patients with CHF. They recommended that the evidence supports routine application of comprehensive discharge planning plus post discharge support for older patients with CHF to optimise the transition from acute hospital care to home.

A more recent British review by Holland and colleagues[186] identified 74 trials, of which 30 contained relevant data for inclusion in a meta-analysis. Multidisciplinary interventions reduced all cause admission (RR 0.87, 95% CI 0.79 to 0.95, p = 0.002). Importantly the inclusion of a further 11 randomised controlled trials since the Phillips report meant that all cause mortality was also reduced (RR 0.79, 95% CI 0.69 to 0.92, p = 0.002) as was heart failure related admissions (RR 0.70, 95% CI 0.61 to 0.81, p < 0.001). The conclusions are that it is possible to achieve major reductions in admissions and deaths of patients with HF by implementing post-discharge interventions delivering education and symptom self management. These interventions appear to be particularly effective when they are at least partly delivered in a patient's own home through visits, telephone calls, or more advanced telemonitoring or televideo techniques[190].

1.6.4.4 Summary and future research suggestions

Clark and Cleland[191] suggest that in the UK setting whilst there was some formal recognition of the possible worth of heart failure nurses with enthusiastic developments of their roles in some areas; uptake was patchy and dependent in large part on the enthusiasm of a heart failure specialist in a local hospital. They pointed out that in many parts of the UK there are not enough cardiologists to serve the population, and certainly no heart failure cardiologist to support such a demanding new role. They felt that HF remains the "Cinderella of cardiology" and called for a National Service Framework for Heart failure with specific targets as a priority. However, they did not mention that it need not be a cardiologist that fronts HF services and the possibility of a general physician or GP specialist with an interest in heart failure may be equally feasible.

It is clear from this review of various clinics and multidisciplinary interventions that there are a variety of approaches with some concentrating on rapid,

accurate diagnosis and others on optimisation of therapies and patient support. A challenge for clinicians involved in the care of patients with HF will be to develop models of care that achieve expedient diagnosis, and offer systematic structured follow up. Such models need to be developed across the primary-secondary care interface and studies designed to study the cost effectiveness of introduction in different settings. Further research is needed to compare the impact of different models including open access echocardiography, hospital based and primary care based specialist clinics in achieving accurate timely diagnosis and evidence based treatment as well as improvements in QOL, morbidity, hospitalisations and mortality.

1.7 Treatment of heart failure

The following section will review the evidence base behind treatment options for CHF from a GP perspective, although all clinicians and allied health professionals responsible for the optimal management of patients with CHF should be familiar with these treatments.

Although the drug treatment of HF is supported by good quality randomised controlled trials, patients in clinical trials of HF often differ from those we see in everyday practice[192]. Applying the results of trials to older people may be limited by the age of the populations studied. Patients included in trials are often younger than the predominant HF population and are less likely to have co-morbidities, renal impairment and be on polypharmacy[193].

1.7.1 Aims of treatment for heart failure

The aims of treating HF are broadly similar in all published guidelines and summarised by the NSF for CHD[132] as improving quality of life of patients by:

- Improving symptoms or slowing their deterioration
- Reducing mortality
- Reducing the frequency of cardiac events and admissions to hospital
- Avoiding adverse events from treatment, and
- Improving end-of-life experiences

1.7.2 Prevention of heart failure

1.7.2.1 Improving the outlook for heart failure

As with any chronic condition, prevention of CHF is better than treating the disease. While this is never going to be fully achievable, targeting those patients at highest risk of CHF (such as patients with previous MI or with hypertension) is the most practical way of trying to tackle this problem.

Drugs that tackle the underlying risk factors for CHF (such as hypertension) are one approach to the management of CHF, and drugs that help reduce left ventricular abnormalities including remodelling, (often detected by a reduction in the left ventricular ejection fraction (LVEF)) can improve the quality of life and life expectancy of these patients by slowing the progression to chronic heart failure. As will be discussed in this section of this review, many drugs have the ability to act in this way. For example, beta-blockers, ACE inhibitors and angiotensin receptor blockers (ARBs) all reduce blood pressure but have additional benefits in patients already showing left ventricular damage or symptoms of CHF.

Recommendations for treating patients with CHF and reduced left ventricular function are clear. In the NICE guidelines, ACE inhibitors are recommended in all patients with CHF due to left ventricular systolic dysfunction before the use of beta-blockers[105]. Similarly, the American College of Cardiology and American Heart Association recommend the use of ACE inhibitors in all post-MI patients regardless of LVEF and in all patients with reduced LVEF in the presence or absence of heart failure symptoms[194].

Taken together, these recommendations highlight the central importance of ACE inhibitors in the prevention of CHF, the prevention of CHF progression when early signs are present, and the management of symptomatic CHF. However, recommendations do not always convince physicians and patients (as is evident with the under use of anti-hypertension treatments) because the evidence supporting them can be weak, contradictory or unclear. In the case of ACE inhibitor use in CHF management, this accusation cannot be made as there is now a solid, and growing, base of evidence that supports them as a first-choice drug.

1.7.2.2 ACE inhibitor use can reduce the risk of heart failure

A number of well designed, large-scale studies have demonstrated the benefits of ACE inhibitors in different patient groups.

The benefit of ACE inhibitor use in patients who do have left ventricular dysfunction is also well established. Several years ago, the SOLVD trial showed that ACE inhibitors (enalapril) improved survival of patients with reduced LVEF and CHF[11]. Although no reduction in mortality was observed in patients with reduced LVEF but no CHF, ACE inhibitor use did reduce the risk of heart failure or MI[195]. After 12 years however, patients in both groups who had received an ACE inhibitor had lower death rates than those who had not received an ACE inhibitor[196].

In the PROGRESS trial[197], patients with no evidence of heart failure or left ventricular dysfunction but with previous cerebrovascular disease were given an ACE inhibitor (perindopril) ± indapamide or placebo. After approximately 4 years, patients receiving perindopril ± indapamide not only experienced less recurrent stroke (28% reduction) and non-fatal MI (38% reduction), but they also had a 26% reduction in the risk of heart failure. The reduction in the risk of CHF was evident in patients who had hypertension and in those who did not have hypertension.

Similarly, in patients with coronary heart disease but no left ventricular dysfunction, the ACE inhibitor ramipril was shown to reduce the risk of a range of cardiovascular diseases and specifically reduced the risk of new onset heart failure by 23% and the risk of hospitalization for heart failure by 12%[198]. This reduction was observed after approximately 5 years in patients at high risk of CVD but whose average blood pressure was in the normal range. However, there is also excellent evidence to show that ACE inhibitors (perindopril) reduce CHF in patients at a much lower risk. In the EUROPA trial[199] of patients with stable coronary heart disease, the risk of hospitalization for heart failure was reduced by 39% after approximately 4 years of ACE inhibitor use. ACE inhibitors also contribute to BP reduction and this may assist in the management of heart failure[200].

1.7.2.3 Summary of prevention of heart failure

A large body of evidence and all national treatment guidelines emphasise the benefits of ACE inhibitors in prevention of heart failure and the prevention of progression of the disease. Since these benefits are seen in virtually all patients with heart failure or at risk of heart failure, and given the excellent safety of ACE inhibitors, this is an important message. Early identification of at-risk patients and early treatment with ACE inhibitors and beta-blockers is the optimum course of action. The only note of caution is that all ACE inhibitors may not be the same and careful selection of the correct drug is essential. Post-MI mortality rates have been shown to differ with different ACE inhibitors (ramipril and perindopril were associated with lower mortality than other ACE inhibitors)[201], and future evidence may help point towards even more specific recommendations for the use of ACE inhibitors in CHF. Likewise beta-blockers that have been shown to have benefits in CHF (carvedilol, bisoprolol and metoprolol) should be preferred to those that have no evidence for use for this indication (propranolol, atenolol) or indeed may worsen outcomes (bucindolol)[202].

GPs have a vital role to play in early detection and treatment of the main risk factors for HF which may help to prevent progression to HF. By provision of CHD clinics in primary care GPs can address post MI care, lifestyle modification, the treatment of hypertension, IHD and diabetes, smoking cessation and hyperlipidaemia. Identifying patients at risk of developing HF and initiation of ACE inhibitors, in particular may help prevent development of HF. Campbell and colleagues[203] in a paper describing a randomised controlled trial of CHD clinics in primary care demonstrated that health outcomes can be improved and commented that primary care can develop holistic, structured, systematic primary and secondary care preventative services which diminish the need for more expensive hospital care in the future.

1.7.3 Non-Pharmacological treatments for heart failure

1.7.3.1 Do lifestyle changes improve heart failure?

Whilst pharmacotherapy remains the cornerstone of CHF management, non-pharmacological interventions may be useful in improving symptoms.

Smoking and cardiovascular disease are integrally linked. Although little direct evidence on prognosis in heart failure exists, patients should be encouraged to stop smoking. Alcohol should be avoided in alcoholic cardiomyopathy, but moderate alcohol intake is permissible in LVSD due to other causes. Salt intake should be controlled especially in moderate to severe heart failure[102].

Overweight patients should be encouraged to lose weight. Conversely, cardiac cachexia is a poor prognostic sign and should be addressed with the help of a dietician. All patients with LVSD should be offered pneumococcal and influenza immunisation[102].

1.7.3.2 Exercise training and cardiac rehabilitation

Exercise training, especially as part of a comprehensive cardiac rehabilitation programme, can increase exercise capacity, improve quality of life and muscle de-conditioning in stable heart failure patients, and should be encouraged[204].

A recent meta-analysis (ExTraMATCH) also confirms exercise training reduces mortality and hospital admissions in patients with CHF[205]. There appears to be no evidence that properly supervised medical training programmes for patients with HF may be dangerous. Further research is needed in identifying appropriate groups of patients to target[205].

1.7.4 Avoidance of detrimental drugs and polypharmacy in patients with heart failure

Clinicians should review medication carefully in the assessment of all patients with HF and exercise caution in prescribing certain groups of drugs to these patients. Studies have shown that NSAIDs can cause CHF in susceptible individuals[206] or lead to deterioration of renal function if co-prescribed with ACE inhibitors[207]. Other drugs that should be used cautiously include rate limiting calcium channel blockers (Verapamil, Diltiazem), corticosteroids, flecainaide, nifedipine and tricyclic antidepressants[208].

With the rise of polypharmacy GPs are increasingly faced with complex drug regimes that may make potentially troublesome drug-drug interactions more likely. This rise is due to various factors including increasing elderly populations with chronic conditions; increasing evidence based therapies for conditions such as HF, hypertension and IHD; increase in preventive treatments for IHD, osteoporosis; lower thresholds for treating hypertension, hyperlipidaemia and diabetes; and increased use of over the counter and complementary therapies. This means that GPs will need to review patients and rationalise drug regimens regularly. Polypharmacy may also contribute to under prescribing and under-dosing of appropriate treatments in HF.

1.7.5 Pharmacological therapies for heart failure

There have been several major systematic reviews and guidelines from the UK, Europe, the US and Canada that have been presented as guidelines for the management of HF[8-10,22,101,102,104,141]. They provide clear recommendations for diagnosis and the appropriate use of evidence based pharmacotherapy. The following sections with outline these treatments.

1.7.5.1 Diuretics

Loop diuretics have been used in the management of heart failure for many years and provide rapid symptomatic relief. Despite the extensive clinical use of loop diuretics in heart failure, there are no large clinical trials on the effects on mortality. Faris and colleagues[209] reviewed the current evidence supporting the role of diuretics in HF and identified 18 eligible small randomised controlled studies for meta-analysis (patient number = 928). Compared to active control, diuretics appear to reduce the risk of worsening disease and improve exercise capacity. Furthermore, conventional diuretics reduce the risk of death and worsening HF compared to placebo.

Diuretics should be considered for patients with signs and symptoms of water retention, but renal function will need to be monitored regularly and the dose should be kept to the lowest effective dose.

1.7.5.2 Angiotensin converting enzyme inhibitors

1.7.5.2.1 Introduction

The Angiotensin-converting enzyme (ACE) inhibitors have been a major development in the treatment of heart failure. The benefits of ACE inhibitor therapy for HF have been established by large-scale clinical trials and several systematic reviews have summarised these trials and clinical benefits[210,211].

1.7.5.2.2 Major trials of ACE inhibitors in HF

The Munich mild heart failure trial[212] in 1992 enrolled 170 patients with LVEF ≤ 35% to captopril or placebo and showed a non significant reduction of deaths (4.8% vs. 12.6%; p = 0.10) and a reduction in progression to severe HF (10.8% vs. 26.4%; p = 0.01). This was one of several small trials that paved the way for several larger, major mortality trials in patients with HF, asymptomatic LVSD and following myocardial infarction. (See Table 1.9)

Table 1.9: Major Trials of ACE-Inhibitors in HF

	Patients (n)	Mean Follow-up	NYHA Class	LVEF (%)	Effects on all-cause mortality
HF					
CONSENSUS (enalapril)	253	188 days	IV	N/A	All-cause mortality: At 6 months ↓ 40% (*p*=0.0022)
SOLVD-Treatment (enalapril)	2569	3.4yrs	II-III	≤35	All-cause mortality: ↓ 16% (*p*<0.0036)
SOLVD-Prevention (enalapril)	4228	3.1yrs	N/A	≤35	All-cause mortality: ↓ 8% (*p*=0.30)
Post-MI HF					
SAVE (captopril)	2231	3.5yrs	N/A	≤35	All-cause mortality: ↓19%(*p*=0.019)
AIRE (ramipril)	2006	1.25yrs	I-III	N/A	All-cause mortality: ↓ 27% (*p*<0.002)
TRACE (trandalopril)	1749	2-4.2yrs	N/A	≤35	All-cause mortality: ↓22% (p=0.001)

Based on the results of these trials ACE inhibitors significantly reduce total mortality with consistent effects in a broad range of patients with heart failure[210]. They slow the progression to heart failure in patients with asymptomatic left ventricular dysfunction[20,195,213]; improve symptoms and quality of life[11,20,52,195,209]; enable reduction of the amount and dosage of other anti-failure drugs[52]; reduce cardiac events[11,20,195,214] and reduce hospitalisations[11,20,195]. European, UK and US guidelines[10,22,101,141] reiterate that patients with symptomatic heart failure and evidence of impaired left ventricular function should receive an ACE inhibitor, unless contraindicated[10,22,101,141]. All patients with a recent myocardial infarction and evidence of left ventricular dysfunction, even if asymptomatic should also receive an ACE inhibitor[10,22,101,141].

Initiation and titration to adequate therapeutic dosages, and subsequent monitoring of ACE inhibitor therapy has been described in detail[127,141]. Practical recommendations for use of ACE inhibitors, beta-blockers and spironolactone have been published[215]. ACE inhibitors can be started safely in primary care[216,217] and remain highly cost effective when the costs of diagnosis and starting treatment are included[141,217-219]. Nine ACE inhibitors are now licensed for use in HF and LVSD in the UK (See Table 1.10)

Table 1.10: ACE inhibitors available for use in the UK. Data from British National Formulary (March 1999)[220].

ACE Inhibitor	Usual maintenance dosage	Licensed indications	Cost of 28 days treatment
Captopril	50mgs tds	CHF and Post MI	£8.90
Cilazapril	2.5mgs-5mgs od	CHF	£8.60-£14.95
Enalapril	10-20mgs bd	CHF and prevention HF	£22.06-£26.20
Fosinopril	10-40mgs od	CHF	£12.04-£26.00
Lisinopril	5-20mgs od	CHF and Post MI	£9.58-£13.38
Perindopril	4mgs od	CHF	£12.74

ACE Inhibitor	Usual maintenance dosage	Licensed indications	Cost of 28 days treatment
Quinapril	10-20mgs od	CHF	£9.79-£10.07
Ramipril	5-10mgs od	CHF and Post MI	£9.95-£13.00
Trandolapril	2-4mgs od	Post MI with LVSD	£12.23-£24.46
Moexipril	15-30mgs	Hypertension only	£9.80-£19.60

1.7.5.2.3 Optimising ACE inhibitor dosage

The Atlas Study[221] was important in demonstrating the importance of using adequate doses of ACE inhibitors in patients with CHF. The purpose of the study was to evaluate the differences in morbidity and mortality between high dose (32.5-35mg once daily) and low dose of lisinopril (2.5mg-5mg once daily) over four years. Both dose regimens were similarly well tolerated but there was a significant 12% additional reduction in the combined end point of all cause mortality plus all cause hospitalization in the high dose group. There was also a significant 15% reduction in the combined end point of all cause mortality and hospitalization for heart failure. These studies suggest that we should be aiming for high dose ACE inhibitors as target doses.

1.7.5.2.4 Current state of management in primary and secondary care.

There have been several studies examining the uptake of ACE inhibitor use over a decade in UK practice, some from primary care, others from secondary care or across the primary-secondary care interface. The following Table 1.11 summarises this data.

Whilst there does appear to be a temporal increase in ACE inhibitor use this still remain unacceptably low given the benefits of treatment with these agents. The studies by Hillis and colleagues[144,145], Missouris and colleagues[222] and the first Lip study[142] were conducted in the hospital setting and show low ACE use even in a specialist care environment. Hillis and colleagues[145] completed an audit cycle and showed that introduction of educational programs for staff increased ACE inhibitor uptake from 40% to

55%. They found that patients managed by a cardiac as opposed to a general medical unit were more likely to have an echocardiogram (52/61 vs. 139/204; p<0.01) and subsequently were more likely to be treated with an ACE inhibitor (41/61 vs. 105/204; p<0.05). They also showed that older patients were less likely to have an echocardiogram (mean age 70 years if echocardiography vs. 76 years if not investigated). As cardiologists tend to see younger patients this could be one reason why patients are more likely to be investigated by echocardiography and then get treated with ACE inhibitor.

Table 1.11: ACE inhibitor use in UK practice

Study authors	Year of study	Patient numbers	ACE inhibitor % prescribed
Hillis et al[144]	1992	325	40.0%
Parameshwar et al[143]	1992	117	10.3%
Clarke et al[41]	1994	281	17.0%
Hillis et al[145]	1996	265	55.1%
Mair et al[40]	1996	266	32.7%
Lip et al[69]	1997	188	30.0%
Lip et al[142]	1997	348	58.5%
Missouris et al[222]	1997	249	57.8%
McCallum et al[70]	2001	100	58.3%

The question of titrating ACE inhibitors to target doses used in clinical trials was addressed by a few of these studies. Missouris and colleagues[222] found that only 16.7% of patients discharged from St. George's Hospital, London were on adequate doses; Hillis and colleagues[144,145] found that 76% in 1992 and 55% in 1996 were not on adequate doses on discharge from Aberdeen teaching hospitals and that in the 1996 cohort 71 patients (26.8%) who had no contraindications and may have benefited from ACE inhibitors were not getting them at all; Mair and colleagues[40] found that patients were generally on conservative doses of ACE inhibitors in a Liverpool GP cohort. They found

that perindopril was the only ACE inhibitor to be used at target doses of 4mgs daily possibly because of its easy two step titration as compared to four or five steps for enalapril and captopril. Furthermore it is a once daily product compared to twice daily for enalapril and thrice daily for captopril. This may make it more attractive to clinicians who may feel patient compliance is increased.

Bungard and colleagues[223] conducted a systematic review assessing prescribing patterns (specifically the use of ACE inhibitors in CHF) identifying 37 studies. Studies assessing use among all patients with CHF document 33% to 67% (median 51%) of all patients discharged from hospital and 10% to 36% (median 26%) of community dwelling patients were prescribed ACE inhibitors. Rates of ACE inhibitor use range from 43% to 90% (median 71%) amongst those discharged from hospital having known systolic dysfunction, and from 67% to 95% (median of 86%) for those monitored in specialty clinics. Suggesting that further investigation and specialist care increases ACE inhibitor uptake. Moreover, the dosages used in the 'real world' are substantially lower than those proven efficacious in randomised, controlled trials, with evaluations reporting only a minority of patients achieving target doses. Factors predicting the use and optimal dose administration of ACE inhibitors were identified, and include variables relating to the setting (previous hospitalisation, specialty clinic follow-up), the physician (cardiology specialty versus family practitioner or general internist, board certification), the patient (increased severity of symptoms, male, younger), and the drug (lower frequency of administration). Bungard et al[223] called for multifaceted programs targeted toward the population at large to try and improve optimal uptake of therapies proven effective in the management of patients with CHF. Recent data from nGMS QOF data suggests uptake of ACE inhibitors in CHD patients with HF due to LVD have increased significantly[381].

However, initiation of evidence-based therapy may be limited by worries about treatment side effects, blood monitoring workload, polypharmacy and drug interactions. Although confidence in using ACE inhibitors is increasing a substantial minority of GPs still had concerns, especially in elderly patients. The lack of evidence of benefit in patients with heart failure over the age of 75

years and of any substantial controlled trial in patients with apparent heart failure and well-preserved left ventricular systolic function, a common finding in elderly patients, may be common reasons why ACE inhibitors appear to be underused in heart failure[224]. Philbin suggested that age bias, use of alternative vasodilators (nitrates), prevalence of renal impairment and 'diastolic' HF, and substandard quality of care led to low ACE inhibitor usage in a US community setting[225]. Monitoring of ACE inhibitors raised some concerns both in terms of workload and uncertainty as to how often monitoring tests are needed. A questionnaire study found that although 85% of GPs checked renal function before ACE inhibitor initiation, only 34% did so after start of treatment and 15% never checked renal function[226]. Observation of guidelines for appropriate monitoring of renal function may help minimize this problem.

1.7.5.2.5 Summary of ACE inhibitor therapy for heart failure

Uncertainty about diagnosis coupled with uncertainties about treating elderly patients and concerns about adverse events of ACE inhibitors[152] may explain the low uptake of treatment in primary care[224]. The benefits of ACE inhibitor therapy are being lost either by their lack of use at all[140,227-230] or by the use of sub-optimal doses[40,222,224,231,232]. This also appears to be the case in hospital practice[143,222].

1.7.5.3 Beta-blockers for heart failure

1.7.5.3.1 Introduction

Until recently it was perceived and accepted that beta-blockers were contraindicated in the management of heart failure[233]. However a Swedish study in the early 1970s indicated that adrenergic beta blocking agents could improve heart function in at least some patients with advanced congestive cardiomyopathy[234]. The evidence for the beneficial role of beta-blockers in the management of heart failure is now very substantial and summarised in several systematic reviews[235-239].

1.7.5.3.2 Landmark beta blocker studies

Over the years a strong evidence base has accumulated from randomised control trials and systematic reviews that adding beta blockers to standard

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therapy with diuretics and ACE inhibitors in patients with moderate or severe heart failure reduces mortality and the rate of hospital admissions. Three trials are considered to represent landmark status in establishing the place of beta-blocker therapy for patients with LVSD. (See Table 1.12)

Table 1.12: Landmark beta blocker trials for heart failure

	USCP 1997[240]	CIBIS II 1999[14]	MERIT-HF 1999[18]
Number of patients	1094	2647	3991
Mean Age	58 (18-85)	61 (18-80)	64 (40-80)
Male Sex (%)	77	81	78
NYHA Class (%) II	53	0	41
III	44	83	56
IV	3	17	3
Primary Endpoint	Various	Mortality	Mortality
Total no. of deaths	54	384	362
Mean Follow-up	6.5 months	1.3 years	1 year
Concomitant medications (%)			
Diuretic	95	99	91
ACE inhibitor	95	96	90
Digoxin	91	52	64
Target dose	25/50 mgs	10 mgs	200 mgs
Proportion reaching target dose (%)	80	43	64
Proportion stopping medication (%)			
Placebo	18	15	15.3
B-blocker	11	15	13.9
Total Mortality	RRR 65% ARR 4.6%	RRR 34% ARR 5.5%	RRR 34% ARR 3.8%
Morbidity			
Hospitalisation	RRR 27%	RRR 20%	Not reported
Combined death and hospitalisation for a cardiac cause	RRR 38%	RRR 21%	Not reported

1.7.5.3.2.1A critical appraisal of the CIBIS II trial

The CIBIS-II trial was based on the first CIBIS study[241], which showed a non-significant 20% reduction in mortality but a significant reduction in hospital admissions as a result of worsening heart failure[241]. CIBIS-II was the first of the very large beta-blocker trials in heart failure with sufficient power to address all cause mortality as the primary endpoint. Hence it can be considered to be a seminal landmark study.

2647 patients, aged 18-80 years, with left ventricular ejection fraction $\leq$ 35% and NYHA class III or IV, receiving standard therapy (diuretic plus ACE inhibitor/other vasodilator) were recruited.

There was a statistically significant reduction in all-cause mortality of 34% (hazard ratio 0.66 (CI 0.54-0.81) p < 0.00001) in the bisoprolol group. All-cause hospital admission, all cause cardiovascular death and combined endpoint were all significantly reduced by 20%, 29% and 21% respectively (p values 0.0006, 0.0049 and 0.0004 respectively) in the bisoprolol group. Permanent withdrawals were virtually identical in each group (15% of total patients) (p value 0.98). Exploratory analyses showed statistically significant reductions in sudden death (44%) and hospital admissions for worsening heart failure (36%) with bisoprolol (p values 0.0011 and 0.0001 respectively).

The bottom line result of this study is a substantial reduction in all cause mortality seen in bisoprolol treated patients with chronic heart failure of moderate severity.

There were some possible weaknesses and limitations on application of these results in pragmatic management of heart failure patients. CIBIS II was a European trial with the greatest percentage of patients (30%) coming from Russia and 11.6% from Poland. This raises concerns as to whether these patients were typical of those from Western Europe as a whole. However, it appeared all patients were receiving ACE inhibitors so there were no reasons to believe they were treated differently from elsewhere in Europe.

Patients studied were relatively young (mean age 61) and mostly male. Although the typical age group and sex is under represented in the data, there were some patients up to 80 years of age included in CIBIS I (and MERIT-HF[18]). Whether we are justified in treating very elderly heart failure patients

with beta-blockers is, as yet, not absolutely clear. However, if patients are in other respects similar to those in CIBIS II, there is no apparent reason why they should not also be started on treatment, providing systems are in place to ensure safety[242]. The SENIORS study recently confirmed the safety, tolerability and mortality benefits of nebivolol in elderly patients with systolic and diastolic heart failure[243].

Most patients had moderately severe heart failure (NYHA III) with an ejection fraction of ≤ 35%. It is not always easy to measure ejection fraction in practice and many patients have mild heart failure (ejection fraction > 35 % and < 45%). This trial does not tell us whether the same mortality benefits apply to patients with mild heart failure, although subsequent trials with metoprolol[18] and carvedilol[12] have shown morbidity and mortality benefits in this group. Benefits were seen in patients in NYHA IV; however only stable patients were enrolled so the use of beta-blocker treatment in non-ambulatory class IV patients, especially with recent instability or decompensation, needs to be defined. Beta-blockers (bisoprolol) also appear to be cost effective[244].

1.7.5.3.2.2 The MERIT-HF trial

MERIT-HF[18] enrolled 3,991 patients with symptomatic CHF and LVEF ≤ 40% at entry. Patients were randomly allocated to either receive Metoprolol (12.5 or 25mg once daily titrated to a target dose of 200mg once daily) or placebo in addition to their standard therapy including ACE inhibitors. Following a clear difference in outcomes which emerged before the scheduled completion date, the study was stopped early. The result showed a highly significant 34% reduction mortality between those who received metoprolol versus those who did not. There was a significant 41% reduction in sudden death and a significant 49% reduction in death from worsening heart failure.

1.7.5.3.2.3 The US Carvedilol program (USCP)

The US Carvedilol Program[240] consisted of 4 separate studies each with a separate primary endpoint other than survival but survival in the overall program was monitored by a single safety committee. 1094 patients (mean age 58 [range 18-85]) randomised to carvedilol or placebo were studied over a relatively short mean follow up period of 6.5 months. There was a 65%

reduction in deaths (3.2% vs. 7.8%); 27% reduction in cardiovascular hospitalisation (14.1% vs. 19.6%) and 38% reduction of combined endpoint of death or hospitalisation for any cause (15.8% vs. 24.6%).

Guidelines[104,105] now suggest that all patients with LVSD of any degree be offered a beta-blocker and these three studies have helped inform evidence-based guidance on which policy statements such as the NSF for CHD are based.

1.7.5.3.3 More recent beta blocker studies

As the first three major trials did not address use of beta blockers in severe HF, elderly patients, mild LVSD after myocardial infarction more recent studies have been conducted to address these important areas. The COMET trial[15] was designed to give a head to head comparison between two beta blockers previously shown to reduce HF mortality. (see Table 1.13)

Table 1.13: Major recent Trials of Beta-Blockade in HF

	Patients (n)	Mean Follow-up	NYHA Class	LVEF (%)	Effects on all-cause mortality
HF					
COPERNICUS[245]	2289	10 months	III-IV	<25	All cause mortality ↓35% (p = 0.00013)
SENIORS[246]	2135	3.5yrs	I-IV	<35	All-cause mortality: ↓14% (p=0.039)
COMET[15]	3029	4.9yrs	II-IV	<35	All-cause mortality: ↓ 17%(p=0.0017)
Post-MI HF					
CAPRICORN[12]	1959	1.25yrs	N/A	<40	All-cause mortality: ↓23%(p=0.03)

The CAPRICORN study[12] recently demonstrated that all cause mortality was lowered by carvedilol compared with placebo (12% vs. 15%; hazard ratio 0.77 [95% CI 0.60-0.98], p = 0.03) in patients after an MI complicated by LVSD (LVEF ≤ 40%). These beneficial effects are additional to those of evidence-based treatments for acute MI including ACE inhibitors.

The COPERNICUS trial[245] found that the addition of carvedilol to standard therapy for about ten months improved survival compared with placebo in 2,289 patients (LVEF<25%) who had symptoms at rest or on minimal exertion. All cause mortality 11.2% vs. 16.8%; (RRR 35% [95% CI 19-48%]; p = 0.00013). In the only head to head comparison of beta blockers previously shown to reduce mortality in HF the COMET trial[15] assigned 1511 patients with CHF (NYHA II-IV) to treatment with carvedilol and 1518 patients to metoprolol. Over 58 months mean study period carvedilol all cause mortality was 34% and metoprolol 40% (Hazard ratio 0.83 [95% CI 0.74-0.93], p = 0.0017). Incidence of side effects and drug withdrawals did not differ by much between the two study groups. These results suggest that carvedilol extends survival compared with metoprolol in CHF patients. Practical applicability of these results are limited in the UK by the fact that metoprolol is not licensed for use in CHF.

The only trial with a beta blocker not to demonstrate benefit was BEST[202]. This showed no significant difference in all-cause mortality between bucindolol (30%) and placebo (33%) after two years in 2,708 patients with moderate to severe HF (LVEF ≤ 35%)

It is likely that the differences in the two above studies relate to differences in the characteristics of the beta blockers rather than differences in the populations studied. It has been suggested that carvedilol has additional properties including alpha blockade and antioxidant activity, which may be important in severe HF in particular[245].

1.7.5.3.4 Systematic review of effect of beta blockers on HF mortality

Doughty RN et al[239] conducted a systematic overview of 24 randomised trials to assess the effect of beta blocker therapy on mortality in patients with heart failure. This involved 3141 patients with stable heart failure. They found a 31% reduction in the odds of death among patients treated with a beta blocker (p = 0.002).

1.7.5.3.5 Systematic review of effects of beta blockers on left ventricular function

Lechat P et al[239] undertook a meta-analysis of 18 published double blind, placebo controlled trials of beta blockers in heart failure with a combined data base of 3023 patients. This showed evidence of a favourable effect of beta blockers on left ventricular ejection fraction, and a combined risk of death and hospitalization for heart failure. Beta blockers increased the ejection fraction by 29% and reduced the combined risk of death or hospitalization for heart failure by 37% (p < 0.001).

1.7.5.3.6 Traditional contraindications and cautions to the use of beta blockers – are they justified?

Recently some of the traditional contraindications and cautions to beta blockers have been questioned; in particular opinion has focused on chronic obstructive pulmonary disease (COPD), peripheral arterial disease, diabetes mellitus and the elderly. It is important to address these areas in order not to deprive patients with these co-morbid conditions and HF the opportunity to benefit from beta blocker therapy.

1.7.5.3.6.1 Beta blockers in chronic obstructive pulmonary disease

A recent Cochrane review assessed the effect of cardio selective beta blockers on lung function in patients with COPD. Eleven randomized blinded controlled trials of single dose treatment, and eight treatments for a longer duration ranging from 2 days to 12 weeks were reviewed. Cardio selective beta blockers given as a single dose or for a longer duration produced no statistically significant change in FEV1 or respiratory symptoms compared to placebo. They also did not significantly affect the FEV1 treatment response to beta$_2$ agonists. Furthermore, there were no COPD exacerbations or hospitalizations during the periods of study in either group[247,248].

This meta-analysis indicated that cardio selective beta blockers are safe in patients who have COPD with or without a reversible component. The Cochrane review concluded that cardio selective beta blockers given to patients with COPD do not produce a significant short term reduction, however these trials were small and of short duration and not applicable to patients with severe COPD[247,248].

Salpeter et al[249] conducted a meta-analysis that also demonstrated that cardio selective beta blockade given in mild to moderate COPD did not produce clinically significant adverse respiratory effects in the short term and that they should not be withheld from such patients. The reviewer stated that long term safety, especially during an acute exacerbation still needed to be established. These findings were in keeping with Cochrane review advice

1.7.5.3.6.2 Beta blockers in peripheral arterial disease

It has been suggested that beta blockers are contraindicated in the presence of peripheral arterial disease. A meta-analysis conducted to determine whether or not beta blockers exacerbate intermittent claudication found no significant impairment of walking capacity compared with placebo[250]. Only one of the studies including in the meta-analysis reported that certain beta blockers were associated with worsening intermittent claudication. These were not the agents currently licensed for the use of heart failure, namely bisoprolol and carvedilol.

The results of the meta-analysis strongly suggested that beta blockers do not adversely affect the symptoms of intermittent claudication in patients with mild to moderate peripheral arterial disease.

Therefore in the absence of other contraindications beta blockers can probably be used safely in such patients with heart failure[250].

1.7.5.3.6.3 Beta blockers in diabetes

It is known that non-selective beta blockers inhibit insulin secretion and can impair glucose tolerance as well decrease catecholamine-mediated response to hypoglycaemia with decreased awareness and delayed recovery of hypoglycaemic episodes. These effects are less pronounced with newer cardio-selective beta blockers.

Shekelle PG et al[251] undertook a meta-analysis of published and individual patient data from 12 large randomized clinical trials of ACE inhibitors and beta blockers and concluded that both groups of drugs provided life-saving benefits in most of the sub-populations assessed in patients with or without diabetes.

Jenas M et al[252] conducted a study looking at the usefulness of beta blocker therapy in patients with non-insulin dependent diabetes mellitus and coronary artery disease. 2,723 non-insulin-dependent diabetic patients were included and three-year mortality was estimated in patients receiving (n = 911) and not receiving beta blockers (n = 1,812). Total mortality during the three-year follow-up was 7.8% in those receiving beta blockers compared with 14% in those who were not. This translates to a 44% relative risk reduction and a further 42% reduction in cardiac mortality was also noted. Multivariate analysis in this study identified beta blocker therapy as a significant independent contributor to improved survival. The evidence would suggest that the benefits of beta blockers in diabetic patients with or without heart failure outweigh the possibility of slight impairment of glucose tolerance.

1.7.5.3.6.4 Beta blockers in older people

Epidemiological data shows that older patients constitute the majority of those with chronic heart failure[30]. However it is apparent that beta blockers are underused in this age group, partially due to the perception of potential adverse effects and drug interactions. Furthermore HF patients in the community tend to be older and with more concomitant disease than those in the majority of clinical trials of beta blockers and indeed most other drugs that are of benefit in LVSD.

In the CIBIS-II trial[14] the age limit was 80 and the mean age 61. In the MERIT-HF trial[18] age limit was 90 and mean age 64. Subsequent analysis from both these studies shows mortality reductions in patients 70 to 80 similar to those in younger patients[253].

Sin-Don D et al[254] observed in a retrospective study of 11,942 older patients over the years of 65 with heart failure (1,162 taking beta-blockers), that beta blocker use was associated with substantial reductions in all-cause mortality, heart failure mortality and hospitalizations due to heart failure.

The recent SENIORS study[246] has shown beta-blockade can be safely initiated, was well tolerated and improved outcomes in over 2000 patients with a clinical diagnosis of chronic heart failure and a mean age of 76 years.

Nebivolol treated patients showed a significantly reduced all-cause mortality or rate of hospitalisation for cardiovascular events (SENIORS).

Whitham and Colleagues[255] evaluated how well older heart failure patients tolerate beta-blockers in everyday clinical practice. In a retrospective case note analysis, 226 patients with a clinical diagnosis of heart failure and evidence of LVSD were studied in the specialist heart failure clinic of a large teaching hospital. They observed that a high proportion of older heart failure patients tolerated beta-blockers, with 60% of those aged 75 or over having been tried on a beta-blocker versus 69% of those aged less than 75, and of those tried, 80% of those aged 75 or over were still taking a beta-blocker at the time of the survey, versus 86% of those aged less than 75. Significant factors identified for failing a trial of beta-blocker therapy were worse NYHA status (3-4) and worse left ventricular function, but importantly not age.

Baxter and colleagues[256] demonstrated in a small prospective observational cohort in Sunderland that 69% of patients with a mean age of 78 (range 70-89 years) tolerated bisoprolol. Mean tolerated dose was 7.6mg (range 1.25mgs to 10mgs), which is similar to that seen in CIBIS II. Despite concerns that beta blockers may worsen HF symptoms in older patients there was no evidence of a negative impact on symptoms or exercise capacity in patients who tolerated bisoprolol.

Whilst age should not be a contraindication to beta-blocker use in heart failure, older patients are more likely to suffer from multiple pathology and concomitant disease. Hence a wise balanced approach needs to be made between the modest survival benefit and the adverse effects on quality of life in elderly patients, when deciding whether or not to use beta-blockers[257].

1.7.5.3.7 Outpatient initiation of beta-blockers for heart failure

There is now overwhelming evidence that beta blockers are beneficial in all grades of heart failure. Large randomised controlled trials confirm that they confer morbidity and mortality benefits, improve quality of life and reduce hospitalisations[236,238,239]. Despite this, it is likely that clinicians including GPs will initially be reticent in initiation of beta-blockers for heart failure patients. The cost of hospitalisation can be decreased by 10% by commencing patients

with heart failure on beta-blockers; however use in clinical practice is still low especially in the UK[13]. It is estimated that only 22% of suitable patients are on beta-blockers in the UK. It is probable that this is partly due to the difficulty of implementing therapy on an outpatient basis.

Currently two beta-blockers (carvedilol and bisoprolol)[220] have a UK licence for the use in heart failure. Both agents should be initiated at a low dose and slowly titrated up to achieve doses achieved in the major clinical trials.

Lee and colleagues[258] looked for a safe regime for outpatient initiation of beta-blockers in heart failure patients. They studied 70 patients with NYHA III-IV heart failure. They were able to establish 88% of these on a beta-blocker with only 12% discontinuing due to side effects. None of these needed hospitalisation. Only 2 patients (3%) reported side effects during the two-hour monitoring period and they experienced mild wheezing that did not need any medical intervention. This study suggests that with simple precautions most patients with heart failure can be safely established on a beta-blocker in an outpatient setting. This can be enhanced by using specialist nurses[260]. Hypotension, a side effect, may be less prevalent than previously believed[243]. These studies would suggest that with simple precautions, most patients with HF can be safely established on a beta-blocker in a community setting.

Reorganisation of heart failure services may be necessary to ensure that suitable patients are considered for beta blockers. Heart failure clinics and liaison nurses may have a useful role in this area[259]. It seems that establishment of programmes across the UK could lead to significant savings on hospitalisation costs for the NHS and this patient group. Further research is needed into initiation and titration of beta-blockers in chronic heart failure within a primary care setting.

1.7.5.3.8 Ongoing Research with beta blockers for heart failure

The introduction of ACE inhibitors and subsequently beta blockers was a major breakthrough in the pharmacological treatment of chronic heart failure. ACE inhibitors and beta blockers significantly reduce mortality and morbidity, favourably alter the cause of this disease, and therefore constitute a fundamental part of CHF therapy.

Despite this significant progress CHF remains a major health problem, and there is an undisputable need to optimize currently established therapy. This issue becomes particularly important with beta-blockers. Despite clear recommendations that beta-blockers should be considered in all stable patients with CHF, they are still underused in every day clinical practice.

There are arguments suggesting it is superior to introduce a beta-blocker prior to an ACE inhibitor in patients with CHF, including early benefits (within 2 weeks) of reduction of incidence of sudden death in some beta blocker mortality studies (CIBIS III – rationale)[260]. The question which drug should be initiated first in CHF is being addressed in CIBIS III[260].

1.7.5.4 Aldosterone receptor antagonists for heart failure

Spironolactone is a competitive aldosterone antagonist. The RALES Study[19] demonstrated that Spironolactone improved all cause mortality (27% RR, p<0.0001), reduced hospitalisations for all cardiac causes (30% RR) and for worsening heart failure (35% RR). Patients with moderate to severe LVSD should be considered for treatment with low dose spironolactone (25-50mgs) if they remain symptomatic on an ACE inhibitor and a beta blocker.

The use of an aldosterone antagonist with diuretics and ACE inhibitors raises concerns about renal impairment and hyperkalaemia. A population-based time-series analysis by Juurlink and colleagues[261] demonstrated an abrupt rise in the rate of prescriptions for spironolactone and in hyperkalaemia-associated morbidity and mortality in Canada following the publication of the RALES study.

In another study by Bozkurt and colleagues[262] of 377 patients started on spironolactone for heart failure following the publication of RALES, 24% developed hyperkalaemia (>6 mmol/L) compared with 2% in RALES. These types of studies are important if we are to see evidence based medicine translated into practice. Large studies often exclude certain groups of patients and certain co-morbidities that are encountered when prescribing to elderly patients in the community. For example in the Bozkurt et al study[262], 40% of patients were taking potassium supplements, 46% were diabetic, 31% had renal insufficiency – all exclusion factors for patients enrolled in RALES[19].

Berry and McMurray described four cases of serious and, occasionally serious hyperkalaemia in patients with CHF (NYHA III) where spironolactone was added to conventional therapy.

Close monitoring and judicious use of spironolactone is necessary when prescribing in real life practice. Berry and McMurray called for mandatory, close monitoring of blood chemistry after starting spironolactone, and advised that spironolactone should be stopped immediately if diarrhoea develops[263].

Eplerenone is a newer aldosterone antagonist with potentially fewer side effects. In the recent EPHESUS study[264] addition of 25-50mgs of eplerenone to optimal therapy reduced morbidity and mortality among patients with acute MI complicated by LVSD and HF. The rate of serious hyperkalaemia was 5.5% in the eplerenone group and 3.9% in the placebo group (p = 0.002). Incidence of gynaecomastia and impotence in the eplerenone group was no greater than in the placebo group. As these are common problems with spironolactone eplerenone should be a suitable alternative in management of HF due to LVSD.

1.7.5.5 Angiotensin II receptor blockers (ARB) for heart failure

ACE inhibitors only partially block the renin-angiotensin system. ARBs act at the angiotensin II receptor site itself and may more completely block its pressor actions. Furthermore, unlike ACE inhibitors they do not inhibit bradykinin breakdown, and are less likely to cause a troublesome cough.

Theoretically ARBs may be combined with an ACE inhibitor therefore offering greater efficacy or be used as an alternative to ACE inhibitors. Many studies have addressed these hypotheses[265].

One meta-analysis demonstrated that the combination did not reduce mortality compared to ACE inhibitor monotherapy. However, a significant reduction in hospitalisations was seen[265].

Neither ELITE II (with losartan)[17] nor Val-HeFT (with valsartan)[21] demonstrated mortality benefits with an ARB over an ACE inhibitor.

ELITE II[17] hypothesised that losartan monotherapy would be superior to captopril in improving survival. 3,152 patients with NYHA II-IV (LVEF ≤ 40%)

were randomised to losartan 50mgs or captopril 50mgs three times a day. No difference in all cause mortality was demonstrated between losartan (17.7%) and captopril (15.9%) (Hazard ratio 1.13 [95% CI 0.95-1.35; p = 0.16]) over a median follow up of 1.5 years. It is important to note that these results do not necessarily mean that losartan is as effective as captopril at improving survival as the study was designed to demonstrate superiority, and not to show equivalence.

The Valsartan Heart Failure Trial (Val-HeFt)[21] compared valsartan with placebo when added to standard therapy including ACE inhibitors and beta blockers in 5,010 patients with mild to moderate heart failure. Patients treated with valsartan and standard therapy were significantly less likely to reach the combined end point of all cause mortality and morbidity (P=0.009). This benefit was mainly due to a reduction in hospitalisation due to heart failure. There was no difference in the other primary end point of all cause mortality[21].

The recent CHARM (Candesatran in HF – Assessment of Reduction in Mortality and Morbidity) studies have addressed 3 groups of patients, including those with preserved systolic function[13].CHARM Alternative (n=2028) enrolled patients intolerant of ACE inhibitors and candesatran significantly reduced the risk of cardiovascular death or hospitalisation for CHF, with an overall risk reduction of 23% (p=0.0004) compared to placebo[13].

In CHARM Added (n=2548) with patients prescribed optimal conventional therapy for CHF including an ACE inhibitor addition of candesatran significantly reduced the risk of cardiovascular death or hospitalisation by 15% (p=0.011). This result is in contrast to Val-HeFT, which had suggested a triple combination of ACE inhibitor, ARB and beta blocker may be associated with adverse outcomes[13].

CHARM Preserved (n=3025) in patients with HF with preserved LV systolic function candesatran did not demonstrate a statistically significant reduction in cardiovascular death or hospitalisation for CHF but did significantly reduce the risk of development of new diabetes, with an overall risk reduction of 40% (p=0.005)[13].

Current advice should be that ARBs might be considered as a replacement for patients with LVSD intolerant of ACE inhibitors. In light of the CHARM Added results a combination of ACE inhibitor and Candesatran may be considered in certain groups of patients still symptomatic on optimal conventional therapies[13]. No other studies have assessed the combination of ACE inhibitor and ARB to date.

1.7.5.6 Digoxin and heart failure

1.7.5.6.1 A historical perspective

Digoxin is a cardiac glycoside derived from *Digitalis purpurea* (Fuchsius 1542) or *lanata*. In 1785 William Withering published '*An Account of the Foxglove and Some of its Medical Uses – With Practical Remarks on Dropsy and Other Diseases*'. James Mackenzie (1835-1925) found that *Digitalis* was effective in slowing the rate of the heart irrespective of correction of heart failure but it was Arthur Cluny (1866-1926) who developed the pharmacology that led to the isolation of digoxin[266].

1.7.5.6.2 Early studies of digoxin in heart failure

Withdrawal studies showed that patients' HF and exercise tolerance deteriorated after withdrawal of digoxin in about a quarter of cases[267,268]. However, the value of digoxin in patients with HF due to LVSD or preserved systolic function was not established from prospective randomised controlled trials.

1.7.5.6.3 The Digitalis Investigators Group (DIG) study – a critical review

This prospective, randomised, placebo controlled trial[16] was designed to test the hypothesis that digoxin would reduce mortality and hospitalisation for patients with heart failure and normal sinus rhythm.

The main study[16] enrolled 6800 patients with heart failure, in sinus rhythm and LVEF $\leq$ 0.45. An ancillary study included 988 patients with heart failure and preserved systolic function (LVEF > 0.45) and in sinus rhythm. The average age was 63 in both groups. The primary endpoint was all cause mortality with secondary endpoints of cardiovascular mortality, death due to worsening heart failure, hospitalisation due to worsening heart failure and other causes.

Digoxin did not reduce all cause or cardiovascular mortality (risk ratios 0.99 (CI 0.91-1.07) and 1.01 (CI 0.93-1.10) respectively, with p values 0.80 and 0.78 respectively), but it reduced the rate of hospitalization for worsening heart failure (0.88 (CI 0.77-1.01) p value 0.06). Pre-specified subgroup analysis showed that those with lower ejection fractions, enlarged hearts and those in NYHA Class III or IV derived more benefit from digoxin[16].

These findings define more precisely the role of digoxin in the management of chronic heart failure.

However there are possible reasons why results may not be applicable in my local setting: the mean age of patients was 63, which is considerably lower than HF population (mean age 76), and it was a US study with high previous digoxin use (44%). Furthermore there were possible methodological weaknesses in that no attempt was made to optimise treatment according to plasma level – many patients may therefore be under treated. Could adjusting the dose according to plasma level have provided additional clinical benefits? This question is likely to remain unanswered. There was also a statistically significantly higher number of patients in the placebo group who were put on open label digoxin and this could have been a possible confounding factor in analysis.

1.7.5.6.4 How should we use and monitor digoxin in heart failure?

NICE guidance[105] recommends that digoxin is used for patients in sinus rhythm with worsening or severe HF due to LVSD despite ACE Inhibitor, beta-blocker and diuretic therapy, and in patients with atrial fibrillation and any degree of HF.

Routine monitoring of serum digoxin concentrations is not recommended. A digoxin concentration measured within 8-12 hours of the last dose may be useful to confirm a clinical impression of toxicity or non-compliance

The serum digoxin concentration should be interpreted in the clinical context as toxicity may occur even when the concentration is within the 'therapeutic range'

1.7.5.7 Summary of main treatments for HF due to LVSD

The following table summarises the use of therapies shown to be of benefit in HF due to LVSD. All patients should be considered for ACE inhibitors and beta blockers unless compelling contraindications exist. Diuretics, digoxin and spironolactone should be considered in selected patients. All GPs should be aware of these indications:

Table 1.14 Summary of Treatment of HF due to LVSD

NYHA I	NYHA II	NYHA III	NYHA IV
	Diuretics if symptomatic		
ACE inhibitors (AIIA or nitrate/hydralazine if ACEi contraindicated)			
Beta-blockers once stable			
	Digoxin if in Atrial Fibrillation or still symptoms on above treatments		
		Spironolactone if symptoms on above treatments	

1.7.5.8 Antithrombotic agents and heart failure

Patients with HF are particularly prone to thrombotic complications. AF, ventricular and atrial dilation, and venous stasis all contribute to the risk. Where there is a clear indication, such as AF, warfarin should be given.

Many patients with CAD and CHF are on aspirin. Systematic review evidence supports the fact that aspirin reduces the risk of vascular events in patients with atherosclerotic arterial disease[269]. However, there have been suggestions that aspirin may reduce the benefits of ACE inhibition in patients with CHF[270], although other systematic reviews refute this claim[271]. Specific randomised controlled trial (RCT) evidence for the benefit of aspirin in CHF patients is lacking. Studies are underway to address this[270]. Until such evidence is available, NICE guidance[105] suggests the use of aspirin (75-

150mgs daily) for patients with the combination of CHF and atherosclerotic arterial disease (including CAD).

1.7.5.9 Lipid lowering agents-should all patients with heart failure be on a statin?

Many patients with coronary artery disease (CAD) and LVSD receive a statin. RCTs have shown that statins reduce the frequency of ischaemic events and prolong life expectancy in patients with CAD, as well as reducing the risk of development of heart failure[272]. However, most statin trials have excluded patients with CHF. Further evidence from large-scale statin trials are needed in CHF[273].

The CORONA study[274] (a double-blind, placebo controlled RCT) with rosuvastatin in subjects with symptomatic LVSD is due to report in 2007. 4950 patients are being enrolled, with a planned primary endpoint of cardiovascular death or non-fatal MI or non-fatal stroke. Until such evidence is available NICE guidance suggests patients with a combination of CHF and CAD should receive a statin in line with current indications for secondary prevention.

1.7.5.10 Anti-arrhythmic agents and heart failure

About half of patients with HF die suddenly. This could be due to arrhythmia, but evidence increasingly suggests that coronary occlusion plays an important role. Both atrial and ventricular arrhythmias occur, especially atrial fibrillation and flutter, and ventricular tachycardia. Palpitations should always be investigated further in HF patients.

The CAST trial[275] demonstrated increased mortality in patients after MI with the once commonly used class 1 and 3 antiarrhythmic drugs (encainide and flecainide) The safest drug in HF is amiodarone as it is the least negatively inotropic of the available drugs. Studies[276] and meta-analyses[277] have suggested it could give a survival advantage to some groups of patients.

However, its use, especially in primary care is limited by the need for specialist initiation, regular monitoring and a poor side effect profile.

Thyroid and liver function tests should be done regularly to check for side-effects of hypothyroidism, hyperthyroidism or hepatitis. Worsening

breathlessness should always raise the suspicion of pulmonary fibrosis, which is rare but can be rapidly fatal. Other amiodarone side-effects include skin photosensitivity or grey-blue discoloration, corneal deposits or optic atrophy, myopathy, neuropathy. Drug interactions can be a problem; in particular it can increase the activity of warfarin or digoxin.

1.7.5.11 Calcium channel blockers and heart failure

There is no place for the routine use of calcium channel blockers in the treatment of HF[104]. In particular, the rate-limiting drugs verapamil and diltiazem are potentially deleterious. The short-acting dihydropyridines, such as nifedipine, should be avoided.

However, amlodipine is helpful in patients who also have IHD and angina. It is safe in HF[278], and could even be of benefit in dilated cardiomyopathy[279]. In the PRAISE study amlodipine (n = 571) did not increase cardiovascular morbidity or mortality in patients with severe heart failure compared to placebo (n = 582)[278].

1.7.6 Monitoring of patients with heart failure

All patients with CHF due to LVSD need regular monitoring, as many of the agents used in its treatment can lead to electrolyte imbalance, renal dysfunction and cardiac rhythm abnormalities. The frequency of monitoring depends on the stage of disease, severity and drug therapy. Monitoring intervals should be short if clinical status or treatment changes have been made (e.g. ACE inhibitor dose increased) and is suggested six monthly for stable patients with LVSD[105]. Minimum requirements are for assessment of fluid status, cardiac rhythm and BP, laboratory assessment of renal function and ideally assessment of functional capacity. Patients should be asked about potential drug side effects and the development of anxiety or depression, a common occurrence in CHF. Appropriate education of patients and carers about self-monitoring is desirable.

There is no evidence for the use of serial cardiac imaging or natriuretic peptides in the monitoring of patients with LVSD, although trials on the latter have commenced and should report within 2-3 years. Specialist HF nurses are playing an increasingly important role in monitoring and education of

patients, and nurse led interventions have been shown to reduce hospital admissions and re-admissions[189].

1.7.7 Device therapies for heart failure

Cardiac resynchronisation therapy (CRT) re-times the failing heart and increases cardiac output and systolic blood pressure, reduces mitral regurgitation and improves left ventricular function without increasing myocardial oxygen demand[280]. CRT should only be considered in patients with documented cardiac dyssynchrony who are symptomatic despite maximal tolerated pharmacotherapy.

Patients with LVSD who have a prolonged QRS duration (>120ms) may benefit from cardiac resynchronisation therapy (CRT) with biventricular pacing. Biventricular pacing improves symptoms and exercise capacity and seems to reduce symptoms of mitral regurgitation. Patients may also be considered for an implantable defibrillator if deemed to be at risk of potentially fatal arrhythmias. The Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) trial was stopped prematurely because of a highly significant 20% reduction in the primary endpoint of all cause mortality or all cause hospitalisation in the CRT arm[281]. Further work is needed to establish the practical application of this new technology for the benefit of patients with LVSD and cardiac dyssynchrony.

1.7.8 The treatment of heart failure with preserved left ventricular ejection fraction or diastolic dysfunction

There is little evidence from clinical trials or observational studies on how to treat PLVEF or LVDD. This means that recommendations offered by various guidelines are speculative and often based on the understanding of the cardiac haemodynamics of PLVEF and LVDD and the knowledge of how various drugs may alter those haemodynamic abnormalities seen in these conditions.

There is little evidence that patients with PLVEF or LVDD benefit from any particular drug therapy[104]. The DIG ancillary study[16] of 988 patients with HF and PLVEF showed some benefit in a composite endpoint of death or

hospitalisations for HF, but no significant reduction in all cause or cardiovascular mortality. The recent CHARM Preserved trial[13] demonstrated that inhibition of the renin-angiotensin system by high dose candesatran (32mgs) reduced cardiovascular mortality or hospitalisations for HF slightly and HF hospitalisations significantly but did not alter mortality. Neither of these studies conducted any objective assessment of diastolic dysfunction, therefore results cannot be extrapolated to those with LVDD.

The mainstay of management of PLVEF and LVDD is aggressive management of risk factors including adequate BP control and treatment of AF. Certain drugs may have theoretical and practical benefits but their use is not based on any clear trial evidence:

- Diuretics may be used to treat fluid overload but over diuresis may be deleterious by reducing preload and therefore cardiac output[104].
- ACE inhibitors lower BP and aid regression of cardiac hypertrophy, as well as improving diastolic relaxation and cardiac distensibility directly[104].
- Beta blockers may help increase diastolic filling time by lowering of heart rate[104].
- Candesatran may reduce hospitalisations from HF[13].
- Verapamil may work in the way beta blockers do and has been shown to improve functional capacity in patients with hypertrophic cardiomyopathy and diastolic dysfunction[282,283]

PLVEF and LVDD treatment can be difficult and unsatisfactory. It should be managed by a specialist in HF and GPs should be encouraged to refer such patients if encountering diagnostic or therapeutic difficulties.

1.8 Guidelines for diagnosis and management of heart failure

1.8.1 Introduction

Evidence-based guidelines for the diagnosis and management of heart failure [8,10,22,101-104,141] all recommend that echocardiography is the "gold standard" investigation for accurate objective determination of cardiac function. Yet,

GPs are faced by a lack of uniform availability of services[146]; difficulty in interpretation of technical results; and disagreements about whether an open-access echocardiography service should be provided[139,140,157,159,161]. Other options suggested are a hospital based and controlled service[162,164,174] or open-access services for echocardiography with specialist follow-up when deemed appropriate by the GP[166].

1.8.2 The National Service Framework for Coronary Heart Disease - what are the implications for primary and secondary care?

The NHS is currently undergoing major reorganization, in part in response to the increasing needs of an ageing population. Among the elderly the incidence of heart failure is rising to epidemic proportions, and the delivery of consistent, coordinated and effective care for sufferers of chronic heart failure (CHF) has become a major challenge. The UK has one of the highest rates of coronary heart disease (CHD) in Europe and heart failure is one of the major consequences of CHD, imposing an enormous clinical and financial burden on UK health services[132,193,284,285].

The National Service Framework (NSF) for CHD[132] acknowledges that death rates from cardiovascular disease remain unacceptably higher in the United Kingdom than in the majority of European countries. A reduction in this mortality is a national priority. The NSF, which aims to "transform the prevention, diagnosis and treatment of coronary heart disease", includes a section (chapter 6) dealing with provision of services for heart failure.

The NSF reinforces the need for accurate identification of CHF patients, and states that patients should be offered appropriate investigation to confirm or refute the diagnosis of CHF. The NSF is clearer in its treatment recommendations. It specifies that all appropriate patients with heart failure should receive first line treatment with an ACE inhibitor, as these agents have been shown to prolong life, delay disease progression and improve symptoms.

The NSF states that both primary care practices and hospitals should undertake an annual audit of CHF care, and that hospital CHF care must be consistent where more than one team is involved. The use of hospital-wide

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protocols is therefore recommended. Clear communication between the secondary and primary care sectors is also vital.

The recommendations contained in the NSF may go some way towards improving some of the current inequalities in CHF care provision across the country. The document does not, however, address key organizational issues at the heart of CHF care in the future, and at best simply consolidates the provision of existing services.

As there is currently no new funding to support implementation of any of the proposals for CHF care in the NSF, development of improved access to diagnostic services and specialist heart failure clinics is likely to remain ad hoc at best, despite the acknowledged attendant mortality and morbidity of heart failure, and despite evidence from other clinical areas such as stroke and cancer that patient care is significantly improved by the provision of specialist services.

1.8.3 National Institute for Clinical Excellence guidelines for CHF

In July 2003 the *National Institute for Clinical Excellence* (NICE)[105] published guidelines for CHF that builds on the NSF for CHD[132]. The NICE guidelines[105] emphasise the need for coordinated application of treatments in a structured manner that includes confirming the diagnosis, coordinating care and involving the individual patient. It is a comprehensive evidence – based document that has 92 recommendations in total with some key recommendations outlined (see Box 1.1 below).

Both the NSF for CHD[132] and NICE guidelines[105] recognise that current care is less than optimal, and in particular acknowledge the need for palliative care for patients with end-stage disease. Neither guideline addresses the management of patients who suffer heart failure in the immediate aftermath of an MI. This group in particular is at risk of further cardiac deterioration due to cardiac damage and remodelling with a mortality of up to 20% at six months. Whilst hospital based services increasingly need to focus on this particular group of patients, multidisciplinary care in general practice will also be needed to deliver ongoing care for those with and without subsequent HF.

Leslie and Colleagues[286] sent a questionnaire to 717 GPs with a 53% response rate. They showed that, although most GPs were aware of the existence of a national guideline, many had not read it. There was little or no difference in the knowledge level for various evidence-based treatments between GPs who had or had not read the guideline, suggesting that reading guidelines may not be a key factor in determining knowledge.

Box 1.1 Key recommendations of NICE CHF guidelines

Diagnosis

- Diagnosis of HF should be reviewed, and confirmed
- Echocardiography should be performed

Treatment

- All patients with LVSD should be considered for an ACE inhibitor
- All patients with LVSD should be considered for beta-blockers, after diuretic and ACE inhibitor therapy even if asymptomatic

Monitoring

- All patients require regular monitoring
- A clinical assessment of functional capacity, fluid status, cardiac rhythm and cognitive and nutritional status
- A review of medication, and investigation including serum urea, electrolytes and creatinine

Discharge from hospital

- Should occur 'only when condition is stable and the management plan is optimised'
- The primary care team, patient and carer must be aware of the management plan

Supporting patients and carers

- Management of heart failure should be seen as a shared responsibility between the patient and healthcare professional

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1.8.4 Implementation strategies in heart failure

Sackett stated that 'evidence is only worthwhile if it translates into clinical benefit'[287]. As has been discussed already many studies suggest that despite the availability of numerous clinical guidelines for the management of HF, care remains suboptimal. The ACC/AHA guidelines[10] suggest that the literature on implementing practice guidelines for patients with HF can be divided into 2 areas: isolated provider interventions and disease management systems. Furthermore the role of general physicians, primary care physicians and cardiologists in the management and implementation of guidelines has attracted considerable study.

Freeman and Sweeney explored the reasons behind why GPs may not implement evidence[288]. They used a qualitative methodology using Balint-style groups with 19 GPs. The particular feature of these groups that distinguished them from standard focus groups was that each meeting focused around the case notes of a particular patient, the doctor-patient relationship, and the feelings that were generated. Six main themes were identified that affected the implementation process: the personal and professional experiences of the GPs; the patient-doctor relationship; a perceived tension between primary and secondary care; GPs' feelings about their patients and the evidence; and logistical problems. One doctor commented on the use of ACE inhibitors, "The problem is starting him on the ACE because he is very anxious about medication change, and every time you change the medication it entails another four or five visits to go and see him and to try and reassure him that he is on the right medication." These themes show the complexity, fluidity and adaptive nature of implementing evidence in everyday clinical practice[288]. Further qualitative work in the context of HF diagnosis and management is needed to identify barriers and potential strategies for implementing evidence based treatments.

1.8.4.1 Isolated provider interventions and academic detailing

Review of the literature suggests that changing physician behaviour is needed to improve care of patients with HF. However a controlled trial has shown that

simple dissemination of a HF guideline followed by written and verbal reminders about recommended actions was unable to change the treatment of HF in the intensive care unit[289]. More recently posting treatment recommendations to primary care physicians did not improve the quality of care for patients recently discharged with MI or HF[290]. Multifactorial interventions that simultaneously attack different barriers to change tend to be more successful than isolated efforts. For example, academic detailing, which involves intensive educational outreach visits that incorporate communication and behavioural change techniques, has been effective and is commonly used by pharmaceutical companies[291].

Academic detailing is one of the few educational interventions that have consistently demonstrated improved physician performance[292]. Several review articles looking at continuing medical education (CME) have concluded that community-based strategies such as academic detailing (and to a lesser extent, opinion leaders), practice-based methods such as reminders, and patient-mediated strategies appeared to be the most effective activities in changing physician performance and/or health care outcomes[293-295]. Methods that are practice and community based rather than didactic also appear to be effective strategies for implementing clinical practice guidelines[296]. Local agents, empowered by resources, are best equipped for co-ordinating implementation activities[297]. Academic detailing and other practice-based education may well form the cornerstone of continuing professional development in general practice[298].

Academic detailing, audit and feedback, as well as individualised teaching in response to real events in practice have been shown to improve physician performance[299,300] and appropriateness of prescribing practices[301,302]. An academic detailing approach has been shown to improve GPs' abilities in the diagnosis of depression[303] and the recognition and treatment of asthma[304]. Several randomised-controlled trials have shown that educational programmes utilising academic detailing can modify prescribing practices within the community setting in a diverse range of therapeutic areas[305-309]. These studies have been successful in reducing the excessive use of drugs[306,309,310], increasing the evidence-based use of medication[305,308] or

improving the dosage prescribing of an agent[307]. Educational outreach ('academic detailing') has been shown to improve clinical decision making to enhance the quality and cost-effectiveness of care[291] and improve drug prescribing in primary care[311].

In summary dissemination of a practice guideline must be accompanied by more intensive educational and behavioural interventions to maximise the chances of improving practice patterns in the management of HF[10]. Some uniformity may be achieved by developing a robust method for integrating evidence into rational, educational, and interventional computer-delivered guidance[312,313].

1.8.4.2 Disease management systems for heart failure

The disease management approach views HF as a chronic illness that spans the home as well as outpatient and inpatient settings. Most patients have multiple medical, social, and behavioural challenges, and effective care requires multidisciplinary systems approaches that address these various difficulties[10]. This area has been discussed elsewhere (Section 1.7.4).

1.8.4.3 Who should provide care for patients with heart failure?

There have been several studies that have addressed the effects of physician specialty on the knowledge, management and outcomes of patients with HF[314]. A study of 5 US states demonstrated substantial hospital to hospital variation in the quality of care for patients with HF[315]. Perhaps not surprisingly several studies indicate that primary care physicians as a group have less knowledge about HF and adhere to guidelines less closely than cardiologists[232,316-318]. Furthermore, studies have noted better utilisation of echocardiography and diagnostic testing[319,320], increased use of ACE inhibitors[321], better adherence to guidelines[322] and better outcomes in patients cared for by cardiologists rather than general physicians[318,320,323]. Whilst some studies suggested that care by cardiologists was not economical[324], others have not shown any cost differences between care provided by cardiologists rather than general physicians[325,326].

Comparisons have also been made between cardiologists and heart failure specialists and whilst both generally manage their patients in conformity with

guidelines, HF specialists are more aggressive in initiation and use of ACE inhibitors at target doses[327]. This may, in part, explain the success of the HF clinic model and raises the question as to whether a clinician (e.g. general practitioners with a specialist interest in cardiology, geriatrician or general physician) with adequate training and experience could manage HF just as well if not better than a cardiologist without a specific interest in HF. This is particularly relevant in the modern NHS climate of sub specialisation in cardiology and the move away from generalist care.

However, there are potential problems with many of these studies of specialty differences. Some were self reported practice and physician knowledge, thus may not correlate with actual practice and are subject to non-responder bias (almost all had less than 60% response rate). All but one were observational studies so may be subject to bias and confounding factors (e.g. patient selection, variable response rates and differential recall) that may affect the validity of the results. Different types of patients are seen by different physicians (a form of selection bias) with cardiologists more likely to see younger patients with less co-morbidities and often higher socio-economic status than geriatricians. All but Davie et al (UK)[321] and Bellotti et al (Italy)[322] were studies conducted in the USA, hence may not be generalisable to the UK setting, especially as types of insurance and health plans in the US setting can affect clinical outcomes in patients (e.g. comprehensive cover means a patient is more likely to receive appropriate investigation and treatment). Finally economic studies tended to be based on costing of single episodes of care rather than long term or continuing costs of care.

In reality close cooperation between cardiologists, general physicians and GPs will be necessary to provide care to all patients with HF, including the elderly and those with co-morbid conditions[328,329]. Primary care physicians with knowledge and experience in HF should be able to care for most patients with uncomplicated HF. By contrast, patients who remain symptomatic despite basic medical therapy and have other cardiac conditions (e.g. AF, VHD, or CAD) may benefit from care directed by physicians who have special expertise and training in the care of patients with HF[10].

Chapter 2.

Barriers to accurate diagnosis and effective management of heart failure in general practice – a qualitative study

Abstract

Background

Heart failure is a common condition with high morbidity and mortality, even when mild. It is largely managed in primary care. Evidence suggests that there are wide variations in the standards of management and the clinical application of guidelines, but there is a paucity of data from general practice as to why this is.

Aim

To ascertain the beliefs, current practices and decision-making of general practitioners in the diagnosis and management of suspected heart failure in primary care, with a view to identifying barriers to good care.

Methods

A qualitative approach utilising focus groups with 30 general practitioners from four primary care groups in North East England using a stratified, purposive sampling strategy. The focus group contents were transcribed and analysis followed the principles of "pragmatic variant" grounded theory and content analysis.

Results

Three categories were identified contributing to variations in medical practice and why general practitioners experienced difficulties in diagnosing and managing heart failure.

1. Clinical practice uncertainty, including lack of confidence in establishing an accurate diagnosis, worries about using ACE inhibitors, beta-blockers and spironolactone in often elderly, frail patients with co-morbidity and polypharmacy. **2. Lack of awareness of relevant research evidence** in what was perceived to be a complex and rapidly changing therapeutic field. Doubts about applicability of research findings in primary care and information overload also emerged. **3. Influences of individual preference and local organisational factors.** Medical training, negative anecdotal experiences and outside agencies influenced general practitioner behaviour and professional

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culture. Local factors included the availability of diagnostic services, resources (e.g. accessible cardiologists) and primary-secondary care professional interactions and seemed to shape primary care practice and decision-making processes.

Conclusions

The National Service Framework for coronary heart disease stresses that the substandard care of patients with heart failure is unacceptable. This study identified barriers to be overcome in locality specific and multifaceted implementation strategies across primary and secondary care. Single strategies e.g. provision of guidelines, are unlikely to have an impact on clinical outcomes and new, conjoint models of care need to be explored.

2.1 Introduction

Heart failure is difficult to define and diagnose[49,103,330]. It is common, increasing in prevalence and incidence[29] and has high morbidity and mortality akin to common cancers[53,331]. It is largely managed in primary care[39,332] imposing a heavy burden on the NHS[60], and accounting for 5% of medical admissions, and high readmission rates[60]. As populations age and patients with ischaemic heart disease, the main cause of heart failure[54], survive cardiac events and live longer, the public health burden of heart failure is likely to increase. Two large studies have shown that heart failure impairs quality of life more than any other common chronic medical condition, including hypertension, arthritis, chronic lung disease and angina[56,57].

Diagnosis by clinical assessment is difficult and is correct in less than half of cases when confirmed by echocardiography[71,140]. Heart failure is relatively poorly managed in general practice for many reasons[40,41,147,152,155,333]. These include diagnostic uncertainty[41,155], lack of access to diagnostic services[147], lack of awareness of research evidence and guidelines[152,333], worries about adverse effects, cost and inconvenience of ACE inhibitors[40,152] and poor communication between primary and secondary care[155]. The detailed reasons behind the apparent variability of practice are in need of further elucidation.

Much of the current evidence on how to diagnose and manage heart failure comes from a secondary care perspective where the difficulties of primary care, including differences in patient populations, are not necessarily appreciated. Studies have usually relied on quantitative methods, with little exploration of the complexity of general practice and its relationship with patients and with secondary care[147,152].

The aim of this study was to ascertain the beliefs, current practices and decision-making of general practitioners around the diagnosis and management of patients with suspected heart failure within primary care with a view to identifying barriers to optimal care.

2.1.1 Choice of methodology

2.1.1.1 Research methodology

A qualitative rather than quantitative methodology was felt to be appropriate in the complex context of decision making by GPs in dealing with heart failure patients. Qualitative methods are useful where it is sought to understand rather than prove; describe and interpret rather than measure and predict with the aim of sharpening discussion and disentangling complexity[334]. Consideration was given to the use of a questionnaire survey, semi-structured interviews or focus group discussions.

Advantages of **questionnaire surveys** are that data collection is systematic and they are easy to administer with respondents completing in their own time; they are easy to use with a large population in a shorter time than interviewing; respondents have relative anonymity; they do not have to speak to the interviewer and thus be personally linked to their responses (this may give more truthful answers, rather than the participant "telling the interviewer what he thinks they want to hear"); and are easy to code and analyse by computer[335-337].

Disadvantages are that appropriate questions may be difficult to devise; the interviewee may be unable to elaborate on their responses and the researcher is unable to probe to find out more; they may have a lower response rate than interviews as they lack the personal touch and it cannot be certain whether the questionnaire was completed by the intended respondent or by someone else[335,336,338]. Questionnaire studies are often hampered by low response rates, ambiguity of questions and doubts as to whether responses accord with actual clinical practice[335].

Face-to-face interviews can be either semi-structured or unstructured and tend to have a higher response rate owing to the presence of the interviewer[339,340]. Generally they are more costly and time consuming than postal questionnaires.

With **semi-structured interviews**, topics and questions are specified in advance and the researcher works through an interview guide using their judgement to decide which questions to ask. Advantages are that data

collection is systematic; interviews are conversational and relaxed and the researcher can use their judgement about which topics and questions to probe and pursue[339,340]. Disadvantages are that if the researcher adapts the topics, questions and sequence for each individual subject, the interview experience is different for each person taking part in the study [339,340]. This may reduce the comparability of responses and it is possible that key questions or topics may be dealt with superficially, or missed out altogether[340,341].

Unstructured interviews are often experienced as informal conversations, rather than a data collection exercise. Advantages are that interviewees are free to respond in their own way and to give as much detail as they wish; they are able to give their opinions and discuss their own experiences; the researcher is able to probe to find out more and can hopefully obtain accurate and truthful information on attitudes and values[339,340]. Audio taping and transcribing the interviews ensures internal validity and credibility[341]. Disadvantages are that analysis can be difficult and time consuming because of the volume and variety, and because each interview is unique, it can be difficult to compare interview results; interviews can last a long time and hence only a small number of respondents can be interviewed and this in turn may reduce generalisability to a specific population[339-341]. Furthermore, general practitioners are busy individuals and difficult to tie down to individual interviews.

Focus groups comprise a group discussion focussed on a particular topic where the members usually have something in common[342]. Discussions are led by a facilitator and are time and task limited. Their strengths are that they are a good way of discovering peoples attitudes, beliefs and perceptions on a particular subject; they provide data rich in human experience (a reflection of real life experiences of group members); researchers are able to collect "beyond the quantitative tick box" and encourage spontaneity and candour; data can be collected in a short time from multiple participants and tape recording and transcription means data is accurate and not missed; they are cost effective and require fewer resources, including time, than personal interviews[343]; results can be generalisable if groups are chosen carefully and

thus representative of the study population[340,342]. Weaknesses are that a good facilitator is needed who can encourage people to talk about their experiences and ideas. They may be dominated by one or two outspoken individuals and may be threatening to some participants, they may "put words in peoples mouths", be time consuming to transcribe and analyse and can be expensive if secretarial time is needed to transcribe and participant expenses are to be paid[340,342].

General practitioners are comfortable with small group meetings. The group dynamics allow for "an informal, supportive group of people with similar backgrounds to put people at ease and encourage them to express their views freely and frankly"[344]. In this study, uni-disciplinary groups encouraged freedom of expression. The direct interaction allows greater potential for the researcher to clarify questions, minimise misunderstandings and observe non-verbal responses[345].

Heart failure is a complex disorder. Focus group methodology was felt to be appropriate for generating "the rich details of complex experiences and the reasoning behind [an individuals] actions, beliefs, perceptions and attitudes"[346]. Focus groups are useful when it comes to investigating what participants think, but they excel at uncovering why participants think as they do[347]. This was felt to be a good method for exploring why gaps between evidence and practice exist in primary care management of heart failure.

The purpose of conducting focus group interviews was to get a detailed view of the thoughts and decision making of GPs as they go through the process of making a diagnosis of heart failure. This is added to by semi-structured interviews of hospital clinicians (see Chapter 3) who may approach the diagnosis from a different angle. This is because their patients are different, often sicker, and with more resources available including rapid access to investigations (such as echocardiography), more time for patients on wards and at clinics and the backup of junior staff. Using specific localities it was possible to investigate if there were local variations in service provision that influenced general practitioners beliefs, practices and decision-making in the those localities.

2.1.1.2 Sampling strategy

Qualitative inquiry typically focuses in depth on relatively small samples selected purposefully (non-probability sampling) whereas quantitative methods typically depend on larger samples selected randomly (probability sampling). Probability sampling depends on selecting a truly random and statistically representative sample that will permit confident generalisation from the sample to a large population, whereas the logic and power behind purposeful sampling lies in selecting information-rich cases for study in depth[348]. Patton has described 16 different strategies for purposefully selecting cases and more than one qualitative sampling strategy may be used. In this study it would not have been appropriate to sample by random probability methods because the large numbers needed would be limited by time and financial constraints. Purposeful sampling allowed the selection of cases for in-depth study, using a smaller sample size that would be manageable within the time and financial constraints of the study. More than one qualitative sampling strategy would be necessary to fit the purpose of this study and to answer the research question. A homogenous group was studied (GPs only) and a combination of stratified purposeful sampling and random sampling was employed. Stratification illustrates the characteristics of particular sub groups (gender, ethnicity, geographical locality, GP partnership size, training practice status, part-time or full-time status) and facilitates comparison. Taking a random sample within localities and within practices adds credibility to sampling when potential purposeful sampling would yield too large a sample to be easily managed. Other potential approaches could have been to employ a convenience or maximum variation sampling strategy. Although convenience sampling saves time, money and effort, it is lower on rationale and credibility. With maximum variation sampling a wide range of variations or dimensions of interest is selected (e.g. low and high ACE inhibitor prescribing, low and high documented heart failure diagnosis, low or high use of open access echocardiography facilities). These may identify common patterns that cut across variations but identification of these variants would be difficult given the fact that (1) ACE inhibitors are also used for hypertension, (2) doubts still exist about the diagnosis of heart failure, (3) not

all practices have access to echocardiography and (4) practitioners may prefer to refer to a consultant more readily or even exclusively when heart failure is considered. Patton suggests that more than one sampling strategy may be necessary dependent on research, and evaluation often serves multiple purposes[348].

2.1.1.3 Sample Size

In qualitative research the quality of the sample is not dependent on the size of the sample. The intent is to achieve 'theoretical saturation' akin to redundancy. Researchers watch for patterns in interview results and will sample until they discover that they have 'saturated' the theory or found redundant information. In focus group research the rule of thumb has been to conduct 3 or 4 focus groups for a particular audience and then decide if additional groups should be added to the study[349]. Large-scale studies of divergent populations often require more groups but the goal is to determine the variability of the concept or an idea. Michael Patton offered examples that may be helpful in explaining a small sample size to quantitative researchers who may be sceptical about the scientific basis of qualitative research[348]; "Piaget contributed a major breakthrough to our understanding of how children think by observing his own 2 children at length and in great depth. Freud established the field of psychoanalysis based on fewer than ten client cases."

The validity, meaningfulness and insights generated from qualitative inquiry have more to do with the information richness of the cases selected and the observational/analytical capabilities of the researcher than with sample size[348]. Sample size will then depend on the research question(s) to be answered, the purpose of the inquiry, how the findings will be used, what is at stake, what will be useful, what will have credibility and what can be done with the available time and resources. In the heart failure context previous studies have explored GP behaviour at breadth rather than in-depth[40,41]. This is helpful in exploring a phenomenon and trying to document diversity or patterns but does not necessarily tell us the causes of diversity. Guba and Lincoln[350] stated that the size of the sample is determined by informational considerations. If the purpose is to maximise information, the sampling is

terminated when no new information is forthcoming from new sampled units, then redundancy is the primary criterion. This is what Glaser and Strauss[351] called "saturation point". In the end sample size adequacy like all aspects of research is subject to peer review, consensual validation and judgement[348]. What is crucial is that the sampling procedures and decisions be fully described, explained and justified so that information users and peer reviewers understand the context of the results.

2.2 Method

2.2.1 Subjects, Setting and sampling strategy

Focus groups of general practitioners were used. The study was set in Northeast England in a locality with six Primary Care Trusts covering a population of 617,532 with 316 general practitioners in 88 practices. Participants were selected using a mixed purposive sampling strategy[348] from an up-to-date health authority general practitioner register. The register was divided into the 6 separate PCG areas (Darlington, Durham-Dales, Sedgefield, Durham and Chester-le-Street, Easington and Derwentside). It was decided that we would conduct 4 focus group interviews initially and the first 4 localities on the above list were chosen at random by my secretary. Initially 8 GPs from each of these localities were chosen randomly from 32 different practices. Stratification of general practitioners allowed proportionate representation of gender, ethnicity, geographical distribution, employment status (part-time or full-time) and practice size (group or single-handed) and attempted to avoid selecting general practitioners from the same practice. Forty-one general practitioners were contacted by telephone and a follow-up letter detailed the broad purpose of the focus groups, venue and timing, and included a brief demographic questionnaire. 9 GPs from the original 32 could not participate for a variety of reasons including work and holiday commitments, and these were replaced at random from the register. 4 groups of 8 GPs were then finalised. 2 GPs were unable to attend on the day of the focus groups. Local venues were used to facilitate maximum general practitioner attendance. Early evening timing was suitable for busy general

practitioners and helped reduce interruptions by surgery staff or patients. Postgraduate education allowance certification and a small honorarium may have helped enhance recruitment. Eleven participants were unable to participipate or did not attend; their demographic and professional characteristics did not differ from those who did attend. The groups comprised six to eight participants and a co-moderator was used in three of the four focus groups. Moderators or facilitators were provided with advice and tips on running a successful focus group.

The 30 participants (males 25, overall age range 33-64 years, years since graduation 10-42 years) represented a wide range of practice size and length of experience, including three from single-handed practices. Twenty-seven were full-time, three part-time and 20 (66%) had open access echocardiography. The male to female ratio of general practitioners in the locality was 3:1 and in the focus groups 5:1.

The full demographic details of the 30 participating general practitioners obtained from a questionnaire collected at the focus group session is illustrated in Table 2.1 below. I believe that conducting focus groups in different localities with variable access to echocardiography and potentially different referral patterns was advantageous in ascertaining more varied views of GP experiences.

A list of points to be considered was compiled from a literature review and was used to assist the discussion (see appendices 8 and 9). The sessions (lasting between 65 to 90 minutes each) were audio taped, transcribed verbatim by a medical secretary and then corrected and verified by the principal investigator (AF).

Sex	Age	Years Qualified	University	Doctors in practice	Patient list size	Part-time or full-time	Open Access Echo	Estimated referrals / month
Darlington PCG								
Male	43	20	Belfast	3	5000	FT	Yes	<1
Male	48	25	St Mary's	7	11700	FT	Yes	0
Female	34	11	Cork	8	14500	PT	Yes	<1
Male	43	20	Newcastle	4	7200	FT	Yes	<1
Female	39	16	Glasgow	5	9300	PT	Yes	1
Male	44	21	St Mary's	5	8500	FT	Yes	1-2
Male	58	31	Glasgow	2	4500	FT	Yes	1
Male	58	31	London	6	16000	FT	Yes	0
Sedgefield PCG								
Male	34	12	Newcastle	7	14500	FT	Yes	0-1
Male	37	16	Newcastle	7	14500	FT	Yes	<1
Female	44	18	Cambridge	1	2100	FT	No	0

Sex	Age	Years Qualified	University	Doctors in practice	Patient list size	Part-time or full-time	Open Access Echo	Estimated referrals / month
Male	36	12	London	5	9000	FT	No	0
Male	51	26	India	1	1200	FT	No	0
Male	36	14	Leeds	5	9600	FT	Yes	<1
Male	37	15	Dundee	10	17000	FT	No	0
Male	64	42	Liverpool	3	6500	FT	Yes	0
Durham & Chester le Street PCG								
Male	42	20	Newcastle	3	4300	FT	Yes	>1
Male	33	11	Leeds	5	10000	FT	Yes	2/3
Male	48	23	Manchester	5	9200	FT	No	0
Male	37	13	Aberdeen	10	20000	FT	Yes	<1
Male	49	26	India	1	2200	FT	Yes	<1
Male	46	24	London	13	23000	FT	No	0
Male	47	14	Birmingham	5	8500	FT	Yes	0

Sex	Age	Years Qualified	University	Doctors in practice	Patient list size	Part-time or full-time	Open Access Echo	Estimated referrals / month
Male	42	19	Dundee	5	8500	FT	Yes	1
The Dales PCG								
Male	35	11	Belfast	5	8600	FT	No	0
Male	49	21	Newcastle	5	10200	FT	No	<1
Male	35	12	Newcastle	6	13000	FT	No	0
Male	42	10	Newcastle	5	7400	FT	No	0
Female	41	13	Aberdeen	7	10500	PT	Yes	<1
Female	42	21	Sheffield	2	2500	FT	Yes	<1
Summary								
25M/5F	33-64	10-42		1-13	2100- 23000	27 FT/ 3 PT	20 Yes/ 10 No	0-2/3

Table 2.1 Characteristics of the 30 participating GPs

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2.2.2 Analysis

The analysis followed "pragmatic variant" grounded theory and content analysis principles[351-355]. Transcripts were read and broad themes identified as the groups progressed. This iterative process allowed ideas and thoughts that were emerging to be brought back to subsequent groups. The iterative process started during the interviews as I took notes of new concepts or ideas as they emerged. The tape recordings were transcribed after each interview and corrected by AF whilst listening to the tape recordings. This allowed me to start coding (indexing) with margin notes as the research progressed. I was then able to take these new ideas back to the next group. Examples of this include the concept of ageism in heart failure diagnosis and treatment, the influence of rural geography on access to investigations, patient choice in determining investigation and treatment from the Durham-Dales group that were then explored further in the subsequent Sedgefield group. These issues had not been discussed in the first (Darlington) group.

Deviant case analysis was used to question widely accepted practice[351]. Examples of this include:

1. A GP who did not use OAE even when available. This was contrary to the prevalent view that OAE should be available to primary care and led to me exploring the reasons behind this in more detail both during subsequent groups and from the data already collected.

2. A GP who would never tell a patient they had heart failure. This was then debated in further groups with some other GPs agreeing with this course of action for fear of affecting patient quality of life. This was challenged by other GPs who believed in openness in patient communication and argued that this would improve compliance with therapy.

3. A GP who admitted all patients with suspected heart failure contrary to the widespread practice of initial treatment and investigation in primary care. This was discussed at subsequent groups and the reasons for investigation in primary care versus admission explored.

No new major themes arose by the end of the fourth focus group implying that 'saturation'[351] was becoming evident. The transcripts were read several times, data organised into codes (within highlighting of data and margin notes) from which categories were identified and major themes constructed by AF and APSH. There was a systematic collection of emergent codes that were organised into outline categories and then outline broad themes. Multiple colour-coded copies (a different colour for each focus group) of transcripts were produced and a cut and paste process using scissors and A1 sheets used to paste into analytical categories. Transcripts (annotated with margin notes) and outline codes/categories/themes were presented to APSH and JJM. All three investigators (Ahmet Fuat, Jerry Murphy, Pali Hungin) contributed to multiple coding by meeting up and after discussing the codes/categories and hence final themes were agreed. Examples of codes include clinical history, symptom presentation, clinical signs, patient examination, definition of heart failure, barriers to diagnosis, diagnostic tests including ecg, chest xray and echocardiogram, defensive medicine, referral to hospital and GP education were all grouped under a category of the diagnostic process which was then included under the broad theme of clinical practice uncertainty along with availability and use of echocardiography and treatment issues. I had initially identified 5 broad themes:

1. The diagnostic process;

2. Treatment issues;

3. Ignorance of relevant research evidence;

4. Influences on individual practice preference and;

5. Local influences.

After our research group meeting this was changed to 3 themes;

1. Clinical practice uncertainty;

2. Lack of awareness of relevant research evidence and

3.Influences of personal preference and local organisational factors

All 3 researchers were then involved in deciding how the research would be written up, presented and also which journals should be targetted for publication.

Analysis was enhanced by constant comparison[351] with the transcripts and available research in this field from the initial literature review. This process allows each item to be checked or compared with the rest of the data to establish analytical categories and is central to the grounded theory approach to analysis[356].

Glaser and Strauss suggested that the grounded theory approach to data analysis produces explanations or theories that are derived from the dataset itself rather than from a researcher's prior theoretical viewpoint. In practice, however it is unlikely that a researcher would not have carried out a thorough literature review or formulated some idea of the content of the data likely to be collected[356].

I adopted the Melia model of pragmatic variant grounded theory[352], whereby added value was achieved by identifying new themes from the data alongside those that could have been anticipated from the outset.

A constant comparative method[357] was used to continuously compare the views and experiences of GPs who had been selected purposively in order to illuminate subtle but potentially important differences. An example of this would be my approach to the issue of underuse of ACE inhibitors where I summarised the potential reasons behind this from the available studies and then explored these in my own study;

1 Diagnostic uncertainty[150]

3 Ignorance of heart failure studies[151]

2 Lack of use of echocardiography services[151]

4 Worries about hypotension[151]

4 Worries about valvular disease (especially aortic stenosis)[151]

6 Cost of drugs[151]

3 Slowness of symptom relief[151]

3 Underestimation of poor prognosis associated with HF[152]

4 Concerns about adverse events[152]

1 Difficulties of securinga diagnosis and differential diagnoses[153-155]

4 Perceived inconvenience of use and adverse effects of ACEi[153-155]

3 View that patients can be managed successfully with diuretics[153-155]

5 Type and quality of information transfer from secondary to primay care[153-155]

2 Lack of open access echocardiography[146]

1 Differences in use of clinical information[77]

Constant comparative analysis of the focus group database and above studies explored and verified the reasons behind underuse of ACE inhibitors and the following categories were constructed (numbers correspond to the numbers in the above list);

1 Diagnostic uncertainty

2 Lack of access to diagnostic echocardiography

3 Ignorance of research evidence

4 Adverse events from ACE inhibitors

5 Poor communications between primary and secondary care

6 Economic considerations

Data analysis was commenced after the first focus group and this iterative process added value to subsequent focus groups.

Multiple coding is felt to equate to the quantitative equivalent of "inter-rater reliability" and is a response to the charge of subjectivity sometimes levelled at the process of qualitative data analysis[356,358]. This demands the cross checking of coding strategies and interpretation of data by independent researchers. Unlike "inter-rater reliability", the degree of concordance between researchers is not that important; what is of value is the content of disagreements, the insights that discussion can provide for refining coding frames and its capacity to furnish alternative interpretations[356].

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2.2.3 Respondent validation

Respondent validation involves cross checking research findings with participants in order to protect against misrepresentation of views expressed during the focus group interviews[359]. All 30 participants were sent a report summarising the study results and conclusions, along with a respondent validation form (Appendix 1). Each report was highlighted on an individual basis for each investigator. This had the advantage of allowing each participant to check that their own responses were represented appropriately as well as giving them an overview of the full research analysis. Of 28 replies, 27 "strongly agreed" or "agreed" and one "neither agreed, nor disagreed" that the report was an accurate representation of their opinions and the group outcomes.

I could have used respondent validation in a more iterative manner by asking participants to check interim findings and transcripts of individual focus groups. The advantage of this could have been that respondents' reactions to emerging findings could have helped refine explanations further. Disadvantages are that the researcher seeks to give an overview of research findings whereas respondents have individual concerns and this could have led to discrepant accounts especially if I had chosen to disregard my own interpretation and accepted those of respondents at face value. Furthermore, asking respondents to read drafts woud have made considerable demands on their time and may have led to delays in analysis.

I therefore opted for a simple respondent validation approach but asked for participant comments. Comments were received from 14 of the participants and some stimulated further analysis as well as leading to adaptation of the final report. An example of this is where a GP made the following comments that led to a review of the final report; "I can recognise a few of my comments and most peoples concerns are broadly similar to mine. One major factor I don't feel is mentioned significantly are the differences treating new and established cases. I tend to follow the guidelines for new cases but not for all 'established' cases for a number of reasons which are reasonably documanted in the summary".

Others agreed with the report; "virtually everything I learnt at medical school has now been turned on its head and shown to be unsafe or unsound. Trying to keep reasonably up to date with everything else one is expected to do makes clinical practice almost impossible. Your paper mirrors pretty much how I feel"

I did find use of respondent validation more than just an approving bumper sticker for this qualitative study[356]

2.3 Results

Three major themes were identified which contributed to reasons for the variation in medical practice and why general practitioners experienced difficulties in diagnosing and managing heart failure. The themes were clinical practice uncertainty, lack of awareness of relevant research evidence and influences of personal preference and local organisational factors.

2.3.1 Clinical practice uncertainty

Most participants expressed a lack of confidence in establishing the diagnosis of heart failure. This affected the management of the individual patient. Under this theme three main categories were identified: the diagnostic process, availability and use of echocardiography services, and treatment issues.

2.3.1.1 The diagnostic process

Heart failure was perceived to be a difficult diagnosis to make in general practice because of several factors:

- Problems with the subtlety of clinical symptoms and signs:

    "Some of the clinical signs, if you have a raised JVP or third heart sound, hepatomegaly, are often difficult in the obese to detect, and ankle oedema is common anyway"

    "The fact that people as they get older tend to get crackles in their chest almost as a matter of normality, well because they have crackles it doesn't usually mean failure does it?"

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- Difficulty in differential diagnosis especially in elderly patients with co-morbidity e.g. chronic obstructive airways disease and obesity:

  "I think heart failure would be not too difficult a subject if it occurred in young fit people but the biggest problem is that it's always inevitably older people who get it. It's a co-pathology intermingled with other things and that makes it often quite difficult to disentangle"

- Time constraints and a generally increasing general practitioner clinical and administrative workload:

  "20 plus patient surgeries and having to try and stick to close to 10 minutes, it can be quite difficult to do a really full assessment"

- Lack of availability of diagnostic tests including electrocardiography, chest X-ray and echocardiography, and lack of confidence in interpretation of the results of these tests:

  "You get a kind of slightly reduced ejection fraction and you know an iffy tricuspid valve or two and you know you're not really that much further forward"

  "We are aware that echocardiograms help but we've had problems with access to them"

  "They [echos] are not as accurate as one sometimes is led to believe and I agree with [other GP], I think sometimes they can confuse the issue rather than clarify it"

- Inertia or fear of initiating action because of anxieties about committing to an intensive course of action, including investigations, initiation, titration and monitoring of therapy:

  "I think it's the milder degrees of heart failure ... that is the difficulty. But once you've diagnosed it you're committed to a course of action and I suppose it seems quite a drastic course of action, you've obviously got the diuretics, ACE inhibitors, and possibly other medication as well, full investigations and I suppose that could lead to a bit of inertia, couldn't it. Somebody

with a bit of swollen ankles, you're not quite sure whether it's HF or orthostatic oedema or whatever and you say we'll see how it goes instead of committing yourself to investigation for fear of what you might have to do in the long term."

- Patient choice, including reluctance to be investigated or treated further:

> *"Some patients obviously don't want to be hospitalised or don't want a second opinion, and sometimes don't want to go to hospital, so you end up treating them yourself"*

2.3.1.2 Availability and use of echocardiography services

Perceived handicaps included the variability of open access echocardiography within the same locality; 66% of the participants had this facility. Some of the inequality was due to the continuation of access acquired previously by general practice fund holders. A number of the open access services had been funded through pharmaceutical sponsorship but disappeared as *"monies dried up."* A further perceived problem was the variability in echocardiography reporting, some by technicians and others by clinicians and a lack of guidance for their use or of standardisation of request forms.

Some general practitioners did not use open access echocardiography even when it was available, chiefly because of not being able to understand technical results and the inconvenience caused to often very ill patients. (See Box 2.1 below)

It was apparent that general practitioners were less likely to use open access echocardiography when reports were technical and lacked a clinical opinion than when a clinician-guided report was available. In these circumstances they either treated symptomatically or referred to hospital; a lack of open access was cited as a reason for increased referrals. Apprehensions were expressed about overloading cardiology services, especially with patients who appeared well:

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"I think there is also a feeling that it's almost an inappropriate cardiac referral… the cardiologists are so busy and when you first make the diagnosis they (the patients) are often actually not that poorly…"

Box 2.1: Difficulties for General Practitioners around Echocardiography

- Uncertainty about the significance of results and interpretation of technical reports:

  "The problem with echocardiograms is that I really just don't understand them. I don't think of myself as being really that old, I mean I'm 43… and when I went through my post-registration years echocardiograms just weren't around… I just don't know where I am with them. When does an ejection fraction of such and such percent stop being reasonable and start being a problem?"

- Not being able to cope with echocardiography many preferred to refer for a consultant opinion:

  "I would rather refer than do an echocardiogram, the interpretation of which I am not confident with"

  "I'm not confident in diagnosis of heart failure. I think I just like to have it rubberstamped"

- Distance to nearest echocardiography clinic may inconvenience patients:

  "It takes a whole day to go to hospital, and for an elderly person with breathlessness that's a long day, ambulance there and back, sit in a waiting room, and patients do it once and they won't do it again and they don't all have relatives to take them in"

2.3.1.3 Treatment issues

Diagnostic uncertainty cast doubts on the development of individual treatment strategies for patients. The treatment process was an area where further barriers to evidence based practice were identified.

There was a good awareness of non-pharmacological advice and interventions such as weight reduction, tailored exercise, salt restriction for patients with heart failure[22]. Most agreed on the importance of patient education but some expressed concerns at informing patients about the diagnosis as this might lead to anxiety. This was countered by those who felt that openness and patient involvement enhanced compliance.

Although attitudes were felt to be changing, there were still worries surrounding the use of ACE inhibitors. Concerns remained about their commencement in primary care as opposed to in hospital, partly because of previous teaching and a fear of side effects, mainly hypotension, in the community setting. (See Box 2.2 below)

Even if ACE inhibitors were initiated in primary care a further barrier was the inability to attain the recommended doses as in major studies and guidelines[22] (See Box 2.3 below)

There was widespread awareness of beta-blocker use in heart failure[259] but a unanimous feeling that it should be a "hospital initiated thing", because of a fear of patients collapsing in the community setting. Most were apprehensive about their use and one GP voicing fears indicated that it was "commonsense for general practitioners to be a little bit reticent." Most general practitioners mentioned medical school teaching that emphasised beta-blockers were contraindicated in heart failure:

> "It still seems a contradiction when we were taught beta-blockers precipitate cardiac failure. I'm sure we've all seen that happen and to turn round and prescribe them, it goes against the grain a bit"

Box 2.2: Concerns about using ACE inhibitors in General Practice

- Concerns about use in elderly patients and those with renal impairment and worries about side effects including cough, postural hypotension and renal failure:

    "I'm not too sure exactly at what degree of renal impairment one should worry too much"

- Polypharmacy and drug interactions was considered a barrier, especially in the elderly:

    "The other thing that raises its head is polypharmacy here, where you have got your people who have been chewing their aspirin for years, that a lot of these will be on statins, anti-arthritic drugs. You've got your ACE inhibitors and diuretics. Well that's five or six (drugs) and I think you're going to have rebellion on your hands from people who say they are on far too many tablets..."

- Ageism was flagged up as a consideration in all four groups:

    "I think there is an ageist agenda with it as well because you know somebody of 60 who has got heart failure, you're going to be much more aggressive with than someone who is 78, not just in terms of making the diagnosis but the investigations and treatment"

- A few general practitioners were happy to keep patients on diuretics and *"spare them the ACE inhibitor unless they are getting worse"*

- There was a minority perception that diuretics alone are *"OK in mild heart failure"*

Box 2.3: Barriers to achieving optimal ACE inhibitor doses in General Practice

- Worry that the diagnosis of heart failure was incorrect:

  "But it worries me that if you are pushing the ACE inhibitors up to the maximum dose which you are recommended to do, that you've got your diagnosis right in the first place"

- Although some awareness of the benefits of high dose existed there appeared to be a lack of knowledge of target doses used in major trials

- Worries expressed about *"huge doses"* leading to side effects and intolerance

- Reluctance to increase dose if patient was asymptomatic or stable:

  "If you've got someone who is stable, you're sometimes a bit reluctant to increase the dosage of any medication if the condition is well controlled"

- It was suggested that it may be more difficult to increase the dose *"if already been on a low dose for a while"*

Most general practitioners indicated that they were unaware of the place for other agents including spironolactone and angiotensin II antagonists in treatment of heart failure[22]. Despite its previous use over many centuries digoxin posed a problem:

"I'm not (even) up to speed with spironolactone or beta-blockers yet"

"But you compartmentalise drugs and my compartment for digoxin is atrial fibrillation and you find it difficult to move digoxin out of that one and I don't think I've ever initiated digoxin for heart failure"

"Digoxin: I wouldn't use it in sinus rhythm" was a common response

2.3.2 Lack of Awareness of Relevant Research Evidence

All focus groups discussed their views on the dissemination of research evidence, guidelines and applicability of evidence in primary care. Information overload was seen as a common cause of stress and concern in primary care. Many worried about the *"rapidity of change in all fields"* and *"keeping up to date with changes"*, but felt that we *"owe it to our patients"* to be in touch with recent developments.

Existing guidelines about the diagnosis and management of heart failure and the use of ACE inhibitor therapy were not familiar to most participants. To some extent this was due to *"guideline fatigue"*; one general practitioner felt *"bombarded and bamboozled by guidelines"*

Specific to heart failure was the lack of awareness of the importance of confirming left ventricular systolic dysfunction, differences between systolic and diastolic heart failure and the significance of New York Heart Association (NYHA) classification (a system of grading the severity of heart failure) in categorising heart failure. There was lack of knowledge as to how NYHA classification could be used to provide a prognosis and guide management.

Some general practitioners were happy to keep patients on diuretics alone, possibly unaware of potential benefits of ACE inhibitors, beta-blockers and spironolactone[22,259]. Most had little knowledge of the place for agents other than diuretics and ACE inhibitors and there was a feeling from some quarters that heart failure should be managed in secondary care:

> *"Can we adequately manage heart failure in general practice, given the modern advances that we are all unsure about?"*

2.3.3 Influences of personal preference and local organisational factors

Medical training, anecdotal experiences and outside agencies (Health Authorities, Primary Care Groups and the pharmaceutical industry) emerged as influences on individual clinician behaviour and professional culture. In some instances this was deeply entrenched and perversely also affected newer influences. An example of this was a participant from a large teaching practice who justified his reluctance to refer all patients for echocardiography;

the factors behind this are likely to be complex and relate to coming to terms with a rapidly changing medical environment:

"I got through the whole of hospital training and we didn't use echocardiograms. In cardiology we managed everyone with heart failure without an echocardiogram"

Another GP was reluctant to accept the use of beta-blockers in heart failure:

"I think that's the trouble with the older generation. Medical school taught us 'Beta-blockers and HF - no', People don't change that thought no matter what the evidence may be"

A clinician's anecdotal experience naturally shapes their thinking and may colour judgement processes in their management of heart failure patients. This seemed to be most prominent when considering treatment options:

"Renal function has always worried me ever since I put a lady on an ACE inhibitor and knocked her into renal failure and I have always been rather sort of worried about that since then"

"So he [cardiologist] tried him on carvedilol and he bombed out straight away. So I've always been a bit wary about its use"

Local organisational factors around the provision of diagnostic services such as open access echocardiography, resources, lack of cardiologists, and primary/secondary care professional interactions shaped general practitioner practice and decision-making processes. A locality based, contextualised approach was found acceptable:

"A locally drawn up set of guidelines which are pertinent to the local situation, that is primary and secondary care situations, drawn up by representatives from both primary and secondary care and other interested stakeholders that is owned by everyone who is going to use them"

"We are in an imperfect health service and we are resource starved, and if like every other medical problem we deal with, if we wanted to manage heart failure as we would like to, it's going to have significant resource implications"

In relation to the referral to cardiologists of patients with suspected heart failure, the general practitioner's decision was influenced by waiting lists and the local availability of consultants:

> "Being pragmatic you look at waiting lists, we've got some very good geriatricians who have excellent clinical skills and certainly if the patient has got multiple pathologies I would have no hesitation in referring to them"

2.4 Discussion

2.4.1 Summary of main findings

It is recognised that heart failure is poorly treated in the United Kingdom, mainly because of inaccurate diagnosis and inappropriate treatment, including the use of heart failure therapy in a large group of patients who do not actually have heart failure[41,44]. A major reason for failing to make an accurate diagnosis is that the symptoms and signs are not highly specific[73]. This study provided information about the difficulties perceived by general practitioners in achieving accurate diagnosis and instituting modern therapy[22].

The most accurate method of diagnosis involves the use of echocardiography, but this study confirmed a variation in its availability[146] and discovered that practitioners were not confident about interpreting results. At the same time, there was a reluctance to refer to a consultant for a definitive diagnosis because of a fear of overloading services and a continuing perception that heart failure remains a primary care problem.

It is evident that the diagnosis and management of heart failure has evolved dramatically such that it relies upon specialised investigations and drug regimens that often require specialist input. Clinicians who trained within the previous paradigm have essentially not come to terms with the more modern approach. In turn, there has been insufficient development of services to capitalise on modern management.

Paradoxically, there was a good appreciation by the general practitioners of the benefits of modern treatment, particularly ACE inhibitors as from large-

scale trials[22]. Although confidence in their use has increased, a substantial minority of general practitioners were reluctant to use them, especially in the elderly. This was related to fears about side effects, especially hypotension and collapse in the community setting, and the lack of contextualised primary care monitoring guidelines.

Polypharmacy was viewed particularly negatively. It is known that if between one and five drugs are prescribed, the likelihood of adverse drug reactions is 3.4% rising to 24% with six or more[360]. The increased numbers of tablets likely to be required by the elderly with concurrent conditions such as diabetes and its associated problems was considered daunting and detracting from compliance. In such situations, decisions about the most appropriate regimens were likely to be weighted by the requirements of the different conditions and perceived returns from intervention. Although chronic heart failure is serious and progressive with proven benefit from appropriate drug intervention many clinicians do not find it easy to judge the extent of worthwhile return in older patients with underlying problems such as ischaemic heart disease. Patients already diagnosed with heart failure who appear stable on conventional therapy but who might benefit from newer interventions[259] also posed a dilemma; many clinicians were reluctant to initiate newer treatments, some of which, such as digoxin and spironolactone[22] have ironically, been around for decades.

The majority of GPs accepted that patient education was essential when making treatment considerations. Discussions around this area were in concordance with published advice on lifestyle and non-pharmacological management[127,361]. Some, however, had difficulty in telling patients that they had heart failure. A recent qualitative study highlighted the fact that patients have questions about their illness that they felt unable to ask their doctors, and that some patients would welcome timely and frank discussion about prognosis. It was suggested that effective and better ways of communicating with patients with chronic heart failure need to be tested[362]. This may then have positive influences on compliance with treatment.

Ageism in cardiology has received much publicity lately[363,364] and was an issue discussed in all four groups. The general feeling was that age should

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not be a barrier to investigation and treatment of HF, but a holistic approach to patient care should guide the physicians' actions. With increasing age, men and women with suspected heart failure are less likely to have undergone echocardiography or to have received an ACE inhibitor[365]. Major trials, physician practice, and service developments have neglected older people. This imbalance needs to be redressed.

Sub-optimal care often results from factors outside the immediate control of the general practitioner[333]. Local circumstances, such as resource allocation, priorities, and consultant attitudes, are crucial. This study confirmed that general practitioners perceived this to be the case for heart failure. The increasing involvement of primary care in planning local services via Primary Care Groups may alleviate this providing they can work effectively with secondary care.

2.4.2 Study Strengths and Limitations

The qualitative methodology for this research lent itself well to discovering the barriers to optimal care. Rigour was enhanced by multiple coding and respondent validation[359]; the personal and intellectual bias of the principal investigator was minimised by using a co-moderator in three groups, by allowing discussions to develop naturally and by reporting the wide range of perspectives. This was aided by the moderator striking a balance being non-prescriptive and attempting to cover the majority of the topics in the discussion list. Open ended questions such as "what areas of heart failure care would you like to discuss" often led to discussion by the majority of participants e.g.

> "I think there is an ageist agenda with it as well because you know
> somebody of 60 who has got heart failure, you're going to be much
> more aggressive with than someone who is 78, not just in terms of
> making the diagnosis but the investigations and treatment"

> "Well it is a major thing throughout cardiology isn't it? When you stop
> offering older people treatments that can prolong their lives."

Deviant case analysis[351] enhanced the validity of the findings by questioning widely accepted practice. Generalisability from qualitative research remains an issue with some. Guba and Lincoln have introduced the concept of

transferability as an alternative to generalisibility[350]. This implies that the onus is on the reader to evaluate the methods, setting and results and decide if these are transferable to their own situation. We believe that the findings of this study can be transferred to the majority of settings in the United Kingdom.

2.5 Conclusions

There is an inherent dilemma in the management of heart failure. Advances in science have outstripped the ability and capacity of NHS delivery systems; rapidly changing therapeutic paradigms have confused clinicians, sometimes because drugs previously regarded as dangerous, such as beta-blockers, are new cornerstones and others expelled from the arena, such as spironolactone, are back in vogue. Previous work has explored general reasons why general practitioners do not always implement best evidence[288]. This study identified specific barriers that need to be overcome if aiming for state of the art management. Particular factors needing attention are better and clearer information, improved availability and a useful translation of results from diagnostic methods, and expedient access to specialist advice when there is doubt. Strategies for this might include the development of heart failure clinics and involving general practitioners and nurses with a specialist interest within an integrated care pathway. The National Service Framework[132] stresses that substandard care for heart failure is unacceptable and there is a pressing need for such new, conjoint strategies.

Chapter 3.

The diagnosis and management of heart failure across primary-secondary care: a qualitative study of specialists' views and attitudes

Abstract

Background

The management of heart failure has altered greatly and good outcomes are dependent on an accurate, specific diagnosis and modern therapy. In 50% of cases heart failure is diagnosed in hospital, with high readmission rates. There is evidence of variation in the diagnosis and management practices between specialists and hospitals, compromising uniformly high standards. In turn, this is likely to affect quality of ongoing management in primary care.

Aim

To explore specialists' attitudes and practices in the diagnosis and management of heart failure with a view to identifying barriers to provision of uniformly high standards of care.

Methods

A qualitative approach utilising semi-structured interviews with twelve clinicians (2 cardiologists, 2 specialist general practitioners, 4 geriatricians and 4 general physicians) in northern England, using a purposive sampling strategy. Interviews were transcribed and analysis followed the principles of "pragmatic variant" grounded theory and constant comparison.

Results

Three major themes were identified that contributed to variations in practice. (a) Diagnostic difficulties including access to echocardiography, failure in establishing the aetiology of heart failure, and the assessment and management of increasingly elderly patients with co-morbidities (b) Treatment issues, dependent on consultant experience and interest in heart failure, and barriers to initiation of evidence-based therapies (c) Service delivery problems influenced locally by NHS resources, competing clinical priorities and a lack of speciality responsibility for heart failure.

Conclusions

Variable opinions and practice in the diagnosis and management of heart failure in hospitals and across primary-secondary care was confirmed. Many of the problems were common to primary care. Newer models, including

expedient diagnostic facilities, inpatient integrated care pathways and structured care protocols need developing. Primary Care Trusts and hospitals need to work together to achieve conjoint working patterns to improve patient care.

3.1 Introduction

The quality of heart failure management in primary care is variable and often sub-optimal. Recent research has shown that clinical practice uncertainty, lack of awareness of relevant evidence, influences of individual practice preference and local organisational factors were major reasons for this variability in general practice[366].

There is evidence that hospital care is also sub-optimal[222] and subject to variability between hospitals[367], especially between different medical specialities such as cardiology and geriatrics[316,323]. Much of these data are from the USA and there is a paucity of similar information from UK hospital practice. Such information is needed for the configuration of services to uniformly high standards. The aim of this study was to ascertain from hospital consultants and specialist general practitioners in cardiology, reasons behind variations in the diagnosis and management of heart failure, and to identify barriers to the provision of uniformly high standards of care.

3.2 Methodology

3.2.1 Justification for the choice of methodology

Qualitative data are often relatively unstructured: they come in the form presented by the subjects of the research rather than being pre-packaged by the researcher[339]. The researcher therefore needs flexibility and adaptability to respond to the research subjects rather than imposing a structure upon them. The researcher is, in effect, creating a natural situation, be it a conversation or a group discussion in order to collect the data[340].

Consideration was given to three methods of collecting the information needed to answer the research question. The possibilities included using a questionnaire, in-depth interviews (structured or semi-structured) or group interviews (often called focus groups). The potential advantages and disadvantages of each method were considered before choosing a data collection strategy.

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Of those, structured questionnaires have the ability to collect unambiguous and easy to count answers leading to quantitative data for analysis[335]. However, they are not good at collecting information about attitudes, behaviour and social processes. Furthermore, questionnaire studies are often hampered by low response rates, ambiguity of questions and doubts as to whether responses accord with actual clinical practice.

Focus groups are used as a research method to find out what groups of people think and how they discuss issues and ideas together[368]. The group dynamics are utilised to generate data[342,369,370]. GPs tend to feel comfortable with small group meetings, which are often employed in primary care for management, education or informal discussion sessions[371-373]. Although this worked in bringing groups of GPs together in a non-threatening environment to discuss the broad area of heart failure[374], it was not felt that this would work with groups of specialists. One reason for this was that group culture might have been dominated by clinicians (possibly cardiologists), who potentially have a deeper understanding of heart failure. This may then have interfered with individual expressions by other clinicians and potentially limited participation by all present. Furthermore, it would have been logistically very difficult to get busy clinicians from different localities together at the same time.

Structured interviewing is a process whereby 'the interviewer asks each respondent a series of pre-established questions with a limited set of response categories'[339]. The disadvantages of this method are similar to those of questionnaire surveys, in particular the responses are recorded according to coding systems that have already been established and the interviewer is usually given guidance on deviating from this sequence and trying not to interpret the meaning of answers. Errors can arise from respondent behaviour; questionnaire design faults and interviewer technique and one of the major disadvantages are that they inadequately assess the emotional and behavioural dimension.

Semi-structured interviews on the other hand allow the respondent to express their ideas in their own way, using their own words and determining the range of aspects and issues they want to raise[339,340]. The advantages are that the

interviewer can probe fully for responses and clarify any ambiguities. More complicated and detailed questions can be asked and information of greater depth can be obtained. Inconsistencies and misinterpretations can be checked and open-ended questions can be used for topics that are largely unknown or complex. This may be of value in pilot studies, which may then inform the development of further projects. They also provide "rich and quotable material, which enlivens research reports"[375]. However, there are potential disadvantages in that interviewer bias[375] can creep in. Interviewer training and use of methods in establishing rapport with participants, putting them at ease and appearing non-judgemental, can reduce this[340]. I was aware of this before starting the interviews and having had training in interviewing and appraisal skills felt comfortable with the process. Additional bias can creep in if language interpreters are used for some participants but this was not necessary in this study.

Use of an interview guide was helpful in remembering the points to be covered and suggesting ways of approaching and talking about topics, as well as reminding the interviewer about probes and ways of asking questions.

Semi-structured interviews were used. In this setting this methodology is useful in understanding the complex behaviour of clinicians, does not impose any pre-determined categorisation limiting the field of inquiry and allows the participants to introduce their own agendas[339].

3.2.2 Subjects, setting and sampling strategy

The study was conducted in North East England. A purposive sample[376] of hospital specialists and specialist general practitioners was taken from five acute hospital trusts involved in the direct management of heart failure across nine primary care trusts in Durham and Tees Strategic Health Authority. Specialist general practitioners were identified as those specifically employed in cardiology on a part-time basis and actively involved in providing cardiology services. Of thirteen clinicians initially contacted twelve agreed to interview, one clinician declining without a reason. The participants comprised two consultant cardiologists (one secondary and one tertiary care based), four geriatricians (one with a cardiology interest who provided echocardiography to

hospital colleagues and a restricted service to general practitioners), four general physicians (one with a cardiology interest providing echocardiography to his hospital) and two general practitioners performing echocardiography within limited open access schemes. Specialists were aged between 36 and 57 (mean 47), had been qualified between 12 to 32 years (mean 23) and had clinical experience as consultants or general practitioners with a specialist interest in cardiology of between 2 to 22 (mean 12) years. For a brief description of demographic data see table 3.1.

Table 3.1 Participant demographics

Sex	Age	Speciality	Hospital	Years qualified	Years as specialist
Male	42	Cardiology	Durham	19	8
Male	56	General Medicine	Darlington	32	22
Male	47	Elderly Care	Bishop Auckland	25	18
Male	38	Cardiology	Middlesbrough	16	6
Male	54	General Medicine	Bishop Auckland	30	19
Male	36	General Medicine	Darlington	12	4
Male	42	GP Specialist	Bishop Auckland	18	2
Female	40	Elderly Care	Durham	14	3
Male	51	Elderly Care	Durham	29	20
Male	52	GP Specialist	Sunderland	25	7
Male	57	General Medicine	Bishop Auckland	30	18
Male	53	Elderly Care	Darlington	24	15

A list of discussion points was formulated following a detailed literature review on the management of heart failure and the identification of barriers to its

management[366](Appendix 2). The interviews were audio taped, transcribed and verified by the principal investigator (AF).

3.2.3 Analysis

Analysis followed "pragmatic variant" grounded theory[352] and content analysis principles[351]. Tape recordings were listened to and new points and ideas emerging were taken back to subsequent interviews. This iterative process allowed re-testing of theories and ideas, which were often of pertinence to a particular locality. The iterative process started during the interviews as I took notes of new concepts or ideas as they emerged. The tape recordings were transcribed after each interview and corrected by AF whilst listening to the tape recordings. This allowed me to start coding (indexing) with margin notes as the research progressed. I was then able to take these new ideas back to the next interview. Examples of this include the concept of "transient" heart failure, palliative and hospice care, the influence of cognitive impairment on initiation of evidence based therapy and dietary assessment of patients with cardiac cachexia that were all new concepts discussed during an interview with an elderly care physician. These were then added to my list of topics to discuss at future interviews as well as acting as a stimulus to review previous studies. None of these concepts had been mentioned in previous qualitative studies in heart failure[153-155].

By the end of the 12 interviews it was apparent that there were no new major themes emerging, that "saturation"[351] was evident and it was decided not to conduct further interviews. The transcripts were read several times, data organised into codes (within highlighting of data and margin notes) from which categories were identified and major themes constructed by AF and APSH. There was a systematic collection of emergent codes that were organised into outline categories and then outline broad themes. Multiple colour-coded copies (a different colour for each focus group) of transcripts were produced and a cut and paste process using scissors and A1 sheets used to paste into analytical categories. Transcripts (annotated with margin notes) and outline codes/categories/themes were presented to APSH and JJM. All three investigators (Ahmet Fuat, Jerry Murphy, Pali Hungin) contributed to multiple

coding[342] by meeting up and after discussing the codes/categories[341] and hence final themes were agreed. Examples of codes included under the category of use of evidence based therapy were co-morbidity, accurate diagnosis, beta-blockers, ACE inhibitors, digoxin, diuretics, spironolactone, ageism, level of patient understanding, cognitive function, polypharmacy, side effects, transalation of evidence into practice, NYHA classification, personal experience in treatment, drug interactions. This category was ultimately included under the broad teme of clinical uncertainty.

Analysis was enhanced by constant comparison[351] with the transcripts and available research in this field from the initial literature review.

Respondent validation[359] to affirm the validity of the findings was conducted by sending all 12 participants a report summarising the results and conclusions and asking for feedback and level of agreement with the report. Of the 12 replies, 8 agreed, 3 strongly agreed and 1 neither agreed nor disagreed that the report was an accurate representation of their comments and views. Each report was highlighted on an individual basis for each investigator. This had the advantage of allowing each participant to check that their own responses were represented appropriately as well as giving them an overview of the full research analysis.

I could have used respondent validation in a more iterative manner by asking participants to check interim findings and transcripts of individual interviews. The advantage of this could have been that respondents' reactions to emerging findings could have helped refine explanations further. Disadvantages are that the researcher seeks to give an overview of research findings whereas respondents have individual concerns and this could have led to discrepant accounts especially if I had chosen to disregard my own interpretation and accepted those of respondents at face value. Furthermore, asking respondents to read drafts woud have made considerable demands on their time and may have led to delays in analysis.

I therefore opted for a simple respondent validation approach but asked for participant comments. Comments were received from 4 of the participants. One example highlighted the fact that individual concerns taken at face value

could have led to a discrepant account if I had not had an overview of all the interview data. "Very interesting. I'm not sure your conclusions stem from the data. Integrated care pathways in particular can cause collateral damage preventing any further thought about the diagnosis, which may be wrong and prevent flexible individual treatment. May be this is just my problem and what is heart failure?" I reviewed the data again around understanding of definition of heart failure and clinical care pathways and felt confident that the report represented a breadth of opinion. The respondent validation process was useful in informing the analysis of this study.

3.3 Results

Three major themes were identified contributing to reasons for variation in clinical practice across the primary-secondary care interface: (a) diagnosis, including access to echocardiography (b) treatment issues relating to patients with heart failure and (c) influences on service delivery.

Introductory comments in the interviews invariably recognised the enormity of heart failure as a problem, and the rapidity with which new managements had evolved. The poor quality of life many of these patients experience was highlighted together with the improved prognosis newer approaches offered.

> "I think for the foreseeable future.... we will see an increasing number of heart failure in the community and think we should be prepared to deal with them" (AM4)

> "I don't think anyone should underestimate the enormity of the problem" (RP5)

> "One of the difficulties in heart failure is keeping up with the changes in treatments" (AH3)

> "Heart failure is changing rapidly" (PT2)

3.3.1 Diagnosis

3.3.1.1 Need for an accurate diagnosis

The participants identified with the difficulties general practitioners face in diagnosing heart failure[366] but were positive about the ability of general practitioners to keep abreast of new knowledge:

> "*What surprises me about general practice is how up to date people do remain... it's surprising how many general practitioners are actually ahead of you. They are sending people up for beta-blockers and it's encouraging that people can self-educate.*" (HB10)

However, only two consultants felt general practitioners could diagnose heart failure clinically without echocardiography. The relative inaccuracy of the diagnosis of heart failure (as confirmed from primary care studies) was understandable as this was a difficult diagnosis unaided. There were particular problems surrounding the identification of systolic and diastolic heart failure, even if echocardiography reports were available. Confirming the diagnosis of left ventricular systolic dysfunction is a prerequisite to maximising the benefits from modern therapy and getting this diagnosis right in a timely manner was important.

> "*Diagnosis of heart failure is difficult even for hospital doctors – forget about general practitioners*" (AM1)

> "*There are some problems sometimes with diagnosing heart failure because you have to make the distinction between systolic and diastolic dysfunction and I'm not sure sometimes whether people know how to handle an echo report that says good ejection fraction, say 55/60% but there is evidence of diastolic filling impairment and they think 'What do I do next?'*" (PC1)

> "*Heart failure is a hard thing to define in the first place, but I think we need to be talking about systolic heart failure...we need to be differentiating those patients with left ventricular systolic dysfunction and getting them onto evidence based therapy*" (MC1)

A clinical diagnosis might be easy in overt left-ventricular failure but was difficult in mild chronic failure. A number of factors were identified contributing to diagnostic problems: a lack of sensitivity and specificity of symptoms and signs; increasing numbers of elderly patients with co-morbidity and time restraints within the consultation.

> *"...I certainly don't find it easy sometimes and again I think signs like that in the elderly can be quite difficult"* (PE1)

> *"It's very time consuming bringing them back and reviewing and that sort of thing"* (RP3)

Specialists appreciated that general practitioners had difficulty with lack of access or delays of access to further investigations including electrocardiography, chest X-ray and echocardiography. There was some disagreement as to the potential utility of chest X-ray and electrocardiography in establishing an accurate diagnosis of heart failure and about the limitations of general practitioners and junior hospital staff in interpreting electrocardiograms.

> *"I think an electrocardiogram is always going to be helpful but that's something you can do in primary care if the general practitioners have the confidence to interpret that, but then again you have to understand that some patients with bad heart failure have normal electrocardiograms"* (AMC1)

> *"I mean some cardiologists would say that someone who has got a normal ECG are unlikely to have heart failure but at the end of the day they have been interpreted by cardiologists or cardiology registrars and I think it's a different ballgame when you've got GPs..."* (AH3).

Several consultants expressed concerns over the use of echocardiography, its reporting and interpretation.

> *"Echocardiography, I have a problem with at times. Interpretation is very subjective and we can get enormous surprises and odd results. We are using a one off number (ejection fraction) – nowhere else in medicine do we do this e.g. blood pressure, peak expiratory flow rate,*

renal function we take a series of results before deciding on a course of action" (PT1)

"I couldn't interpret them. If you gave me images or technical data I couldn't – there are one or two figures I understand but I would not feel competent without a clinical interpretation of it" (AMC3).

3.3.1.2 Presenting picture

Many clinicians felt that the importance of past history and assessment of risk factors for developing heart failure were being forgotten. It was pointed out that the search for the cause of heart failure was often neglected and this had a major bearing on further treatment.

"I think we have to have a high level of suspicion and people who are presenting with symptoms suggesting heart failure we should concentrate on high risk people with ischaemic heart disease, hypertension, diabetes, especially if they have atrial fibrillation and if they had a suspicion of thyroid disease and alcoholism" (AM1).

"The other problem I have with open access clinics is that there is this feeling that sometimes that's the diagnosis completed. They (the patients) are breathless so get an echo and it says left ventricular dysfunction so they've got heart failure. Fine. They haven't looked at the cause and personally I do an angiogram on all my heart failure patients who are reasonably young" (MS3).

3.3.1.3 Transient Heart Failure

One consultant talked about the phenomenon of *'transient heart failure'* (HB1) causing difficulties in establishing a confident diagnosis and establishing a management plan. Only two consultants (both geriatricians) mentioned the potential use of biochemical markers such as B-type natriuretic peptide in guiding general practitioners in further investigation and diagnosis of heart failure:

"Not that I am au fait with it but obviously there is B-type natriuretic peptide coming out. People say that it's going to be good but without

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having any personal experience…. It sounds a nice idea to have a blood test (for heart failure)". (RP4)

Table 3.2: Difficulties in diagnosing and managing Left Ventricular Systolic Dysfunction

o Lack of sensitivity and specificity of symptoms and signs

o Increasing number of elderly patients with co-morbidity

o Time constraints faced by consultants and general practitioners

o Difficulties in definition of systolic and diastolic heart failure

o Lack of, and delays in, access to diagnostic tests

o Difficulties in diagnostic utility of chest X-ray and electrocardiogram – including difficulties in interpretation by general practitioners and junior hospital physicians

o Concerns over use, reporting and interpretation of echocardiogram

o Phenomenon of "transient" heart failure

3.3.2 Treatment

3.3.2.1 An accurate diagnosis as a pre-requisite

It was felt the first step had to be the establishment of an accurate diagnosis. There was broad consensus that categorisation of the degree of failure (mild, moderate or severe) should guide treatment and follow up but there was little mention of the New York Heart Association classification which is broadly accepted as a means of heart failure categorisation which links with prognosis and treatment strategies. Pinpointing the aetiology of the heart failure prior to embarking on treatment was emphasised. One cardiologist felt strongly that all younger patients with ischaemic heart failure should have angiography.

"In terms of the New York Heart Association classification we all have a rough idea what it is but you don't ever put down that this patient has a class 1, class 2 etc – we don't do that." (PC5).

"I think the ischaemic heart failure patient is still getting a slightly raw deal in that as soon as they clearly co-exist, I think they should be getting referred for full assessment at a very early stage to work out

which ones actually need to be treated with revascularisation by whatever means, maybe bypass surgery or angioplasty. I believe that will be helpful in terms of prognosis" (MS3)

3.3.2.2 Use of therapies

It was noted by some participants that there was a lack of confidence and reluctance in the initiation of therapy by general practitioners and even by some hospital consultants. Consultant experience and 'interest' in heart failure in both inpatients and outpatients was considered a potential influence on whether or not patients received evidence-based therapy.

> *"There is a reluctance and lack of confidence in introducing angiotensin converting enzyme inhibitors and if they (general practitioners) introduce them they keep them on the smallest dose and they don't progress the dose to be compatible with the clinical trials... and beta-blockers are new to the hospital doctors- forget resistance and difficulty to introduce beta-blockers in general practice"* (AM1)

> *"I think the majority (of consultants) are comfortable with heart failure but they have different degrees of interest... The degree of effort that's put into it and the degree of follow up do vary between consultants. Some consultants will just stick them on a diuretic because they are symptomatically better".* (RP3)

The practice of inappropriate diuretic use (both under and over use) by general practitioners and consultants was mentioned. A cardiologist discussed the concept of "dynamic diuretic dose" rather than the static diuretic dose employed by most physicians. He went on to suggest that patients be given the authority and education to change diuretic dose and implied that this may keep patients out of hospital. Despite this he admitted that this was something primary and secondary care clinicians had not addressed yet:

> *"The dose of diuretic should be seen as something dynamic rather than being fixed and we haven't addressed that yet"* (MC5).

> *"General practitioners don't feel comfortable changing medication but patients should be taught how to change that depending on their symptoms.... And we haven't focussed on that enough in the past. I*

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haven't. I just put them on a certain amount of diuretic. They come back and they get more and more congested and end up in hospital or they come back dry as a stick" (MC5).

Only two clinicians mentioned non-pharmacological treatments. These included training and conditioning, and the dietary assessment of patients with heart failure. Overall it was felt that clinicians did not deal with this area well.

"The other thing I think we're bad at, not necessarily on the wards because the nurses are very clued up, is getting dietary assessments on people with cardiac failure..." (HB9)

3.3.2.3 Elderly patients

The treatment of elderly patients was also discussed in terms of poor quality of life, lack of compliance with medication and potentially high levels of psychomotor side effects from use of multiple medications. Preference for a holistic patient-centred approach was expressed and a geriatrician mentioned a lack of consideration of the presence of cognitive impairment in elderly patients when it came to deciding on treatment strategies.

"It's less easy to advise them on what to do. I would say that over three quarters of the patients I see haven't got the cognitive function to make judgements themselves. So you say to patients 'weigh yourself daily' well they wouldn't" (HB6)

3.3.2.4 Constraints on the use of evidence-based drugs

Many of the barriers perceived by general practitioners[366] were also experienced in secondary care when it came to usage of beta-blockers, spironolactone and digoxin, and to a lesser extent, ACE inhibitors. These barriers included worries about the treatment of elderly patients, allowances for co-morbid conditions, such as chronic obstructive airways disease which might preclude treatment with beta-blockers, drug interactions, poor cognitive function, problems associated with polypharmacy and the fear of inducing iatrogenic disease

"Particularly there is an ageist thing – the older you are the more likely you are just to be stuck on a diuretic and sent home, without thinking of

the other issues like aspirin, warfarin, God forbid, ACE inhibitors, spironolactone, beta blockers – all that sort of thing"; (RP3)

"The other is co-morbidity. A lot of these people will have chronic obstructive pulmonary disease so you would be worried about beta-blockers. They may be real vasculopaths so you would be worried about the ACE inhibitor in relation to putting them into renal failure." (RP3)

"...and also the difficulty in instructing patients (about medication) because I do think you have to have a certain level of understanding. (HB8)

"And also you have got multiple pathology leading to multiple drugs and these weren't the only drugs on offer. You have a gut instinct that to send somebody out on 10 different drugs is not good medicine" (RP3);

"Well it (beta-blockers) won't save any of my 89 year olds if the blood pressure is too low." (HB6)

The majority of consultants felt they were 'hesitant' at prescribing beta-blockers even though they understood the strong evidence-base for their use. Part of this hesitancy related to frequent monitoring of patients once a beta blocker had been initiated.

"To be honest with you I'm not terribly good at the beta blockers idea. I'm learning twenty years of avoiding beta-blockers and also it's a hassle. You have to be honest – it means you have to keep the person under frequent review. You have to bring them back to you outpatient department – I'm not so good on that but I know that's something we should be doing" (RP3)

"You are speaking to someone who is just coming to terms with use of beta blockers in heart failure. Five years ago you would fail your membership for saying it. Rightly or wrongly my view of the management of heart failure or left ventricular dysfunction is ACE inhibitors plus a minor diuretic as a first line approach and I suspect that many patients could be managed in that way" (AMC3)

3.3.2.5 Palliative care

The question of palliative care for these patients was flagged up as being an overlooked area, despite the fact that the National Service Framework for CHD[23] and guidelines[34] recommend end of life support for patients with end-stage heart failure:

> "*There is the palliation issue. That's cropped up in the National Service Framework and that is an area that cardiologists at any rate have not paid a huge amount of attention to in the past... The palliation issue is very important as they have got someone to contact for support and the Macmillan nurses could be roped in when people have a very short life expectancy. That wouldn't be unreasonable. You would like to think that patients get that sort of support*". (MC5)

Table 3.3: **Reasons behind reluctance in initiation of evidence-based therapy**

- o Lack of an accurate diagnosis of left ventricular systolic dysfunction
- o Lack of consultant and general practitioner experience and interest in heart failure
- o Lack of application of New York Heart Association classification in deciding treatment options
- o Managing increasingly elderly and frail patients
- o Co-morbid illnesses e.g. chronic obstructive pulmonary disease, peripheral vascular disease
- o Contraindications and fear of drug interactions; polypharmacy
- o Physician variability in knowledge of evidence base for heart failure
- o Fear of inducing iatrogenic disease
- o Reluctance in treating "mild" left ventricular systolic dysfunction
- o Time constraints – especially to monitoring and follow up
- o Hesitance in beta-blocker use due to prior conditioning
- o Lack of palliative care services and support
- o Inappropriate diuretic use – lack of "dynamic diuretic dosing"

3.3.3 Influences on Service Delivery

3.3.3.1 Gaps between evidence and practice

This raised animated responses amongst all the participants. There was a common feeling that despite the availability of evidence and even good resources in many places it was essentially the current organisation of the pathways of care that compromised the quality of delivery of heart failure care (see Table 3.4).

"To do a good job people have got to have time and the resources to do it and if that means more specialtst nurses or more delegation – I don't think anybody should underestimate the enormity of the problem"

".... there doesn't seem to be any standardisation of care [for heart failure] across the country"

There were problems common to each of primary and secondary care: lack of clinicians' experience and interest in heart failure, availability and access problems around diagnostic facilities, competing health priorities and the influence of policy makers, including national initiatives such as the National Service Framework (see Table 3.4). Most interviewees offered their vision of how services could be reconfigured to overcome barriers and to improve the overall management of heart failure patients (see Table 3.5).

3.3.3.2 Who should manage heart failure?

There was disagreement as to whether heart failure should be managed in primary or secondary care. Half of the interviewees felt that it could be adequately managed in primary care:

> *"Heart failure ought to be a general practice disease"* (PT1)

> *"General practitioners can treat mild and moderate cases themselves"* (EE1)

> *"So I have to say no, again there will be some general practitioners who are interested and follow literature and give a good service to their patients and there are others who will not – definitely there are some who will not read the literature…. because heart failure may not feature as a problem in general practice. They may see few cases in a year unless they have an interest"* (AM3)

> *"Increasingly… I think people are moving towards saying it is a sufficiently difficult diagnosis with additional resource implications, that specialist heart failure clinics are the best way of doing it"* (MS2)

One cardiologist questioned the definition of open access echocardiography and highlighted problems. Furthermore, it was felt that open-access service discouraged the search for aetiology of heart failure:

> *"If, by open access, it is a clinician led service with a clinical report then it's not a general practitioner diagnosing it. All he's doing is reading the clinician's letter. So I have a problem with the concept of open access… what people refer to are not open access echo they are one-stop heart failure assessment clinics. The clinic that started it all off*

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was run by a cardiology registrar and patients had electrocardiograms done, they had a clinical examination done, they got blood pressure measured and then an echocardiogram and then the clinical report was issued with recommendations for treatment ... I think that's very different from open access echo where a technician just writes the same technical report...." (MC1)

Many of the participants felt that it was desirable that one clinician in a locality take the responsibility for heart failure management. The choice of speciality would be dependent on the interests of the key players: local cardiologists, general physicians, geriatricians or general practitioner specialists.

"I think it should be referred to somebody who is interested in management of heart failure and who has knowledge of echocardiography and able to interpret the results and have some input. I feel heart failure is a general physician and geriatrician responsibility – it's not a pure specialist cardiology domain because (patients) don't always see the cardiologist". (AM3)

Waiting times in cardiology were seen as a problem and changes in out of hours care in general practice were seen by some hospital clinicians to be increasing the admission rates of patients with heart failure. Also, it was considered that specialist cardiology care was not necessarily the answer because of the increasing numbers of patients with heart failure referred.

"I suspect certainly 10-15 years ago some people might have stayed at home in the evening or the middle of the night with a shot of frusemide and some diuretic to take the following morning. That's not an option any more really in the way urgent care is now practised". (RP5)

The majority of the participants felt that heart failure should be managed by conjoint working between primary and secondary care. Doctor and carer education, multidisciplinary guideline production and dissemination and clinical governance were desirable as potential answers to remedying shortfalls but models with joint primary and secondary care were needed to attain National Service Framework targets[132]. There were parallels with other chronic diseases such as diabetes and hypertension. In these chronic

conditions, shared care is now becoming the norm. Under a similar shared care scheme general practitioners could manage patients in certain categories with hospitals managing others.

"I think there are parallels for any chronic disease process and how we actually work better together..." (AMC5).

"There are some patients who you never get stable. ...That sort of patient is often just better continuing to attend the hospital clinic and because that way we can give very ready access to inpatient treatment... I agree that there could be a model for the patient just presenting in middle to late life with classical heart failure. They get referred to hospital, and get the diagnosis confirmed. Over the course of two or three months they get established on standard therapy, the balance gets optimised and then they return for long-term follow up to the general practitioners. That could certainly work for a large proportion of these people" (MS3).

"Disseminating the expertise outwards rather than sucking everything in because logistically I don't think we can cope with it. Not unless we acquire a whole load of cardiologists" (AMC5).

Table 3.4: Influences on Service Delivery

- o Clinician experience and "interest" in heart failure
- o Lack of availability of diagnostic services
- o NHS resources (financial and manpower)
- o Competing clinical priorities
- o Influences of local policy makers (primary and secondary care)
- o Lack of specialty responsibility for heart failure in a locality setting

Table 3.5: Suggestions for Service Delivery

- o Shared care schemes across primary and secondary care
- o Inpatient integrated care pathways
- o Specialist heart failure clinics including "one-stop" option
- o General practitioners with a specialist interest in heart failure

- o Specialist heart failure nurses working across the interface
- o Palliative care for heart failure
- o General practitioner academic detailing
- o Locally owned protocols

3.4 Discussion

This qualitative study confirmed variable opinions and practice in the diagnosis and management of heart failure in UK hospital practice and across the primary-secondary care interface. Difficulty in establishing an accurate diagnosis, concerns about availability, reporting and interpretation of echocardiography, multiple barriers to initiation of evidence-based therapy and local organisational influences were similar to themes identified from research with general practitioners[366].

3.4.1 Methodological considerations and limitations

This methodology proved to be effective to this research. The rigour of the study was increased by multiple coding[342] and respondent validation[359]. Although the number of participants was small, purposive sampling[376] generated rich data from the interviews. The characteristics of the participants were felt to be broadly similar to specialists across British hospitals. The personal and intellectual bias the principal investigator (AF) may have exerted on the interviews was minimised by allowing discussions to develop naturally, tape recording all data and by reporting a wide range of different perspectives from all twelve interviews.

Questions are often raised about generalisability of the results of qualitative studies of this nature. Qualitative studies are not intended to be generalisable to all clinical situations or localities. However, as the organisational factors are unlikely to vary across the country we believe the results are transferable to other localities wishing to tackle heart failure diagnosis and management.

3.4.2 Potential solutions

Standard 11 of the National Service Framework for coronary heart disease[132] recommends that all patients with suspected heart failure should have

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echocardiography. Thus there needs to be a consistent and systematic approach to identify patients with heart failure or those at high risk of its development, deliver appropriate care to those so diagnosed and to offer regular review. Currently, management of heart failure is variable in both primary and secondary care sectors. One of the problems in hospitals seems to be that care is frequently fragmented with different specialty consultants and often-inexperienced junior staff looking after such patients. The increasing sub-specialisation of consultants, the admission of patients under an on-call consultant who may have little experience or interest in heart failure, and pressure for early discharge before investigations are completed are likely contributory factors to sub-optimal management. Of pressures facing clinicians, trying to determine optimal drug regimens, polypharmacy, drug interactions, co-morbidity and the reduced cognition of some elderly patients were seen as the greatest.

Recently, structured care in hospital based nurse-led clinics, such as provided by the Omada programme[377], has demonstrated an improved outcome in heart failure patients and is an example of models of care suggested in the National Service Framework[132]. Systematic structured care has also been shown to increase the uptake of ACE inhibitors in primary care patients with heart failure[70]. However, it is likely that there will be reticence in the uptake of beta-blockers and spironolactone without a definitive, accurate diagnosis of left ventricular systolic dysfunction and at least some expert input.

There has been much debate as to how the diagnosis of heart failure should be secured. Some argue for open access echocardiography to be available to all general practitioners[139,140,157] others feel that a specialist opinion should be sought[163,166]. However, open access is not uniformly available across the UK[146], largely due to lack of trained technicians and some general practitioners have concerns about interpretation of technical results[366]. A specialist opinion in every situation is impractical due to long hospital waiting lists and the increasing numbers of patients with heart failure[378].

Newer models of care are needed. An integrated care pathway that bridges primary and secondary care is desirable. A question which arises is whether every patient with suspected heart failure needs to be seen by a cardiologist

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or another physician with good access to diagnostic facilities, or whether by a hospital clinician at all. There is a good argument from the views collected that a diagnostic service could be established without the intervention of a hospital specialist, although treatment itself may require a clinician with special expertise. One way of delivering this could be a general practitioner specialist/nurse specialist run one-stop heart failure clinic, taking referrals from primary and secondary care. Inpatient care pathways for those admitted with heart failure also need to be introduced to ensure uniform procedures for diagnosis and treatment. Specialist heart failure nurses could then follow patients discharged back to primary care[184] as well as responding to referrals of patients felt to be decompensating or needing palliative care. Newer screening methods such as B-type natriuretic peptide offer opportunities for diagnostic strategies[379] but need further evaluation within a pragmatic primary care setting.

The findings of this study confirm that there is a lack of uniformity in the diagnostic and management services for heart failure in the secondary care sector, between clinicians and between institutions. Specialists' opinions about the ability of general practitioners to deliver effective care vary; in general, primary care alone cannot deliver a uniformly high standard service even with the provision of diagnostic facilities. Conversely, a service geared entirely toward secondary care provision is untenable because of workload and follow-up implications. There is a pressing need for the exploration of conjoint service provision encompassing the possibility of a non-cardiologist centred service. From this research, exploring the views and experiences of specialists, there is much variation in practice within secondary care itself; a specific heart failure service would benefit patients across the interface.

Chapter 4.

One stop diagnostic clinic for suspected heart failure and the Darlington integrated heart failure service - a descriptive study

Abstract

Heart failure due to left ventricular systolic dysfunction (LVSD) carries a high morbidity and mortality. LVSD merits rapid, accurate diagnosis in order to initiate evidence based management strategies. The Darlington heart failure services model, part of the South Durham Heart Failure Network, was devised to overcome barriers to accurate diagnosis and effective management of heart failure. It involves rapid diagnosis of LVSD and ongoing heart failure management. A weekly one-stop diagnostic clinic, run by a GP specialist and a heart failure nurse, is jointly funded by the PCT and the NHS Trust. If LVSD is confirmed, a management plan is formulated which includes patient education and initiation of evidence-based therapy. The heart failure nursing service is invaluable in bridging the gap between primary and secondary care. Local guidelines, together with continuing education of GPs and practice nurses, and the new GMS contract, should further increase the uptake of evidence-based therapies at target doses.

4.1 Background

Chapters 2 and 3 have highlighted significant barriers to accurate diagnosis and effective management of heart failure across primary and secondary care. Even when facilities for the accurate diagnosis of HF exist (open-access or consultant screened echocardiography) the application of effective therapy remains a problem in general practice[40,366,380]. Relatively low rates of usage of ACE inhibitors, beta-blockers and spironolactone are likely to be related to a number of complex factors, e.g., difficulties in interpretation of echocardiography results, waiting times, lack of familiarity of regimens, apprehensions about adverse effects, and workload pressures[155,366]. Furthermore target doses of these agents are often not achieved[40,41,44,70,223]. There is a pressing need to explore alternative management approaches, which eliminate or minimise obstacles and are conducive to the appropriate management of that group of patients most likely to benefit from modern therapy.

In addition, (i) there needs to be equity of access for patients with heart failure to the most effective and cost-effective treatment available. General Practitioners should be in a position to be able to offer or arrange optimal management. However, there is a widening "practice-evidence" gap (ii) although evidence based guidelines[105,127,141,233] have established the need for an accurate diagnosis of heart failure, essentially with echocardiography, the rate of "over-diagnosis" remains around 40%[39,71], with less than 40% of patients receiving ACE inhibitors[41] (iii) doubts remain about the effective use of echocardiography services, and many secondary care clinicians favour referral to hospital[163,164] (iv) there is increasing pressure within the NHS towards the implementation of evidence-based clinical guidelines[105,127,141,233] (v) the needs of PCTs to collaborate with secondary care for the provision of services creates an urgent need to resolve this clinical / health services issue. (vi) the advent of clinical governance is a further imperative towards streamlining the provision of care in this field.

The National Service Framework for Coronary Heart Disease (NSF for CHD) recommendations include echocardiography for all patients with suspected heart failure, and development of a consistent and systematic approach to

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identify patients with heart failure or at high risk of developing it, and delivery of appropriate care to those diagnosed with heart failure, together with regular review[132].

Hence, possible drivers for change in the management of heart failure due to left ventricular systolic dysfunction (LVSD) include the extensive evidence base and the various national guidelines[22,105,379]. In addition, the NSF for CHD[132], the new General Medical Services contract[381] and the CHD and Primary Care Collaborative (including MINAP, the Myocardial Infarction National Audit Project) are policy-based strategies that are helping to close the evidence-treatment gap.

The NSF for CHD proposes development of newer models of care for diagnosis and management of LVSD[132]. Coinciding with a government call for more GPs with a specialist interest we established a GP specialist led one-stop diagnostic clinic to enable expedient diagnosis and appropriate initiation of evidence based therapy if LVSD confirmed. Development of the service considered barriers to accurate diagnosis and effective management of heart failure across primary and secondary care identified from qualitative research projects described in chapters 2 and 3, and incorporated some of the solutions proffered by participants and researchers.

4.2   Aims of the service

The aims of the heart failure diagnosis clinic are:

- To provide rapid access to diagnostic facilities for patients with symptoms consistent with heart failure.
- To provide a consistent approach to the diagnosis of heart failure in the locality.
- To maximise treatment, according to evidence-based guidance and local protocols for patients with confirmed LVSD.
- To be innovative in the approach to service provision and share our successes with others.

4.3 Clinic structure

4.3.1 Service outline and funding

The current heart failure service is outlined below:

Figure 4.1 Heart failure services in Darlington

Rapid diagnosis of LVSD – one-stop clinic

South Durham Local Guideline/Protocol/Care Pathway and basic formulary

Heart failure nursing service

Ongoing LVSD management including drug titration

— Primary care (CHD and HF clinics/HF nursing service)

— Secondary care (nurse/pharmacist titration clinics)

Palliative care

The one-stop diagnostic clinic was established in January 2002 as a joint venture between Darlington PCT and South Durham NHS Trust and the British Heart Foundation funds a specialist nurse. Whilst there have been other reports of rapid access clinics[172-174] we believe this is the first GP specialist led diagnostic and management clinic.

The one-stop clinic is run by a GP specialist and a heart failure nurse. The service is based upon local heart failure guidelines and protocols. The weekly clinic runs in parallel to a consultant cardiologist's clinic and is sited within the general medical outpatient department of Darlington Memorial Hospital. The clinic template allows for 6 new and 5 follow up patients.

There was much discussion about where the clinic should be based. PCT managers were keen on the clinic being in primary care, in line with an NHS push to moving services from secondary care into primary care and the introduction of payment by results. We argued that the hospital setting had the advantage of having the best echocardiography equipment and the best, fully trained, highly skilled technicians; access to a consultant opinion if needed; availability of other diagnostic tests including ECG, Chest X-ray and exercise

treadmill test; follow up of abnormal blood test results by consultant when GP specialist not available; immediate access to the warfarin clinic and availability of secretarial and administrative support.

4.3.2 Referral criteria

Patients access the clinic via:

- GP referral for patients with suspected heart failure.
- GP or heart failure specialist nurse may refer patients with confirmed heart failure who require symptomatic assessment.
- Referral from cardiology clinic or other physicians who require evaluation of patient's symptoms.

For GP referrals there is a standard one page referral form (Appendix 3). Referral forms for the heart failure diagnosis clinic are received and processed by the central appointments patient office; patients then receive clinic appointments via post. All patients are sent an information leaflet regarding the diagnostic clinic and which has been produced by the heart failure team (Appendix 4).

The GP is asked to undertake baseline blood tests; ECG and chest X-ray.

At the clinic all patients have clinical assessment, relevant blood tests, chest X-ray (if not done by GP), ECG, echocardiography and selected patients undergo pulmonary function tests. The decision to include a chest x-ray was debated but it was felt that as NICE guidance recommends this investigation in assessment of patients with suspected heart failure, it should be included[105]. British Society of Echocardiography accredited cardiac physiologists perform echocardiography. Left ventricular function is assessed by "eyeball" assessment, with Simpson's rule and wall motion index measurements when possible. The patient brings the report back to the clinic in a sealed envelope. The cardio-respiratory laboratory provides 6 dedicated echocardiography slots for use by the clinic. Appendix 5 outlines the clinic function and patient pathway.

Patients in whom heart failure or LVSD is not confirmed are discharged back to the GP or, if necessary, to another physician (e.g. respiratory physician or

general cardiologist). If LVSD is confirmed, a management plan is formulated which includes patient education and initiation of evidence-based treatment.

BNP and NT proBNP[16] were used initially as research tools in the clinic (funded respectively by the PCT and Roche Diagnostics). This study identified a cut off point of 150pg/ml for NT proBNP[382], which was used by GPs to triage referrals to the diagnostic clinic within the setting of a pilot project. These studies were designed to answer some pragmatic questions around the practicability of use in primary care, appropriate cut off points, cost benefit, and the role of electrocardiography in this setting. These studies are reported in detail in chapters 6 and 7 of this thesis.

4.3.3 Staffing of clinic

4.3.3.1 Role of the GP specialist in cardiology

The GP specialist in cardiology provides the main clinical leadership to the HF team and was instrumental in persuading Darlington PCT and South Durham NHS Trust to adopt and fund a one-stop diagnostic clinic model.

The role of the GP specialist includes:

- Clinical assessment of all referred patients.
- Order appropriate baseline investigations (bloods, Chest X-ray, ECG and echocardiogram).
- Assimilation of all clinical and investigative data to establish a working diagnosis.
- Once LVSD confirmed determine a management plan.
- Decide on referral to tertiary care for specialist services e.g. cardiac resynchronisation therapy, coronary angiography (CABG or angioplasty), valve replacement.
- Decision to discharge or follow up patients.
- Refer onto other secondary care specialists including cardiology and respiratory medicine.
- Offer clinical advice to local GPs and others working with HF. Patients who are deteriorating clinically can be fitted into the one stop clinic for review and management.

- Further education of local GPs, district and practice nurses, specialist nurses, patients and carers.

- Sharing good practice - other GP specialists from across the UK have sat in the clinic and taken away ideas for initiating similar services in their own localities (from Isle of Lewis to London)

- Clinical audit and evaluation of the service

4.3.3.2 Role of the specialist heart failure and auxiliary nurse

The specialist nurses see patients in clinic after they have received the appropriate diagnostic tests and heart failure confirmed by medical practitioner at the clinic.

The specialist and auxiliary nurses provide the link between the diagnosing clinician, the patient and the organisation of community based care. They collate the results, counsel the patients and carers and ensure follow-up in the clinic, GP or domiciliary setting. They are also responsible for effecting the day to day management of the HF patient in relation to specific items such as daily weighing to evaluate fluid overload and exercise regimes.

If patients require a home visit after diagnosis, an appointment will be made during the heart failure clinic.

4.3.3.3 Role of the consultant cardiologist

Dr Jerry Murphy was supportive in the setting up and running of the clinic.

His main roles include:

- Overall clinical responsibility for patient care and

- Advice to GP specialist and specialist nurses in interpretation of complex or difficult investigative data (including ECG, Chest X-ray, echocardiograms, CT scans) and management issues

4.3.4 Heart failure review clinic

Pressures on workload generated by follow up patients, especially those needing beta-blocker titration in the one stop diagnostic clinic led to development of a nurse led review clinic, complemented by involvement of a

pharmacist. Continuing education of GPs to up titrate beta-blockers was also undertaken.

The underpinning rationale for the heart failure review clinic was to provide a consistent approach to the optimisation of medications, and reduction of symptoms in patients with heart failure. The unique approach to the clinic aims to integrate specialist nursing, pharmacy and cardiology services to provide high quality evidence based care for patients with heart failure. Patients can be referred to the clinic by the GP with a specialist interest, cardiologists or general physicians.

4.4 Summary of services and referral pathways

The Darlington Integrated Heart Failure Service is built around partnership working between primary care staff, secondary care staff, patients and carers, palliative care services, voluntary agencies and charitable organisations.

Figure 4.2. The Darlington integrated heart failure service
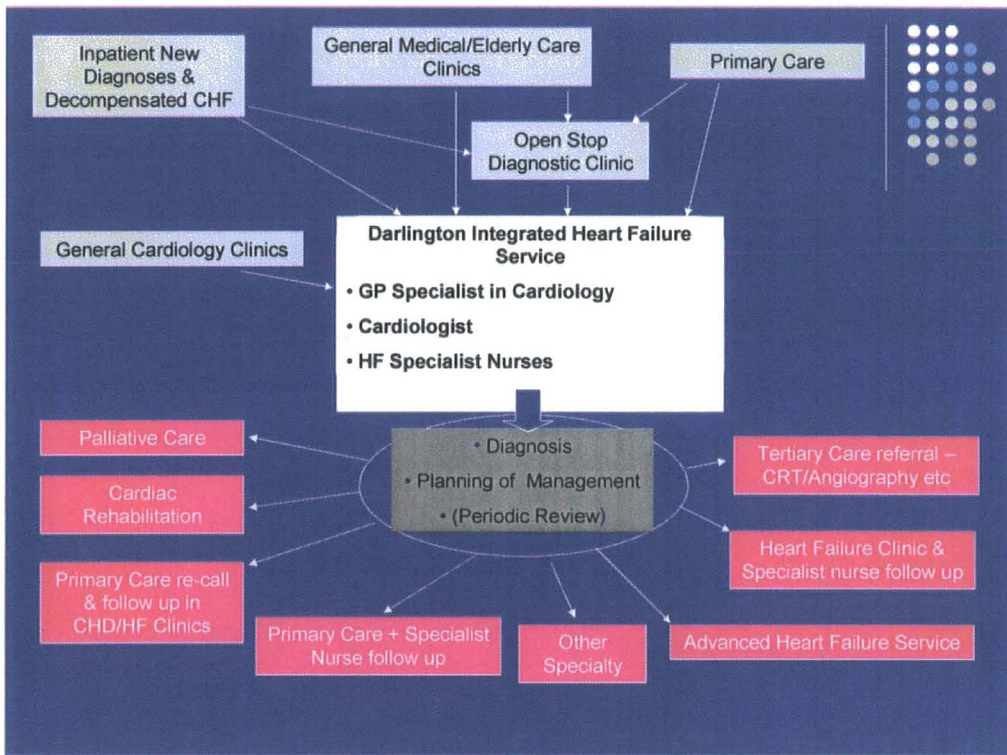
4.5 Facts and figures

4.5.1 Referrals

55 (98%) Darlington GPs referred at least one patient to the diagnostic clinic within the first 14 months. 6 GPs from adjoining PCTs (Dales, Sedgefield and North Yorkshire) also referred patients to the clinic. The Darlington PCT area covers a population of around 100,000 with a hospital catchment population of around 150,000.

4.5.2 Diagnoses

In the first 14 months, 217 consecutive patients were seen in the one-stop diagnostic clinic. The age range of patients was 34-93 years, with a mean of 72.9, and 61.3% were female. 82 (37.8%) had LVSD. Of these 33 (40.2%) were mild, 17 (20.8%) moderate and 32 (39%) severe LVSD. This diagnosis was based on a semi-quantitative eyeball assessment of LVSD rather than NYHA clasasification. However, these would correspond to NYHA I, II and III respectively. A further 82 (37.8%) had other significant cardiac abnormalities that could have accounted for symptoms and/or signs suggestive of heart failure. There were also non-cardiac conditions that led to patient referral. Many patients have multiple pathologies. Table 4.1 lists these alternative diagnoses. These alternative results are similar to other studies and should be rigorously sought and mamaged accordingly[137].

Table 4.1: Diagnosis in patients without LVSD 2002/3

Diagnosis	Number of patients	Diagnosis	Number of patients
LVH	43 (19.8%)	Mitral Regurgitation	29 (13.4%)
Atrial Fibrillation	20 (9.2%)	Diastolic dysfunction	20 (9.2%)
PHT	9 (4.1%)	COPD	6 (2.8%)
Cor Pulmonale	3 (1.4%)	Aortic regurgitation	4 (1.8%)

Diagnosis	Number of patients	Diagnosis	Number of patients
Left ventricular aneurysm	4 (1.8%)	Tricuspid regurgitation	4 (1.8%)
Aortic stenosis	4 (1.8%)	Atrial flutter	2 (0.9%)
Right ventricular hypertrophy	3 (1.4%)	Lung cancer	2 (0.9%)
SLE	1 (0.5%)	Cardiac amyloid	1 (0.5%)
Paraproteinaemia	1 (0.5%)	Waldenstroms' macroglobuline mia	1 (0.5%)

4.5.3 Initiation of evidence-based therapy

All patients with a diagnosis of LVSD had a detailed explanation of the illness given by the GP and HF nurse. Evidence based therapy was initiated and titrated to target doses. In the majority of patients this titration was supervised by the specialist heart failure nurses and GPSI. Some patients were titrated by their GP, especially in those patients from rural communities. These GPs had received educational sessions on use of beta-blockers in heart failure. We did not document the number of visits patients had to make to reach target doses but estimate this to be between 6 to 8 visits if achieving maximal doses of ACE inhibitor and beta-blocker. In terms of medication prescribed at the clinic, there was a high level of use of ACE inhibitors[211] and beta-blockers[235] (see Table 4.2)

Table 4.2. One-stop clinic medication for patients with LVSD 2002/3

Drug	Proportion of patients receiving
Diuretics	89%
ACE inhibitor	87.8% (intolerant 3.7%; contraindicated 1.2%)
Angiotensin II receptor antagonist	7.3%
ACE inhibitor or angiotensin II receptor	95.1%

Drug	Proportion of patients receiving
antagonist	
Beta-blocker	69.5% (intolerant 8.5%; contraindicated 20.7%)
Digoxin	11%
Spironolactone	8.5%
Nitrate	8.5%
Statin	43.9%
ACE inhibitor at target dose	73.6%
Beta-blocker at target dose	63.2%

95.1% of patients were taking an ACE inhibitor or angiotensin II receptor antagonist[265], and 69.5% were taking a beta-blocker (29.2% had contraindications or were intolerant). Target doses were achieved in 73.6% of patients taking ACE inhibitors and in 63.2% of those taking beta-blockers. Spironolactone[19] has been more difficult: many patients have experienced side effects and have had to discontinue treatment with this drug.

4.5.4 Admission data

Table 4.3. DMH admissions with a primary diagnosis of heart failure

	Congestive Heart Failure	Left ventricular failure	Heart Failure unspecified	Total
2000	168 (57.5%)	117 (40.1%)	7 (2.4%)	**292**
2001	156 (60.7%)	97 (37.7%)	4 (1.6%)	**257**
2002	178 (65%)	82 (29.9%)	14 (5.1%)	**274**
2003	166 (59.9%)	102 (36.8%)	9 (3.3%)	**277**
2004	149 (69.6%)	54 (25.2%)	11 (5.2%)	**214**
2005	124 (59.9%)	64 (30.9%)	19 (9.2%)	**207**

Table 4.4. DMH admissions with a secondary diagnosis of heart failure

	Congestive Heart Failure	Left ventricular failure	Heart Failure unspecified	Total
2000	85 (42%)	109 (54%)	8 (4%)	**202**
2001	101 (52.3%)	75 (38.9%)	17 (8.8%)	**193**
2002	103 (60.2%)	51 (29.8%	17 (10%)	**171**
2003	147 (59.5%)	88 (35.6%)	12 (4.9%)	**247**
2004	114 (50.4%)	83 (36.7%)	29 (12.9%)	**226**
2005	109 (60.6%)	53 (29.4%)	18 (10%)	**180**

The heart failure diagnostic clinic and the heart failure nursing services were introduced in January 2002. Using primary diagnosis data it appears that admissions increased in the first two years and now are showing a downward trend (see Table 4.3). The initial increase could have been due to increased awareness and knowledge about heart failure by local GPs attended in practice educational sessions on diagnosis and management of heart failure. This may have led to increased referrals for confirmation of a diagnosis. It may be that thereafter admissions fell as a result of patients being established on evidence-based therapies; patients being managed more in the community by specialist heart failure nurses and GPs referring patients as emergencies into the clinics and home based service rather than admitting. Obviously this is retrospective audit data which is open to confounding factors such as coding errors, privatisation and availability of nursing and residential homes, social services, GP and district nursing workload. It will be interesting to observe the continuing trend over the next few years. Admissions to DMH with a secondary diagnosis of heart failure are variable from year to year and most probably reflect difficulty in coding such admissions (see Table 4.4).

Table 4.5. Average length of stay for heart failure patients DMH 2003-2005

Calendar year	Average LOS
2003	12.86
2004	11.67
2005	10.40
Average	11.80

The average length of hospital stay for patients with heart failure exceeds that of all other condition apart from stroke, averaging 14 days in 2002[24].

The figures for DMH show a decline of 2.46 days between 2003 and 2005 (see Table 4.5). Whilst this may not be as substantial as one would hope it represents a move in the right direction that has cost savings implications for the NHS. Furthermore it compares favourably with average lengths of inpatient stay of 14 and 16.5 days in studies from Scotland[61] and the Netherlands[62] respectively. It cannot be said that the local heart failure services have directly lead to this decline in length of stay but may certainly have contributed by specialist nurse involvement in discharge planning, follow up at home and quicker access to echocardiography.

4.5.5 Patient follow-up

The integration of the one-stop diagnostic clinic into the Darlington heart failure service is shown in Figure 4.2. The clinic takes referrals from different outpatient and inpatient specialties. Once a diagnosis has been reached, the patient either returns to primary care, or attends the heart failure clinic or other specialties as appropriate. Ongoing LVSD management is carried out in both primary and secondary care. After receiving further education, many GPs are now confident in up titrating the doses of beta-blockers and other drugs. In secondary care, ongoing management is carried out by a specialist nurse and a pharmacist. A project to assess the effectiveness of heart failure rehabilitation and exercise training is planned.

4.6 Service evaluation

Service evaluation has been carried out with feedback from GPs and patients (see section 4.8.2).

These will be reported elsewhere. In brief the results indicated that;

- A majority of GPs preferred the one stop clinic model to open access echocardiography or traditional cardiology outpatient clinics
- Whilst GPs were happy to initiate diuretics and ACE inhibitors, only a minority felt confident in using beta-blockers in HF
- Over 95% of patients were satisfied with the service they received at the one stop clinic

The results were used to improve and further optimise the service offered to NHS patients.

4.7 Changing GP contractual obligations

4.7.1 The new GMS contract

The new GMS contract[381] should further increase the uptake of evidence-based therapies. The contract enables separate agreements to be negotiated for each practice. It rewards quality, with a system in which all work is converted into points. For 2004/5, one point is worth £75 and for 2005/6 one point will be worth £120. The four main domains of quality are clinical, organisational, patient experience, and additional services (including child health surveillance, childhood immunisation, cervical screening). There are also 50 bonus points for achieving access targets. Clinical issues account for the highest number of points and 346 of the 550 clinical quality points are broadly based around cardiovascular disease. 20 of those points are specifically to meet indicators for left ventricular dysfunction (LVD). See table 4.6 below:

Table 4.6   New GMS Quality Indicators for Left Ventricular Dysfunction (LVD)

Indicator	Points	Payment stages
LVD 1. Practice can produce register of patients with CHD and LVD	4	
LVD 2. Percentage of patients with CHD and LVD (Diagnosis after 1/4/03) confirmed by echo	6	25-90%
LVD 3. Percentage of patients with CHD and LVD currently treated with ACEi or ARB	10	25-70%

4.7.1.1 New GMS contract LVD data

The first new GMS/QMAS[381] data was collected in March 2005 and all 11 Darlington practices achieved 100% for LVD 2, suggesting that the one stop clinic is enabling GPs to have all their patients investigated. Only one practice did not achieve maximum payment for LVD 3 by achieving 68% ACEi/ARB use. The other ten all met targets with a range from 70-100% achievement. (See table 4.7 below)

Table 4.7 Summary of Quality Outcome Framework data for Darlington practices - March 2005

	Practice number	1	2	3	4	5	6	7	8	9	10	11
Indicator	Denominator	25	26	105	14	43	97	96	42	52	58	22
	Target											
LVD 1	100%	100	100	100	100	100	100	100	100	100	100	100
LVD 2	90%	100	100	100	100	100	100	100	100	100	100	100
LVD 3	70%	100	89	68	100	75	89	81	97	76	98	90
Total points	121	121	121	120.3	121	121	121	121	121	121	121	121

4.7.2 Potential hospital influences on new GMS contract

There are several ways in which secondary care colleagues can help GPs meet the targets in the GMS contract. Good communication and interaction with primary care is essential. It is important to agree local management guidelines, and to have rapid, clear and accurate correspondence, perhaps

using a template for clinic letters to highlight the data that are required (as we do from the one stop clinic). In the Darlington area, pharmacists now indicate on discharge letters why a drug has been stopped or started and this information is very useful to GPs. There is a need for education of hospital medical staff about the contract.

4.7.2.2 Myocardial Infarct National Audit Program (MINAP) data

MINAP data for the Darlington Memorial Hospital show that the NSF target for prescribing of ACE inhibitors and beta-blockers to eligible patients on discharge after MI is being met in 86% and 83% of patients, respectively. As many patients develop LVSD after an MI this will help GPs achieve targets.

4.8 Discussion

4.8.1 Strengths of the service

Whilst HF care varies substantially across the country this project shows that good HF care can be delivered in the NHS and has been singled out as a model of excellence by a recent Royal College of Physicians report[383]. Although many new referrals to the clinic did not in fact have HF, a reliably accurate diagnosis can be achieved which is important for correct management. Particular strengths of the service are emphasis on patient involvement and education, improving patient compliance with treatment and improving communication between health care professionals and patients as well as between primary, secondary and tertiary care. Local palliative care access is a great strength of our service model.

The candesatran on mortality and morbidity in patients with chronic heart failure (CHARM) screening programme[13] and the Euro-Heart survey[148] showed the UK to have lower use of beta-blockers and spironolactone than other European countries. Our clinic experience demonstrates that beta-blocker usage can be improved. We experienced difficulty establishing elderly patients on spironolactone, largely due to side effects of renal impairment, postural hypotension and gynaecomastia. The recent introduction of

eplerenone, an aldosterone antagonist with mortality benefits and fewer side effects is a welcome development[264].

The service meets all of the 8 key recommendations of NICE guidance for HF management[105] :

- *The basis for historical diagnoses of HF should be reviewed, and only patients whose diagnosis is confirmed should be managed according to the guideline* (Our data show that of primary care referrals, only two in every five patients had the diagnosis confirmed – thus three out of every five could have been treated inappropriately)

- *Doppler 2D echocardiographic examination should be performed to exclude important valve disease, assess the systolic (and diastolic) function of the (left) ventricle and detect intracardiac shunts* (We would argue that just providing an echocardiogram does not equate to making a diagnosis of heart failure, and that the more broadly based service provides diagnosis and management planning)

- *All patients with heart failure due to left ventricular systolic dysfunction should be considered for treatment with an ACE inhibitor*

- *Beta-blockers licensed for use in heart failure should be initiated in patients with heart failure due to LVSD after diuretic and ACE inhibitor therapy (regardless of whether or not symptoms persist)* (Our service demonstrated high uptake of both Ace inhibitors and beta-blockers at evidence based target doses)

- *Patients should generally be discharged from hospital only when their clinical condition is stable and the management plan is optimised* (Involvement of specialist heart failure nurse and pharmacists in identification of HF patients for referral into the service contributes to appropriate discharge of these vulnerable patients)

- *The primary care team, patient and carer must be aware of the management plan* (Our letters back to GPs are structured and educational in their content with a clearly outlined management plan)

- *Management of heart failure should be seen as a shared responsibility between patient and health care professional* (Our service is based on shared responsibility, patient and carer education and empowerment. Interventions are individualised and tailored for each patient as it is clearly not feasible for all patients with HF to be asymptomatic, even on optimal therapy)

- *All patients with chronic heart failure require monitoring. This monitoring should include:*

  - *a clinical assessment of functional capacity, fluid status, cardiac rhythm, cognitive and nutritional status*

  - *a review of medication, including need for changes and possible side effects*

  - *serum urea, electrolytes and creatinine*

  (All patients are closely monitored in the clinics and GPs advised on future monitoring on discharge from the clinic. GP specialist and pharmacist review all medication)

4.8.2 GP and patient satisfaction surveys

The diagnosis of heart failure due to left ventricular systolic dysfunction cannot be made by clinical assessment alone or by electrocardiography or chest X-ray in isolation or combination[139]. Echocardiography is the optimal way of confirming left ventricular systolic dysfunction[127,233]. Yet, five general practitioners (11.6%) from a survey of forty three respondents (response rate 77%), felt that they could diagnose left ventricular systolic dysfunction by clinical assessment alone. 62.8% of general practitioners felt chest X-ray could be used to diagnose heart failure. Only a third (32.5%) felt an electrocardiogram and the majority (83.7%) felt echocardiography was useful. Three general practitioners (7%) felt an echocardiogram was not useful in making a diagnosis. This suggests that there is still lack of awareness of the need for echocardiography in accurately diagnosing left ventricular systolic dysfunction.

When asked about treatment of heart failure, all general practitioners were happy to initiate diuretics and ACE inhibitors. However, almost three quarters (74.4%) were not happy to use beta-blockers. A third (32.6%) were unhappy using spironolactone and 37.2% did not feel they could use digoxin. This would seem at odds with evidence-based guidelines recommending consideration of beta-blockers for patients with stable heart failure and spironolactone and digoxin in selected patients[127,233]. Guidelines do suggest that beta-blockers should be initiated and titrated by a clinician skilled in the management of heart failure[127,233]. Recent reports from outpatient and primary care settings advise that beta-blockers can be initiated safely using simple protocols[258,384]. However, until all general practitioners are confident in the use of beta-blockers, spironolactone and digoxin in heart failure, a GP service that is able to initiate these agents and to contribute to better understanding is one way of addressing these shortcomings.

The majority of general practitioners (58.1%) preferred the 'one stop heart failure clinic' run by a general practitioner with a specialist interest. Around a quarter (25.6%) favoured an open access service. Four general practitioners (9.3%) liked all three options, and two (4.7%) preferred a combination of open access echocardiography and a one-stop clinic for more difficult patients. Only one (2.3%) would refer to a consultant for all cases.

Notably five of the GPs who wanted OAE with a clinical report did not feel confident in prescribing beta-blockers or spironolactone and one did not feel confident in prescribing digoxin. This raised the question as to whether OAE alone would facilitate evidence-based treatments to patients with LVSD.

Having an interested/trained general practitioner within a practice who is confident in the management of all aspects of heart failure may be a way of increasing the uptake of newer therapies. 91% of general practitioners were happy to refer to another colleague with heart failure expertise within the practice. It would seem that identifying a general practitioner in each practice and training them up to the standard of a 'Heart Failure Certificate' may be a useful way of advancing and improving the management of heart failure in a locality.

The implications from this survey are that following the one-stop HF clinic GPs are not comfortable with the introduction of evidence-based therapies such as beta-blockers. Despite the risk of becoming de-skilled, over 90% of the doctors in this sample were happy to refer to a GP trained in HF from within the practice for long term management.

Service design is often dictated by the availability of resources in secondary care. GPs expressed a strong preference for the one-stop HF clinic and only a minority wanted OAE. The traditional general cardiology clinic was not supported.

A literature search and verbal contact with experts in the field of heart failure failed to identify a validated questionnaire for use in assessing patient satisfaction. A postal questionnaire was designed and sent to 47 of 51 consecutive patients accessing the clinic. To ensure the questionnaire was appropriate and to minimise bias it was reviewed by Primary Care Trust clinical governance and changes made accordingly. Whilst being mainly yes/no answers we also provided space for subjective patient comment.

Prior to the survey, a flyer was sent out giving patients the opportunity to refuse being a part of the survey. A total of 51 people were approached to take part in the survey. 47 agreed to receive a postal questionnaire.

Patient satisfaction was assessed in 39 patients (83% response rate)

- 95% felt they had enough information prior to attendance
- 100% had enough information about tests received
- 97% said results were clearly explained
- 97% were made aware of the diagnosis at the clinic
- 87% received enough advice at clinic
- 95% said it was beneficial to have all tests and receive diagnosis at the same appointment – 2 (5%) did not answer
- 95% said the waiting time for initial appointment was acceptable – 2 (5%) did not answer
- 95% said they were treated with courtesy and respect and the same number felt there was adequate privacy – 2 (5%) did not answer

The questionnaire showed that the open stop clinic was popular and well received by a large majority of patients. Undertaking the patient satisfaction survey has proved a useful tool in making changes to the clinic. The changes that have been made include:

❖ Patients may have a robe should they request it.

❖ Summing up after the tests has become more structured and in words that patients and carers can understand. Patients (and carers) are offered the opportunity to discuss their diagnosis with medical and nursing staff at the clinic. Patients with concerns or educational needs may be followed up at home, and will be given a Helpline number to contact the specialist heart failure nurse if a visit is required.

❖ Patient information sheet sent with appointment time and date has been adapted to give more clarity about the length of time in different diagnostic areas, having to undress more than once and general clinic procedures, including potential invitations to participate in research projects

❖ Patients from outside of the Darlington PCT area are referred to their local CHD Nurse or Heart Failure Nurse at the point of discharge from the clinic to ensure continuity of care. Letters will be copied to the appropriate nurse.

❖ Option to refer to dietician for obesity and cardiac cachexia has been formalised with the dietetic department

One patient expressed a desire to be reviewed by myself and the specialist nurse after their cardioversion for atrial fibrillation. We need to explain follow up arrangements to patients, but if they do not have LVSD they tend to be reviewed at the general cardiology clinic, hence maintaining capacity in our clinic for new patients and those with LVSD.

Potential changes which could be made to improve the patients experience include copying patients into communication about them made between clinicians. This has been recommended by two patients at the clinic and is suggested by the Department of Health. The initiative to copy clinician's letters to patients is part of the government's policy to increase patient involvement

in their care and treatment and to keep patients up to date about these matters. Both the NHS plan and the Kennedy Report of the Public Inquiry into children's heart surgery at the Bristol Royal Infirmary refer to copying to patients letters that are written between clinicians about them. There is wide spread support that the partnership between doctors and their patients should be improved and strengthened, and that providing better and timely information to patients is an essential element of a modern and effective health service. It is one strand in the many different ways needed to improve and enhance communications between patients and professionals in the NHS

4.8.3 Weaknesses of the service

The service concentrates on patients with systolic dysfunction due to the benefits these patients derive from evidence-based therapy. As diastolic heart failure is harder to diagnose and we know little about effective therapies these patients were excluded from the heart failure nursing service and follow up. However, patients with diastolic heart failure are often admitted and also have a poor quality of life and may stand to benefit from nursing interventions[138]. We plan to study the impact of such interventions in this group of patients in future service developments and research projects.

It is easy to presume that simply measuring the process of prescribing more will reduce morbidity and mortality. This assumption is based on the premise that the process of prescribing ACE inhibitors[211] and beta-blockers[259] is a reasonable proxy for outcome improvement extrapolated from the clinical trial data to real life practice. Unfortunately it is difficult to show that reduction of mortality and hospital re-admissions, and improvements in quality of life are as a direct result of interventions implemented in the heart failure clinic. However, measurements of mortality, hospital re-admissions and quality of life parameters are required by politicians, PCT audit and clinical governance managers, and may persuade commissioners of care to continue investing in a service.

Reliance on a single GP specialist means that clinic waiting times can increase with sickness or holiday absence of the GP specialist. We have been

unable to attract a second GP specialist but have arranged for a consultant cardiologist or staff grade cardiologist to cover the clinic if waiting times become unacceptable (over 4 weeks).

Hospital IT databases are cumbersome and have hindered the process of data collection. Improvements in hospital IT and its interface with primary care are urgently needed.

4.9 Future service developments

A number of key developments to the service are underway. These include a secondary care integrated pathway, establishment of a heart failure rehabilitation/exercise training programme, and development of a common IT database. These developments should lead to a comprehensive heart failure service that delivers seamless care to patients across primary, secondary and tertiary care.

4.10 Conclusions

A GP specialist led diagnostic clinic facilitated accurate diagnosis of LVSD in a single clinic visit rather than after repeated visits for further diagnostic tests, and was well received by GPs and patients. The majority of patients received evidence based therapy and attained target doses of ACE inhibitors and beta-blockers. Contrary to perceived anxieties regarding use of BBs in outpatients we achieved a high level of use (70%), even in patients with severe LVSD, without observation of clinical parameters at initiation of therapy. The heart failure nursing and review clinic component and other elements of this integrated service deliver high quality care[189]. Similar models of care should offer expedient care for patients with suspected LVSD, deliver NSF targets, compliment secondary care services and in my opinion urgently need to be developed across other NHS sites.

Despite the success of our model and other heart failure clinics[21-23], the importance of accurate diagnosis of heart failure[9-12] and the continuing debate around optimal service delivery[15, 16] with some areas in the NHS still offering

traditional cardiology clinic referral or open access echocardiography there are no comparative studies of traditional outpatient care (usual care), open access echocardiography or heart failure diagnostic clinics. Further research is needed to determine the optimal service delivery model. Outcomes that would need to be considered would need to include uptake rates of ACE inhibitors and beta blockers for patients with LVSD; quality of control of heart failure symptoms; rates of referral to hospital and numbers of patients requiring emergency admission for heart failure; health economics outcomes; quality-of-life analyses; rates of inappropriate use of ACE inhibitors and beta blockers in patients with non-LVSD heart failure; proportions of patients achieving target doses of ACE inhibitors and beta blockers and rates of diagnosis of LVSD between the two groups. Furthermore, the practical management of patients with left ventricular diastolic dysfunction or heart failure with PLVEF needs further study.