

Full version of
NICE Guideline No. 5

CHRONIC HEART FAILURE

National clinical guideline for diagnosis and management
in primary and secondary care

Developed by

The National Collaborating Centre

for Chronic Conditions

Acknowledgements

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Preface

It is a pleasure to welcome you to this guideline on the management of chronic heart failure which aims to describe best practice for the healthcare management of a complex disorder that affects individuals and their carers in many and varied ways. Heart failure is common and causes considerable morbidity and mortality – much of which can be prevented or delayed by appropriate management. It is hoped that if the principles set out in this document are followed, then service provision will be improved and those with heart failure will benefit with reduced future levels of disability.

The guideline was commissioned by NICE and the scope for the project was developed by the National Collaborating Centre for Chronic Conditions with input from all the stakeholders registered with NICE. Because the guideline relates to care within the NHS, its scope is limited in the main to health aspects of heart failure. However, as effective care requires support from other agencies, including social services, the document touches on but does not discuss in detail their involvement. There was also a stipulation that if a particular topic was already covered by an existing NICE appraisal report, then the recommendations of the report should be incorporated without reassessing all the original evidence.

This guideline has examined the published evidence on heart failure with considerable thoroughness. Because its scope was so wide ranging, even with an extremely hard-working and dedicated team, it was not possible to examine every paper on every topic. Some pragmatic choices had to be made: we searched first for the best research designs and if several were found that provided a strong evidence base, did not continue to consider papers of less methodological rigour. The searching for, and systematic critical appraisal of, studies was done using standard techniques and all the searches will be available to future researchers. We believe it is unlikely that important papers have been missed either by the technical team in their searches or by the expertise of the guideline groups.

For many areas of management there is weak or no evidence upon which to base recommendations. However, the guideline has to cover all aspects of the disease if users are to develop their local care pathways from the document. The gaps between the published evidence have been filled with best practice recommendations based on a formal consensus of the experts on our guideline groups. In each section of the document the level of supporting evidence is made clear on the understanding that the stronger the evidence, the greater likelihood that the recommendations based on it are sound. However, the reader should not equate level of evidence strength with strength of recommendation – some of the most important recommendations with greatest consequences for the health service, or for patients with heart failure, have been made by group consensus. This is what the experts believe to be best practice, ie what they would recommend for their patients or relatives.

While the details of local implementation of this guideline may vary (according to local facilities and geography), the main recommendations, if adopted across the country, should lead to better standards of care and thus better outcomes from this debilitating condition. There will

be some readers who will find particular recommendations, especially those reached by consensus, hard to accept. To them the challenge is to go out and produce and publish evidence to either confirm or refute what this guideline sets out. Such additional research and thought should make future versions of this guideline even stronger.

The final challenge is to all those involved in healthcare (those that commission care, those that deliver care, and the patient and carer groups) to ensure that these guidelines are used. We know that the lot of those with heart failure can be improved, but we have to find ways of translating the knowledge set out in this document into organised systems that actually deliver high quality care wherever it is needed.

Mike Pearson FRCP
Director, National Collaborating Centre for Chronic Conditions

DEVELOPMENT OF THE GUIDELINE

1 Introduction

1.1 Definition of heart failure

Heart failure is a complex syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the heart to function as a pump to support a physiological circulation. The syndrome of heart failure is characterised by symptoms such as breathlessness and fatigue, and signs such as fluid retention.

There is no single diagnostic test for heart failure, and diagnosis relies on clinical judgement based on a combination of history, physical examination and appropriate investigations. These are discussed in more detail in the diagnosis section (Section 6).

1.2 Clinical context

Around 900,000 people in the UK today have heart failure – with almost as many with damaged hearts but, as yet, no symptoms of heart failure.¹ Both the incidence and prevalence of heart failure increase steeply with age, with the average age at first diagnosis being 76 years.² While around 1 in 35 people aged 65–74 years has heart failure, this increases to about 1 in 15 of those aged 75–84 years, and to just over 1 in 7 in those aged 85 years and above.³ The risk of heart failure is higher in men than in women in all age groups, but there are more women than men with heart failure due to population demographics.¹

The most common cause of heart failure in the UK is coronary artery disease – with many patients having suffered a myocardial infarction in the past.¹ A history of hypertension is also common, as is atrial fibrillation. Heart damage of unknown cause – such as dilated cardiomyopathy – accounts for just under 15% of cases under the age of 75.⁴ There are few reliable data for different ethnic groups; it is likely that people of African or Afro-Caribbean origin are more likely to develop heart failure due to hypertension rather than coronary artery disease, whereas those of Asian origin have a greater risk of developing heart failure due to coronary artery disease – often accompanied by obesity and diabetes mellitus.

Heart failure has a poor prognosis: just under 40% of patients diagnosed with heart failure die within a year – but thereafter the mortality is less than 10% per year.⁵ Survival rates are similar to those from cancer of the colon, and worse than those from cancer of the breast or prostate.⁶ Younger patients do better, as do patients with no other medical problems.

On average, a general practitioner will look after 30 patients with heart failure, and suspect a new diagnosis of heart failure in perhaps 10 patients annually. Those who work in more deprived areas are likely to have more cases. The cost of general practitioner consultations has been estimated at £45 million per year, with an additional £35 million for GP referrals to outpatient clinics. In addition, community-based drug therapy costs the NHS around £129 million per year.⁷

Heart failure accounts for a total of 1 million inpatient bed days – 2% of all NHS inpatient bed-days – and 5% of all emergency medical admissions to hospital. Hospital admissions due to heart failure are projected to rise by 50% over the next 25 years – largely due to the ageing of the population. It is estimated that the total annual cost of heart failure to the NHS is around £716 million, or around 1.8% of the total NHS budget: approximately 70% of this total is due

to the costs of hospitalisation.^{1,7} The costs increase with disease severity, with the healthcare costs for patients with the most severe symptoms between 8 and 30 times greater than those with mild symptoms.⁸

As well as NHS costs, heart failure also places a burden on other agencies such as social services and the benefits system, and of course on the patients with heart failure and their families and caregivers.

For patients and their carers, the costs are more difficult to quantify but the burden is both financial and via adverse effects on their quality of life. The financial costs of heart failure to the patient and family arise from prescription charges (in patients under the age of 60), attendance at GP surgeries and outpatient clinics, hospital stays, modifications to the home and loss of earnings due to absence from work or loss of employment (although given that heart failure is more common in older people, productivity losses may not be as great as for other chronic conditions).

Quality of life is affected by the physical limitations imposed by the disease, and also by the social limitations that follow from this and the emotional problems that may also arise. These symptoms can be caused by the disease itself, by co-morbidities, or can result from the side effects of treatment. There is, however, evidence that both pharmacological and non-pharmacological treatments can improve patient quality of life, both in terms of physical functioning and well-being.⁹

1.3 Guideline aims

This guideline offers best practice advice on the care of adult patients (aged 18 years or older) who have symptoms or a diagnosis of chronic heart failure. It aims to define the most effective combination of symptoms, signs and investigations required to establish a diagnosis of heart failure, and those which will influence therapy or provide important prognostic information. It also gives guidance on the treatment, monitoring and support of patients with heart failure.

1.4 For whom is the guideline intended?

Clinical guidelines have been defined as ‘systematically developed statements to assist both practitioner and patient decisions in specific circumstances’.¹⁰

These guidelines are aimed at helping all healthcare professionals provide optimal services for patients with heart failure by:

- providing individual clinicians with a set of explicit statements on the best way to manage the most common clinical problems, and to maximise the effectiveness of the service
- providing commissioning organisations and provider services with specific guidance on the best way to provide complex services, to maximise efficiency and equity.

Others, including the general public, may find the guideline of use in understanding the clinical approach to heart failure. Separate short form documents for the public and clinical staff are available which summarise the recommendations without full details of the supporting evidence. These documents are available from the NICE website (www.nice.org.uk) or, within the UK, from the NHS Response Line (0541 555 455).

1.5 Underlying guideline principles

The main principles behind the development of this guideline were that it should:

- consider all issues that are important in the management of patients with chronic heart failure
- use published evidence wherever this is available
- be useful and usable to all professionals
- take full account of the perspective of the person with heart failure and their carers
- indicate areas of uncertainty or controversy needing further research.

1.6 Definition of a specialist

The term ‘specialist’ is applicable to a wide range of healthcare professionals; however within the context of this guideline, the term specialist is most often used in relation to the prescription of drugs or the decision to perform invasive investigations or procedures.

As such, a specialist is defined as a healthcare professional with special knowledge and experience in heart failure. As well as cardiologists, this could include a wide range of physicians and (increasingly) other professional groups in primary and secondary care.

1.7 Structure of document

Sections 6–13 of the document contain the guidelines, each of which covers a set of related topics. For each topic the layout is similar.

The **background** to the topic is provided in one or two paragraphs that simply set the recommendations in context.

Then the **evidence statements** are given which summarise the evidence detailed in the **evidence tables** (Appendix J or www.rcplondon.ac.uk/pubs/books/chf/). In addition, there is an evidence statement about the health economic evidence where this is available. These evidence statements and tables aim to provide context and aid the reader’s understanding of why each recommendation was made.

The main **recommendations** follow. These are graded to indicate the strength of the evidence behind the recommendation (see Section 3). In some sections of the guideline, additional text providing more detailed guidance follows a recommendation.

1.8 Guideline limitations

The document and recommendations are subject to various limitations. The sponsoring authority, NICE, is concerned primarily with health services, and so these recommendations only indirectly refer to social services, the voluntary sector and post-transplant care. Nonetheless, the importance of other agencies cannot be over-stated and in each locality the aim should be to integrate heart failure care across all relevant sectors.

A systematic approach was used to locate and appraise the evidence and explicit inclusion criteria were applied. Due to the magnitude of the literature potentially relevant to heart failure, the inclusion criteria aimed to limit the included studies to those of a higher quality conducted primarily in patients with heart failure. Where these were not available, well-conducted studies outside heart failure, or lower level studies in patients with heart failure, were included.

1.9 Scope

The guideline was developed in accordance with a predetermined scope, which detailed the remit of the guideline development and specified those aspects of heart failure to be included and excluded.

Before the guideline development began, this scope was subjected to stakeholder consultation in accordance with processes established by NICE.¹¹

The scope is detailed below.

▷ Inclusions

The guideline covers the care provided by primary and secondary healthcare professionals who have direct contact with, and make decisions concerning the care of, patients with heart failure. The guideline also addresses the interface between primary and secondary care, including in what circumstances patients should be referred to or admitted to secondary care.

Where available, evidence for the following circumstances was considered:

- referral for invasive procedures including pacing, implantable cardiac defibrillators, coronary artery bypass grafting, angioplasty, valve surgery and transplantation surgery
- referral to supportive and palliative care.

The guideline addresses all the key areas of managing chronic heart failure.

Diagnosis – Systolic and diastolic dysfunction, valve disease and the other causes of heart failure. The value of a range of diagnostic techniques including ECG, chest X-ray, biochemical markers and imaging techniques.

Treatments – The goals of treatment are defined in terms of symptom reduction, functional ability, hospitalisation and mortality.

Pharmacological treatments – The initiation, dosage, sequence and monitoring of the following preparations:

- ACE inhibitors
- angiotensin-II receptor antagonists
- beta-blockers
- digoxin
- diuretics
- nitrates and other vasodilators
- spironolactone.

The guideline usually recommends within the licence indications. Exceptionally, where there was clear supporting evidence, recommendations outside the licence indications have been included. Where this is the case, it is clearly indicated to alert the reader.

Non-pharmacological treatment – Exercise programmes and rehabilitation. Lifestyle advice on diet, physical activity, weight reduction and smoking cessation.

Management of depression and/or anxiety – Only as it pertains directly to patients with heart failure.

▷ Exclusions

This guideline does not include specific reference to ‘acute’ heart failure, but does include comment on exacerbation of the syndrome and the causes and treatment of this, recognising that chronic heart failure often has an undulating course.

The guideline does not address the screening or diagnosis of people who are asymptomatic, nor does it address the management of patients with right heart failure as a consequence of respiratory disease.

In addition, the guideline does not cover the organisational aspects of heart failure management. It does not therefore address models of care, the roles or composition of primary or secondary healthcare teams and competencies, skillmix or training requirements.

This guideline is relevant to the work of, but does not cover the practice of, social services, the voluntary sector and those working in post-transplant care.

▷ Presentation

This heart failure guideline is available in three forms:

- this full guideline, which contains the complete evidence statements and recommendations (with evidence tables accessible in web-based format)
- a short form version
- a version of the short form prepared specifically for the public, including patients and their carers.

1.10 Plans for guideline revision

The process of reviewing the evidence is expected to begin four years after the date of issue of this guideline (July 2007). Reviewing may begin earlier than four years if significant evidence that affects the guideline recommendations is identified sooner. The updated guideline will be available within two years of the start of the review process.

2 Methodology

2.1 The developers

The National Collaborating Centre for Chronic Conditions (NCC-CC) is housed by the Royal College of Physicians (RCP) but governed by a multi-professional partners board inclusive of patient groups and NHS management. The Collaborating Centre was set up in 2000 to undertake commissions from the National Institute for Clinical Excellence (NICE) to develop clinical guidelines for the National Health Service.

Editorial responsibility for the guideline rests solely with the development group.

Each commission is systematically developed from the current evidence base. Two multi-professional groups, supported by a technical team from the NCC-CC, were involved in the development of the guideline:

- a small **guideline development group** (GDG) that met monthly for twelve months and undertook the detailed evidence assessment and recommendation drafting
- an extension of the GDG, the larger **consensus/reference group** (CRG), which met twice throughout the process: once early in the development to ensure the clinical questions and aims were appropriate, and again at the end of the process to review the recommendations drafted by the GDG. The group employed formal consensus techniques in their consideration of clinically important areas where there was insufficient evidence.

Nominations for group members were invited from various stakeholder organisations, which were selected to ensure an appropriate mix of clinical professions and patient groups. Each nominee was expected to serve as an individual expert in their own right and not as a mandated representative, although they were encouraged to keep their parent organisation informed of the process. Group membership details can be found on pp v–vi of this document.

All group members made a formal ‘declaration of interests’ at the start of the guideline development and provided updates throughout the process. The NCC-CC and the group leaders monitored these.

2.2 Involvement of patients with heart failure

As part of the development process, the NCC-CC was keen to ensure that the guideline development process was informed by the views of patients with heart failure and their carers. This was achieved in two ways:

- by securing patient organisation representation on the guideline development group
- by carrying out a focus group to ensure that the views of people directly affected by heart failure informed the development of the guideline.

Patient representatives from the Cardiomyopathy Association and the British Heart Foundation were members of the GDG. They were therefore involved at every stage of the guideline development process and were able to consult with their wider constituencies throughout the process.

2.3 Searching for the evidence

There are three stages to evidence identification and retrieval:

- 1) The technical team set out a series of specific clinical questions (Appendix A) that covered the issues identified in the project scope. The CRG met to discuss, refine and approve these questions as suitable for identifying appropriate evidence within the published literature.
- 2) The information scientist developed a search strategy for each question to identify the available evidence. Identified titles and abstracts were reviewed for relevance to the agreed clinical questions and full papers obtained as appropriate. Full papers were assessed for inclusion according to predefined criteria (Appendix B).
- 3) The full papers were critically appraised and the pertinent data entered into evidence tables that were then reviewed and analysed by the GDG as the basis upon which to formulate recommendations.

Limited details of the searches with regard to databases and constraints applied can be found in Appendix B. Grey literature was searched for using the System for Information on Grey Literature in Europe (SIGLE). No formal contact was made with authors of identified studies. Additional contemporary articles were identified by the GDG on an *ad hoc* basis. Stakeholder evidence identified via a process established by NICE¹¹ was incorporated where appropriate, and was assessed for inclusion by the same criteria as evidence provided by the electronic searches.

Searches were re-run at the end of the guideline development process, thus including evidence published up to the end of September 2002. Studies recommended by stakeholders or GDG members that were published after this date were not considered for inclusion. This time-point should be the starting point for searching for new evidence for future updates to this guideline.

2.4 Synthesising the evidence

Abstracts of articles identified from the searches were screened for irrelevant items, and hard copies were ordered of papers that appeared to provide useful evidence relevant to each clinical question. Each paper was assessed for its methodological quality against pre-defined criteria using a validated evaluation tool. Papers that met the inclusion criteria were then assigned a level according to the evidence hierarchy as detailed in Section 3. Owing to practical limitations, selection, critical appraisal and data extraction were undertaken by one reviewer only. However evidence was considered carefully by the GDG group for accuracy and completeness.

Each clinical question dictated the appropriate study design that should be prioritised in the search strategy. In addition certain topics within any one clinical question at times required different evidence types to be considered. Randomised control trials (RCTs) were the most appropriate study design for a number of clinical questions as they lend themselves particularly well to research into medicines. They were not, however, the most appropriate study design for all clinical questions. For example, the evaluation of diagnostic tests is more suited to alternative research designs. Furthermore, RCTs are more difficult to perform in areas such as rehabilitation and lifestyle, where interventions may be tailored to the needs of the individual. As such, pharmaceutical interventions tend to be placed higher in the evidence hierarchy than other equally important interventions. This should not be interpreted as a preference for a

particular type of intervention or as a reflection of the quality of the evidence, particularly for those clinical areas where non-RCT evidence is valid and most appropriate.

Where available, evidence from well-conducted systematic reviews was appraised and presented. Trials included within these reviews are listed in the evidence table but were not critically appraised. Studies identified in addition to those included in the systematic review were included in the appraisal process.

The study populations considered varied between clinical questions. At times evidence was not available from studies that included a heart failure population; therefore it was necessary to consider studies in other chronic conditions. Where this occurred it is indicated in the relevant evidence statement.

Study quality, although formally assessed, was not used as a basis for informing the evidence level assigned to evidence statements. Descriptive limitations of studies are, however, included in the statements as appropriate. On occasion the GDG identified a clinical question that could not be appropriately answered through undertaking a systematic review (where the evidence was scarce, or where the question could not usefully be answered with the largely dichotomous output of a review). These questions were addressed via an expert-drafted discussion paper, subject to consideration by the GDG. In these instances there was no formal search strategy used by the clinical expert or assessment of the studies cited. These review papers were developed and used as a basis for discussion by the GDG as a whole.

Finally, national and international evidence based guidelines were referred to during the development process. These were not formally appraised owing to the inherent difficulties of such a process, in that the consistency of process and of evidence base can be difficult to ascertain across such documents.

2.5 Health economics evidence

While evidence on cost effectiveness was extracted from the main searches wherever it existed, this was rare; hence it was necessary to undertake a separate search for information on the potential costs and benefits of the interventions and management strategies considered in this guideline. The information scientist carried out these searches with guidance on search terms from the health economist. The GDG realised that few formal cost effectiveness analyses would be identified, therefore the search for economic evidence was very broad and designed to identify information about the resources used in providing a service or intervention and/or the benefits that can be attributed to it. No study design criteria were imposed *a priori*, ie the searches were not limited to RCTs or formal economic evaluations. Further details of the searches for economic evidence are given in Appendix C.

Identified titles and abstracts from the economics searches were reviewed by the health economist and full papers obtained as appropriate. The full papers were critically appraised by the health economist and the relevant data was conveyed to the GDG alongside the clinical evidence for each question. Given that the economics searches were so broad and that no standard measure of assessing the quality of economic evidence is available, careful consideration was given to each study design and the applicability of the results to the guideline context. An important issue in this respect is that much of the evidence on costs and benefits comes from the healthcare system in the United States and is therefore of limited applicability to a UK guideline.

As well as presenting existing evidence on the costs and benefits of a broad range of interventions to the GDG, the issue of echocardiography in the diagnosis of heart failure was identified as an important area for further economic analysis. This choice was made on the grounds that the diagnostic procedure may be associated with:

- potentially large health benefits
- a potentially large effect on NHS resources
- uncertainty surrounding the benefits and resources
- a potentially large service impact.

While health economic analysis can provide a framework for collating information from a variety of sources in order to estimate, and systematically compare, costs and benefits, this is a complex and labour intensive process and it does require a level of clinical evidence that is not always readily available. As a result the cost effectiveness of echocardiography in the diagnosis of heart failure was the only issue prioritised for further analysis. The results of this analysis are discussed briefly in section 6.1, with further detail in Appendix G.

2.6 Unpublished trials

We have referred in the text to all key ongoing trials which we were aware were going to publish within months of the cut-off date for literature searches, and which, in the opinion of the GDG, could conceivably impact on the guideline. This is intended to help the reader in using the guideline in the near future. The findings of such trials did not influence the formulation of recommendations in any way.

2.7 Drafting the recommendations

Evidence for each topic was extracted into tables and summarised in evidence statements. The GDG reviewed the evidence tables and statements at each meeting and reached a group opinion. Recommendations were explicitly linked to the evidence supporting them and graded according to the level of the evidence upon which they were based, using the grading system detailed in Section 3. **It should be noted that the level of evidence determines the grade assigned to each recommendation and as such does not necessarily reflect the importance attached to the recommendation.**

2.8 Agreeing the recommendations

Once the evidence review had been completed and an early draft of the guideline produced, a one-day meeting of the CRG was held to finalise the recommendations. This included a pre-meeting vote on the recommendations and a further vote at the CRG meeting, where the group were asked to consider the draft guideline in two stages.

- 1) Are the evidence-based statements acceptable and is the evidence cited sufficient to justify the grading attached?
- 2) Are the recommendations derived from the evidence justified and are they sufficiently practical so that those at the clinical front line can implement them prospectively?

There were three types of recommendation to be considered:

- a) A recommendation from the GDG based on strong evidence – usually non-controversial unless there was important evidence that had been missed or misinterpreted.

- b) A recommendation that was based on good evidence but where it was necessary to extrapolate the findings to make it useful in the NHS – the extrapolation approved by consensus.
- c) Recommendations for which no evidence exists but which address important aspects of heart failure care or management – and for which a consensus on best practice could be reached.

This formal consensus method has been established within the NCC-CC, drawing on the knowledge set out in the health technology appraisal,¹² and practical experience. It approximates to a modification of the RAND Nominal Group Process¹³ and will be fully described in future publications.

2.9 Writing the guideline

The guideline was drawn up by the technical team in accordance with the decisions of the guideline groups. The draft guideline was circulated to stakeholders according to the formal NICE stakeholder consultation and validation phase¹¹ prior to publication, and modifications, agreed by the GDG, were made as a result.

3 Hierarchy of evidence and grading of recommendations

Each recommendation has been allocated a grading which directly reflects the level of the evidence upon which it is based.

The gradings are as follows.

A hierarchy of evidence		Typical grading of recommendations	
Level	Type of evidence	Grade	Evidence
Ia	Evidence obtained from systematic review of meta-analysis of randomised controlled trials.	A	At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels Ia and Ib).
Ib	Evidence obtained from at least one randomised controlled trial.		
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.	B	Well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels IIa, IIb, III).
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study.		
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.		
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.	C	Expert committee reports or opinions and/or clinical experience of respected authorities. This grading indicates that directly applicable clinical studies or good quality are absent (evidence level IV).
		GPP	Recommended good practice based on the clinical experience of the Guideline Development Group.
DS	Diagnostic studies.	DS	Diagnostic studies.
NICE	Evidence from NICE guidelines or health technology appraisal programme.	NICE	Evidence from NICE guidelines or health technology appraisal programme.

The levels of evidence are included at the end of each evidence statement in bold type. Gradings of recommendations appear at the right of the text in each recommendation in bold type.

4 Glossary of terms

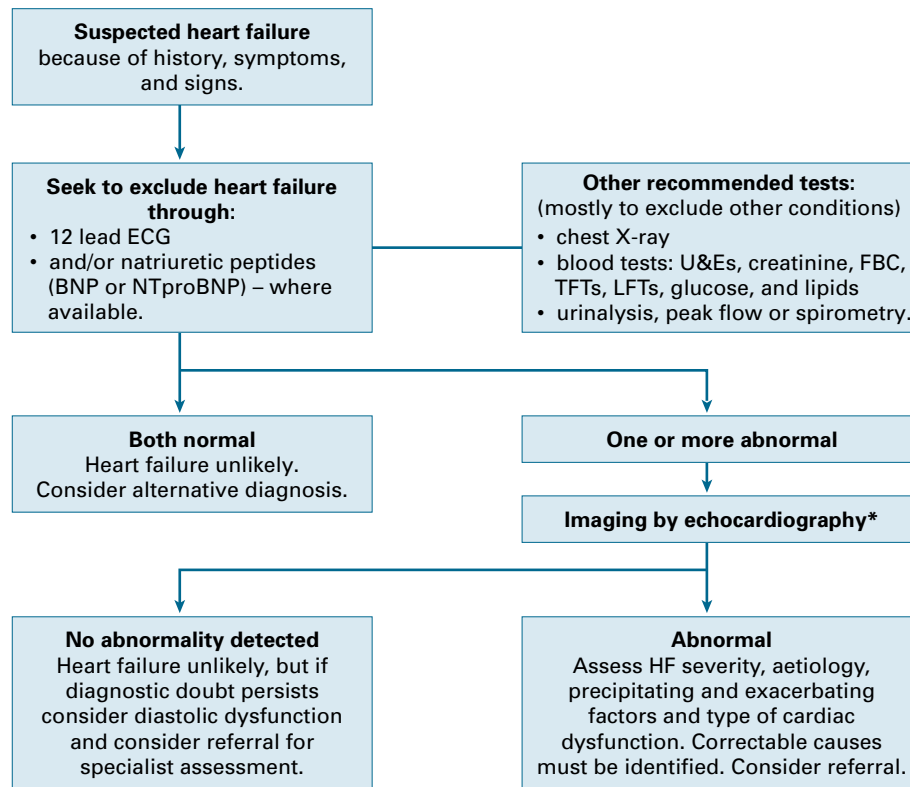
ACE inhibitor	Angiotensin-converting enzyme inhibitors.
AF	Atrial fibrillation.
ARVD	Arrhythmogenic right ventricular dysplasia.
BNP	B-type natriuretic peptide.
Bridge to transplantation	Mechanical support for the heart pending heart transplantation.
Brugada syndrome	Syndrome characterised by a structurally normal heart but a propensity to the potentially life-threatening heart rhythm problem, ventricular fibrillation.
CABG	Coronary artery bypass grafting.
CHD	Coronary heart disease.
CHF	Chronic heart failure.
CI	Confidence interval.
CMRI	Cardiac magnetic resonance imaging.
CRG	Consensus reference group.
CTR	Cardiothoracic ratio.
CXR	Chest X-ray.
DSMB	Data and safety monitoring board.
ECFV	Extra cellular fluid volume.
ECG	Electrocardiogram.
Exercise performance	Level of physical activity.
FEV1	Forced expiratory volume in one second.
FS	Fractional shortening.
FVC	Forced vital capacity.
GDG	Guideline development group.
GP	General practitioner.
GPP	Good practice point.
Haemodynamic	Relating to the circulation of the blood.
Hibernation	Heart muscle that is not contracting but still alive and may recover function if its blood supply is restored.
HBI	Home-based intervention.
HF	Heart failure.
Hypertrophic cardiomyopathy	Heart abnormality characterised by thickening of the heart muscle due to a genetic cause.
ICD	Implantable cardioverter defibrillator.
INR	International normalised ratio.
Ischaemia	Insufficient blood supply to an organ or tissue.
ISDN+Hyd	Isosorbide dinitrate and hydralazine.

K⁺	Potassium.
LBBB	Left bundle branch block.
Long QT syndrome	Syndrome with a characteristic change on the electrocardiogram, and a propensity to serious heart rhythm problems.
LV	Left ventricular.
LVADs	Left ventricular assist devices.
LVEF	Left ventricular ejection fraction.
LVSD	Left ventricular systolic dysfunction.
MI	Myocardial infarction.
NCC-CC	National Collaborating Centre – Chronic Conditions.
NICE	National Institute for Clinical Excellence.
NNT	Numbers needed to treat.
NSAID	Non-steroidal anti-inflammatory drug.
NSF	National Service Framework.
NTproBNP	N-terminal pro-B-type natriuretic peptide.
NYHA	New York Heart Association (functional classification).
PCI	Percutaneous coronary intervention.
PCT	Primary care trust.
PTCA	Percutaneous transluminal coronary angioplasty.
PVR	Pulmonary vascular resistance.
RBBB	Right bundle branch block.
Rehabilitation	Process to assist patients to achieve optimal function. May include a period of exercise training.
RNVG	Radionuclide ventriculography.
SIGN (Guidelines)	Scottish Intercollegiate Guideline Network.
Syncope	Blackout.
Tetralogy of Fallot	A type of congenital heart disease.
Titration	The administration of small incremental doses of a drug until a desired clinical effect is observed.
UK	United Kingdom.
Ventricular fibrillation	A type of serious heart rhythm problem with very rapid, irregular and uncoordinated electrical activity of the ventricles.
Ventricular tachycardia	A type of serious heart rhythm problem arising in the ventricles resulting in (usually) very rapid contraction of the ventricles.
Viable myocardium	Heart muscle that is still alive but may not be contracting.
VO₂	Oxygen uptake.
WMI	Wall motion index (an echocardiographic scoring system for assessing the function of the left ventricle).

THE GUIDELINE

5 Implementation summary of recommendations

5.1 Algorithm summarising recommendations for the diagnosis of heart failure



* Alternative methods of imaging the heart should be considered when a poor image is produced by transthoracic Doppler 2D-echocardiography – alternatives include transoesophageal echocardiography, radionuclide imaging or cardiac magnetic resonance imaging.

BNP = B-type natriuretic peptide; ECG = Electrocardiogram; FBC = Full blood count; LFTs = Liver function tests; NTproBNP = N-terminal pro-B-type natriuretic peptide; TFTs = Thyroid function tests; U&Es = Urea & electrolytes.

5.2 Recommendations for specialist referral

Patients with heart failure require specialist advice in the following situations:

- heart failure due to valve disease, diastolic dysfunction or any other cause except LV systolic dysfunction
- one or more of the co-morbidities outlined in Table 9
- angina, atrial fibrillation or other symptomatic arrhythmia
- women who are planning a pregnancy or who are pregnant.

The following situations also require specialist advice:

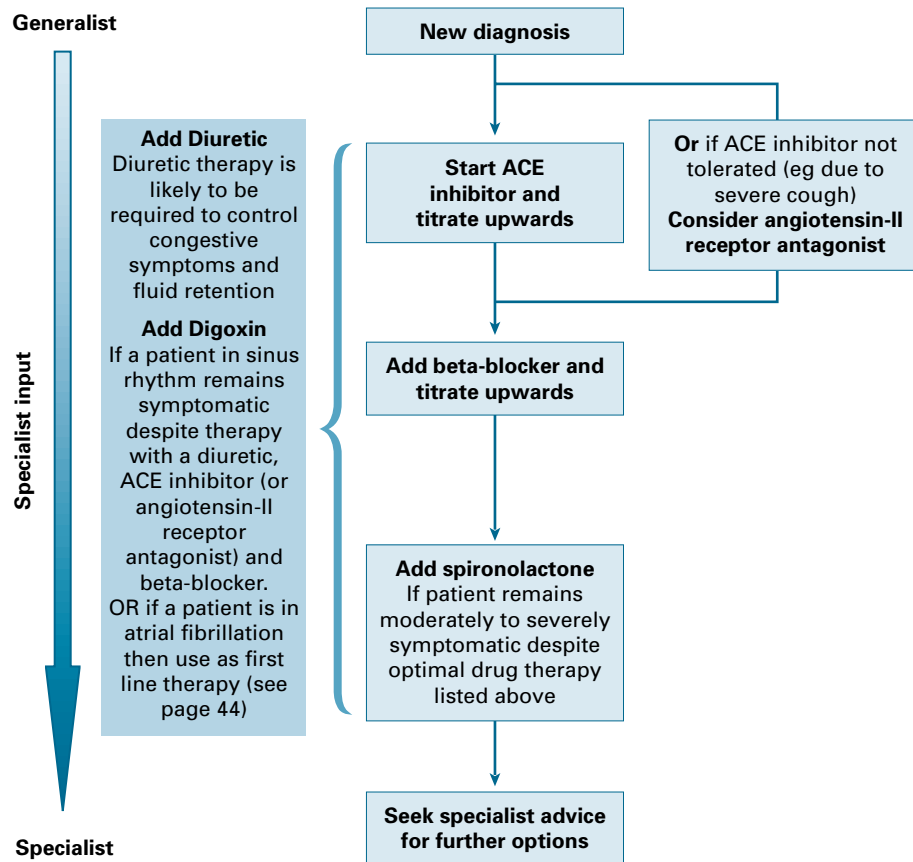
- severe heart failure
- heart failure that does not respond to treatment as discussed in this guideline and outlined in the algorithm
- heart failure that can no longer be managed effectively in the home setting.

5.3 Algorithm for the pharmacological treatment of symptomatic heart failure due to LV systolic dysfunction

Patients with symptomatic heart failure due to LV systolic dysfunction should be treated with the following drugs (if tolerated and not contraindicated) and in the sequence indicated. The reader must refer to the text of the main guideline for more detailed discussion and explanation.

Please note:

- Diuretic is first line therapy when a patient presents with acute pulmonary oedema
- Please refer to tables 3–7 (in Section 7) for starting doses of drugs
- The arrow on the left indicates the increasing likelihood of the need for specialist input.



5.4 Suggested audit criteria for implementation

Audit criteria				
Key recommendations	Criterion	Other relevant recommendations	Exceptions	Definition of terms
The basis for historical diagnoses of heart failure should be reviewed, and only patients whose diagnosis is confirmed should be managed in accordance with this guideline.	1. 'Disease register' % of patients on general practice heart failure registers who have had this diagnosis confirmed.	Where the diagnosis of heart failure is still suspected, but confirmation of the underlying cardiac abnormality has not occurred then the patient should have appropriate further investigation.	Patient choice; or where this would be inappropriate (eg terminal illness).	The diagnostic algorithm (see page 29) summarises how a diagnosis of heart failure should be confirmed.
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.	2. Echocardiography % of patients with a new diagnosis of heart failure (in the previous 12 months) who have had an echocardiogram.		Patient choice; or where this would be inappropriate (eg terminal illness).	
All patients with heart failure due to left ventricular systolic dysfunction should be considered for treatment with an ACE inhibitor.	3. ACE inhibitors % of patients with heart failure due to left ventricular systolic dysfunction who are prescribed an ACE inhibitor or an angiotensin-II receptor antagonist, if ACE inhibitors are not tolerated (eg due to cough).	At the time of issue of this guideline angiotensin-II receptor antagonists (see Table 8) are not licensed in the UK for heart failure and studies are ongoing. However, angiotensin-II receptor antagonists may provide an alternative to ACE inhibitors for patients intolerant of ACE inhibitors (for example, because of cough).	Patient choice; contraindications (see guideline text); or documented adverse events led to withdrawal of ACE inhibitor; heart failure not due to LV systolic dysfunction.	
Beta blockers licensed for use in heart failure should be initiated in patients with heart failure due to LV systolic dysfunction after diuretic and ACE inhibitor therapy (regardless of whether or not symptoms persist).	4. Beta-blockers % of patients with heart failure due to left ventricular systolic dysfunction who are prescribed a beta-blocker.	Patients who develop heart failure due to LV systolic dysfunction and who are already on treatment with a beta-blocker for a concomitant condition should continue with a beta-blocker – either their current beta-blocker or an alternative licensed for heart failure treatment.	Patient choice; contraindications (see guideline text); or documented adverse events led to withdrawal of beta-blocker; heart failure not due to LV systolic dysfunction.	

continued

Audit criteria – continued			
Key recommendations	Criterion	Other relevant recommendations	Definition of terms
<p>All patients with chronic heart failure require monitoring. This monitoring should include:</p> <ul style="list-style-type: none"> 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. 	<p>5. Monitoring % of patients with proven heart failure who are reviewed on a six-monthly* basis. * – this is a minimum</p>	<p>The frequency of monitoring should depend on the clinical status and stability of the patient. Monitoring interval should be short (days to weeks) if the clinical condition or medication has changed, but is required at least six monthly for stable patients with proven heart failure.</p>	<p>Patient choice.</p>
<p>Patients with heart failure should generally be discharged from hospital only when their clinical condition is stable and the management plan is optimised. The primary care team, patient and carer must be aware of the management plan.</p>	<p>6. Discharge planning a. % of patients with heart failure who have a pre-discharge management plan in place. b. % of patients discharged from hospital with a (primary or secondary) diagnosis of heart failure for whom a management plan has been rapidly communicated to the primary care team. c. 'Rapidly' will need to be defined and agreed at a local level, for audit purposes.</p>		<p>Patient choice.</p>
<p>Management of heart failure should be seen as a shared responsibility between patient and health care professional.</p>	<p>7. Patient understanding All patients with heart failure receive a copy of the public version of the guideline.</p>		<p>Patient choice.</p>

6 Diagnosing heart failure

▷ Introduction

The full evaluation of the patient with heart failure involves more than stating whether the syndrome is present or not; it requires consideration of the underlying abnormality of the heart, the severity of the syndrome, the aetiology, precipitating and exacerbating factors, identification of concomitant disease relevant to the management, and an estimation of prognosis.

6.1 Symptoms, signs and non-cardiac investigation

▷ Symptoms

Patients with heart failure may have a number of symptoms, the most common being breathlessness, fatigue, exercise intolerance, and fluid retention.^{14,15} (DS)

One of the primary symptoms of heart failure is breathlessness. The degree of exertion required to elicit symptoms such as breathlessness may be used to grade the severity of symptoms into one of four functional classes (Table 1).¹⁶ The functional class tends to deteriorate unevenly over time and the severity of symptoms does not necessarily equate with the severity of the underlying heart problem – mild symptoms may be found in patients with severe damage to the heart, and vice versa.^{15,17} Changes in medication and diet can have very favourable or adverse effects on functional capacity in the absence of any measurable change in heart function, however the severity of symptoms may fluctuate even in the absence of changes in medication.¹⁸ (IV)

Class	Symptoms
I	No limitations. Ordinary physical activity does not cause fatigue, breathlessness or palpitation. (Asymptomatic left ventricular dysfunction is included in this category.)
II	Slight limitation of physical activity. Such patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, breathlessness or angina pectoris (symptomatically 'mild' heart failure).
III	Marked limitation of physical activity. Although patients are comfortable at rest, less than ordinary physical activity will lead to symptoms (symptomatically 'moderate' heart failure).
IV	Inability to carry on any physical activity without discomfort. Symptoms of congestive cardiac failure are present even at rest. With any physical activity increased discomfort is experienced (symptomatically 'severe' heart failure).

Other non-specific symptoms of heart failure include nocturia, anorexia, abdominal bloating and discomfort, constipation, and cerebral symptoms such as confusion, dizziness and memory impairment.^{19,20} (IV)

None of the symptoms discussed above is specific to heart failure, and several other disorders may present in a similar manner (Table 2, overleaf). Therefore, symptoms alone cannot be relied upon to make the diagnosis^{21,22} which depends upon a combination of good clinical skills with history taking and physical examination, supplemented by tests (see below). (DS)

Table 2 Other conditions that may present with symptoms similar to those of heart failure

- Obesity.
- Chest disease – including lung, diaphragm or chest wall.
- Venous insufficiency in lower limbs.
- Drug-induced ankle swelling (eg dihydropyridine calcium channel blockers).
- Drug-induced fluid retention (eg NSAIDs).
- Hypoalbuminaemia.
- Intrinsic renal or hepatic disease.
- Pulmonary embolic disease.
- Depression and/or anxiety disorders.
- Severe anaemia or thyroid disease.
- Bilateral renal artery stenosis.

NB Elderly patients are particularly likely to have a number of concomitant medical problems.

▷ Signs

An elevated jugular venous pressure has a high predictive value in the diagnosis of heart failure,¹⁹ but is often not present. Several studies have shown that other clinical signs such as tachycardia, third heart sound, and displaced apex beat, have less predictive value if found in isolation.^{15,18,20,22–24} (IIb)

When multiple signs and symptoms are present, a diagnosis can be made with greater confidence, but further assessment is required to identify the underlying functional abnormalities. (IV)

▷ Cardiac assessment

Heart failure is most unlikely in a patient with a normal ECG^{25–27} or normal plasma concentration of BNP or NT-proBNP, given the high sensitivity of these tests.^{28–33} Normal results may, therefore, be useful in guiding the doctor to consider other diagnoses and investigations. Any abnormality of the initial 12-lead ECG, or plasma BNP does not confirm a diagnosis of heart failure and further investigation is required.^{23,26,34} The sensitivity of plasma BNP depends upon the assay and the cut-off value that is used, but may be as high as 90–97% for patients presenting with new symptoms.^{28,29} Cut-off values should be determined in consultation with the local biochemical laboratory. The sensitivity of the ECG will depend upon what features are considered abnormal and the experience of the ECG reader, and may be as high as 94%.^{25,26} (IIb)

Echocardiography and its interpretation is a crucial component in diagnosing heart failure.^{35–38} A high quality Doppler and 2D echocardiographic examination can provide much detailed information about the heart but is most informative after a careful history, physical examination, electrocardiogram (ECG) and chest radiograph have been obtained so that appropriate questions can be addressed. In general the more information provided with a request for this test, in particular the clinical reasons for requesting the test, the more specific and useful the interpretation will be. (IIb)

Most doctors will require the technical findings of echocardiography and other methods of imaging the heart to be interpreted, and are likely to need clinical advice regarding possible

further investigation and management decisions. Interpretation of the ECG may also be required. (IV)

Small case series have indicated that alternative methods of imaging the heart such as radio-nuclide angiography and cardiac magnetic resonance imaging can provide useful information on cardiac structure and function.^{39–41} (III)

Health economic evidence: A critical question is whether all patients with suspected heart failure should be referred for echocardiography, which would have substantial service implications. An economic model was constructed to compare this option with performing echocardiography only in patients with an abnormal ECG or BNP test (Appendix G). The model found that the cost per life year gained of echocardiography is very sensitive to the proportion of patients being sent for echocardiography who have the diagnosis of heart failure ultimately confirmed. The use of BNP (or NTproBNP) and ECG raises this proportion, and thus results in more efficient use of echocardiography facilities.

▷ Diastolic heart failure

Isolated diastolic dysfunction of the left ventricle may be the underlying cause of heart failure in a sizeable minority of patients with heart failure, particularly in the elderly. A definite diagnosis of isolated diastolic dysfunction can be made through cardiac catheterisation. There is no evidence that such investigation is justified for most patients with suspected heart failure, but it may be required in cases of serious diagnostic doubt.^{19,42–44} (IV)

Considerable debate continues as to how best to confirm a diagnosis of ‘diastolic’ heart failure. In practice, the diagnosis is generally based on the findings of typical symptoms and signs of heart failure in a patient who is shown to have normal left ventricular systolic function and no valvular abnormalities on echocardiography. The diagnosis of such ‘diastolic’ heart failure is thus usually by *exclusion* of other cardiac abnormalities. Further research in this area is required. It is important that other conditions that may masquerade as heart failure are excluded (see Table 2). (IV)

DIAGNOSTIC RECOMMENDATIONS*

- | | | |
|----|---|-----|
| R1 | Take a careful and detailed history, and perform a clinical examination. These should be combined with tests to confirm the presence of heart failure and make a complete diagnosis. | GPP |
| R2 | <p>Healthcare professionals should seek to exclude a diagnosis of heart failure through the following investigations:</p> <ul style="list-style-type: none"> ● 12 lead ECG ● and/or Natriuretic peptides (BNP or NTproBNP) – where available. <p>If one or both are abnormal a diagnosis of heart failure cannot be excluded and transthoracic echocardiography should be performed because it consolidates the diagnosis and provides information on the underlying functional abnormality of the heart.</p> | B |
| R3 | Efforts should be made to exclude other disorders that may present in a similar manner. | GPP |

*For explanation of recommendation grade, see p15.

R4	To evaluate possible aggravating factors and/or alternative diagnoses the following tests are recommended:	GPP
	<ul style="list-style-type: none"> ● chest X-ray ● blood tests: <ul style="list-style-type: none"> – biochemical profile including electrolytes, urea and creatinine – full blood count – thyroid function tests – liver function tests – fasting lipids – fasting glucose ● urinalysis ● peak flow or spirometry. 	
R5	Transthoracic 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.	GPP
R6	Transthoracic Doppler 2D echocardiographic studies should be performed on high-resolution equipment, by experienced operators trained to the relevant professional standards. Need and demand for these studies should not compromise quality.	GPP
R7	The reporting of Doppler 2D echocardiography should be by those experienced in doing so.	GPP
R8	Alternative methods of imaging the heart should be considered when a poor image is produced by Doppler 2D echocardiography. Such methods may include radionuclide angiography, cardiac magnetic resonance imaging, or transoesophageal Doppler 2D echocardiography.	B
R9	Where the diagnosis is unclear, or if a diagnosis of diastolic heart failure is being considered, the patient should be referred for more specialist assessment.	GPP

6.2 Review of existing diagnoses

The approach to the diagnosis and management of heart failure has changed considerably over the last ten years. Past diagnoses of heart failure as identified in GP registers may be inaccurate, since the label of heart failure may have been applied without following the investigations as recommended above.

The advice in this guideline should be followed for the confirmation of the clinical suspicion of heart failure.

RECOMMENDATIONS

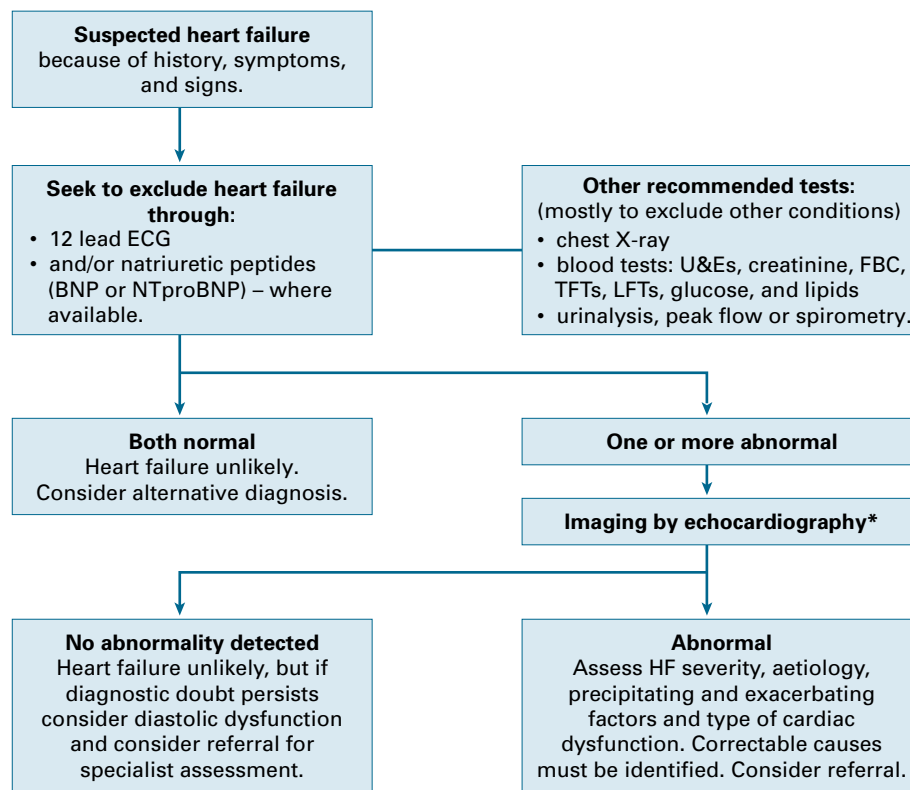
R10	The basis for historical diagnoses of heart failure should be reviewed, and only patients whose diagnosis is confirmed should be managed in accordance with this guideline.	GPP
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- R11 If the diagnosis of heart failure is still suspected, but confirmation of the underlying cardiac abnormality has not occurred, then the patient should have appropriate further investigation. GPP

6.3 Specialist referral

There are several circumstances where the GDG recommends further specialist input – please see the section on referral and approach to care for full details (Section 9).

6.4 Algorithm summarising recommendations for the diagnosis of heart failure



* Alternative methods of imaging the heart should be considered when a poor image is produced by transthoracic Doppler 2D-echocardiography – alternatives include transoesophageal echocardiography, radionuclide imaging or cardiac magnetic resonance imaging.

BNP = B-type natriuretic peptide; ECG = Electrocardiogram; FBC = Full blood count; LFTs = Liver function tests; NTproBNP = N-terminal pro-B-type natriuretic peptide; TFTs = Thyroid function tests; U&Es = Urea & electrolytes.

7 Treating heart failure

Introduction

The aims of therapy in heart failure are to:

- improve life expectancy
- improve quality of life.

The relative importance of these aims will vary between individual patients, should take into account patients' preferences, and may change with time. Clinical trials have measured achievement of these aims in different ways. Improvements in life expectancy are usually measured in terms of reductions in all-cause mortality and/or heart failure-related mortality. Improvements in quality of life have been assessed using generic measures of health status such as the Short Form-36, and through the use of more disease-specific measures, such as scoring systems that assess symptom control, ability to perform certain activities and exercise capacity. Hospitalisation rates are also often reported in clinical trials. These are relevant in that they reflect both morbidity and cost.

It may also be helpful to consider the aims of heart failure treatment in terms of the process of the delivery of care. These process-oriented aims, such as keeping patients fully informed about their condition and the treatment options, are reflected in the recommendations that appear in later sections.

Much of the evidence base for the management of heart failure relates to heart failure due to left ventricular systolic dysfunction. Although this is the most common underlying cardiac abnormality in patients with heart failure in the UK, it should not be forgotten that other cardiac abnormalities may be the cause of the heart failure – for example valve disease, or 'diastolic' dysfunction of the left ventricle. In some patients several abnormalities may co-exist. The evidence on which to base clinical management of these other cardiac abnormalities is much smaller than that for LV systolic dysfunction, and is covered briefly in 7.6. Specialist advice is recommended.

The guidance for the treatment of heart failure is presented under the following headings:

- 7.1 Lifestyle
- 7.2 Pharmacological treatment of heart failure due to LV systolic dysfunction
- 7.3 Algorithm for the pharmacological treatment of symptomatic heart failure due to LV systolic dysfunction
- 7.4 Invasive procedures
- 7.5 Oxygen therapy and continuous positive airways pressure treatment
- 7.6 Treatment of heart failure not due to LV systolic dysfunction

7.1 Lifestyle

7.1.1 Exercise training

Inactivity can lead to physical deconditioning, which leads to a worsening of symptoms and exercise performance.⁴⁵ Training can improve exercise performance – through adaptations to peripheral muscles – without adversely affecting cardiac function.⁴⁶ Both aerobic exercise (such as brisk walking) and resistive exercise (such as weight training) will improve a patient's symptoms, exercise performance and quality of life without deleterious effects on central haemodynamics.^{46,47} The long-term effects of exercise training (greater than a year) are not well defined. A forthcoming systematic review may clarify this (please visit www.nelh.nhs.uk/cochrane.asp). (Ia)

Breathing exercise training has been suggested to improve exercise performance.⁴⁸ In one small study this yoga-derived type of respiration (a particular form of slow deep breathing) was reported to decrease breathlessness and increase oxygen saturation by about half of that found in full exercise training programmes. This has yet to be confirmed in controlled trials. (III)

Health economic evidence: There is very little economic evidence on the cost effectiveness of exercise training. Costs and benefits are specific to the particular programme adopted and it is important to consider patient borne costs, such as travel time and expenses, when considering cost effectiveness (see Appendix F).

7.1.2 Rehabilitation programmes

The World Health Organization defined rehabilitation as the sum of the activities required to ensure the patient the best possible physical, mental and social conditions so that they may, by their own efforts, resume as normal a place as possible in the life of the community.⁴⁹

Rehabilitation programmes have been shown to be effective in patients with coronary heart disease, reducing hospitalisation rates, improving quality of life, and improving exercise performance.⁵⁰ It is likely that widening the remit of cardiac rehabilitation programmes to include patients with heart failure will lead to benefit for these patients, as several small RCTs have reported similar benefits to those gained by patients after myocardial infarction.^{50,51} (Ia)

Programmes that combine exercise, psychological support, and education, can be of greater benefit than programmes that provide only one of these components.⁵⁰ Such a combined approach has also been shown to improve cardiac risk factors for patients with coronary heart disease.⁵⁰ (Ia)

There are no characteristics of programme design in terms of frequency or duration that have been shown to be superior to others, and it has been suggested that the most effective regimes are those tailored to individual patients with a 'menu'-based approach.⁵¹ (IV)

Health economic evidence: Very little is known about the health economics of rehabilitation programmes for patients with heart failure. Evidence from other disease areas suggests that if a rehabilitation programme can reduce the risk of hospitalisation they often represent a very cost effective use of resources.

RECOMMENDATIONS ON EXERCISE TRAINING AND REHABILITATION

- R12** Patients with heart failure should be encouraged to adopt regular aerobic and/or resistive exercise. This may be more effective when part of an exercise programme or a programme of rehabilitation. **B**

7.1.3 Smoking

There are no published studies of the effects of stopping smoking in patients with heart failure. Smoking has many potentially adverse effects on, for example, haemodynamics and oxygen delivery. There was consensus amongst the guideline development group that total abstinence from smoking was beneficial to the clinical status of patients with heart failure. (IV)

Counselling and education programmes can provide assistance with quitting.^{52,53} (Ia)

RECOMMENDATION

- R13** Patients must be strongly advised not to smoke. Referral to smoking cessation services should be considered. **GPP**

7.1.4 Alcohol

Chronic excessive alcohol consumption may damage cardiac muscle and lead to heart failure.⁵⁴ Cardiac function may improve, or completely recover, in such patients if they abstain from alcohol. For patients in whom alcohol is not the cause of their heart failure, alcohol may still have clinically important effects such as precipitating arrhythmias (eg atrial fibrillation) or causing acute deterioration in cardiac function leading to clinical decompensation.⁵⁵ The volume load of alcoholic beverages varies – drinking beer or lager involves a greater volume of fluid than drinking the same amount of alcohol in the form of spirits. For patients with heart failure with fluid retention that is difficult to control, this extra fluid consumption may exacerbate the problem. Many patients with heart failure, however, continue to drink alcohol without any obvious harm, and there is no evidence that alcohol should be prohibited for all patients with heart failure.⁵¹ (III)

RECOMMENDATIONS

- R14** Patients with alcohol-related heart failure should abstain from drinking alcohol. **C**
- R15** Healthcare professionals should discuss alcohol consumption with the patient and tailor their advice appropriately to the clinical circumstances. **GPP**

7.1.5 Diet and nutrition

The evidence base for diet and nutrition for patients with heart failure is limited. One small randomised trial of non-pharmacological therapy, with exercise training, dietary control, and cognitive behaviour therapy in group sessions found improvements in indices of anxiety and depression in the short term; however, potential methodological limitations to the study makes this an unreliable evidence base on which to make recommendations.⁵⁶

Particular issues include:

- Nutritional status and its assessment. Many patients with heart failure may be malnourished, but this may be partially masked by fluid retention. Assessment is not straightforward.

- Weight reduction may be appropriate in some people with heart failure.
- Fluid restriction is commonly advocated for those with heart failure, but this may cause dehydration in some, and may exacerbate confusion in the elderly.
- Salt reduction is also commonly recommended by physicians to help control fluid status, but may make food less palatable.

Further research in this area is required.

7.1.6 'Natural' supplementary therapies

Several supplements have been considered for treatment in heart failure, including Co-enzyme Q₁₀, hawthorn extract, and Myrobalan (*Terminalia arjuna*). Neither observational nor controlled trials show evidence of benefit in terms of hospitalisation and mortality. Where trials have shown benefit they have been of poor quality⁵⁷ or have small sample size.⁵⁸ The mechanism of action of these therapies is not clearly understood. Studies have shown little risk of side effects or complications, although there is a potential for interactions with prescribed therapies. As supplements may be obtained without advice from a healthcare professional enquiries should be made as to the use of supplements during patient consultations (see p 63). (IIb)

Co-enzyme Q₁₀ shows no benefit compared to placebo in terms of mortality and morbidity and the long-term safety profile is not as yet known.^{59–61} (Ib)

No recommendations are made.

7.1.7 Sexual activity

The systematic search did not identify any published studies of the effect of sexual activity in patients with heart failure. Breathlessness on exertion and inability to lie flat may limit activity. Patients and their partners may be concerned about the possible risk of sexual activity, and may wish guidance from a healthcare professional. There was consensus among the guideline development group that these issues should be discussed with patients and their partners, where appropriate.

Sexual intercourse increases energy expenditure by a factor of 3 to 5 in healthy men, but with a wide variation.⁶² Related American expert consensus guidance suggests that if a patient with coronary heart disease can achieve 5 or 6 METS on the exercise tolerance test without demonstrating arrhythmias or ischaemia electrocardiographically, they most likely are not at high risk for developing myocardial ischaemia as a result of their normal sexual activities.⁶³ (IV)

RECOMMENDATION

- R16 Healthcare professionals should be prepared to broach sensitive issues with patients, GPP such as sexual activity, as these are unlikely to be raised by the patient.

7.1.8 Vaccination

There are no randomised controlled studies of vaccination against influenza in patients with heart failure. There was consensus among the guideline development group that the current UK recommendations for annual influenza vaccination for patients at high risk of developing complications from influenza infection should apply to patients with heart failure.

Patients with heart failure should also receive vaccination against pneumococcal disease (following guidance in the BNF). (IV)

RECOMMENDATIONS

- R17 Patients with heart failure should be offered an annual vaccination against influenza. **GPP**
- R18 Patients with heart failure should be offered vaccination against pneumococcal disease (only required once). **GPP**

7.1.9 Air travel

There are no pathophysiological reasons why most patients with stable heart failure and well-controlled symptoms should not be able to travel by air. Patients with decompensated heart failure, including pulmonary oedema, may become more hypoxic during air travel, and those who are symptomatic at rest or on minimal exertion may also not be fit to fly. The British Heart Foundation's factfile on air travel states that 'in general, if a patient can manage a flight of stairs without stopping and without significant symptoms whilst holding a conversation, he/she should be fit enough to fly... In the event of significant left ventricular dysfunction/failure flying is contra-indicated if oxygen is needed at rest on the ground.'⁶⁴

For many patients the most difficult part of air travel is the long walk within the airport. Assistance may be required. (IV)

RECOMMENDATION

- R19 Air travel will be possible for the majority of patients with heart failure, depending on their clinical condition at the time of travel. **GPP**

7.1.10 Driving regulations

The Driver and Vehicle Licensing Agency (DVLA) is responsible for licensing drivers of all motor vehicles in the UK. The regulations are updated from time to time, and are much stricter for those who wish to hold or retain a licence for a public service vehicle (PSV) or heavy goods vehicle (HGV) than for driving a car for personal use only. Patients with symptomatic heart failure are likely to be disqualified from holding a PSV or HGV licence, but may be re-licensed if they fulfil certain criteria. It is the responsibility of the patient to inform DVLA of any medical condition that may impact on their ability to drive, but the guideline development group considered it important to recommend that physicians are up to date with current guidelines. The ultimate decision regarding licensing rests with the DVLA.

RECOMMENDATION

- R20 HGV and PSV licence: Physicians should be up to date with the latest DVLA guidelines. Check the website for regular updates: www.dvla.gov.uk **GPP**

7.2 Pharmacological treatment of heart failure due to LV systolic dysfunction

Drug therapy is required for the vast majority of patients with heart failure. This section should be read in conjunction with the guidance on the sequencing of therapy, in particular the treatment algorithm (p 54). It is the responsibility of the individual prescriber to check the dosage of medication, as well as the cautions and contra-indications. This document should be read as a guide to treatment rather than being considered a protocol that must be followed prescriptively in all patients. Treatment should be tailored to the individual patient, with referral for more specialist advice being considered where appropriate.

In general, the dose of drugs used for improving symptoms and exercise capacity can be adjusted according to patient responses, but drugs used with the aim of improving longevity or reducing hospitalisation rates should not usually be adjusted on this basis; instead attempts should be made to ensure that the patient is treated with the doses proven to be effective in RCTs (details in tables 4–7), or if this is not possible, the maximum tolerated dose.

Table 3 Drugs in this guideline unlicensed for the treatment of heart failure or its common signs and symptoms in the UK at the time of issue of this guideline

Class (drug name)

- Angiotensin-II receptor antagonists
- Positive inotropic agents (Dobutamine and Dopamine)
- Calcium-channel blockers (Amlodipine)

Evidence statements and recommendations on specific drugs

7.2.1 Diuretics

Diuretics remain a key element in the treatment of heart failure. Diuretics preceded the advent of randomised control trials, and there are no large or long-term placebo controlled trials of their use. A systematic review of a number of small randomised trials indicated a possible benefit from diuretics in terms of mortality, compared to placebo.⁶⁵

One small study⁶⁶ demonstrated that patients with symptomatic heart failure deteriorated (increased body weight, reduced walking distance and worse quality of life) when diuretic therapy was withdrawn. (III)

Diuretics improve symptoms (breathlessness) and exercise performance in patients with heart failure.⁶⁷ It is common practice to initiate diuretic therapy at low doses,⁶⁸ and to increase the dose as required to control fluid retention – provided renal function does not deteriorate substantially. Most patients with heart failure who require diuretic therapy are treated with loop diuretics, rather than thiazides, as they are more powerful agents. Combination diuretic therapy, with a loop diuretic and a potassium sparing diuretic, may be used to increase the diuresis and also reduce the risk of hypokalaemia. The risk of hypokalaemia is less if an ACE inhibitor is used (see section on ACE Inhibitors, p 37). (Ib)

Health economic evidence: There are no economic evaluations of the use of diuretics in the treatment of heart failure. There is some evidence from the United States which suggests that the total costs of treatment with torasemide are less than those with furosemide, despite the higher acquisition cost of the newer drug (see Appendix D).

Table 4 Diuretics (oral): dosages and side effects

Drug	Initial dose (mg)		Maximum recommended daily dose (mg)	
Loop diuretics				
Bumetanide	0.5–1.0		5–10	
Furosemide	20–40		250–500	
Torasemide	5–10		100–200	
Thiazides*				
Bendroflumethiazide (previously called bendrofluazide)	2.5		5	
Indapamide	2.5		2.5	
Metolazone	2.5		10	
Potassium-sparing diuretic	+ACEI	–ACEI	+ACEI	–ACEI
Amiloride	2.5	5	20	40
Triamterene	25	50	100	200
For spironolactone , see p 43				
*May be effective when added to loop diuretics when fluid retention is resistant, but can promote dramatic diuresis and disturbance in fluid balance and electrolytes. Patients must be closely monitored and specialist advice is required. ACEI: ACE inhibitor				

RECOMMENDATION

- R21** Diuretics should be routinely used for the relief of congestive symptoms and fluid retention in patients with heart failure, and titrated (up and down) according to need following the initiation of subsequent heart failure therapies. **C**

7.2.2 Angiotensin converting enzyme (ACE) inhibitors

Systematic reviews of randomised controlled trials comparing ACE inhibitor to placebo have found that ACE inhibitor therapy in patients with heart failure due to left ventricular systolic dysfunction increases life expectancy^{69,70} compared to placebo.⁷¹ The effect is more marked in patients with more severe LV systolic impairment, or more severe symptoms – although there is benefit for all NYHA classes.⁷⁰ Compared with placebo, ACE inhibitor therapy also reduces the risk of hospitalisation for heart failure in such patients, and also for patients with asymptomatic left ventricular systolic dysfunction.^{69,70,72} (Ia)

The symptoms of heart failure in patients with heart failure due to left ventricular systolic dysfunction improve on therapy with an ACE inhibitor.^{72,73} There is some evidence from a

randomised controlled trial that quality of life improves with ACE inhibitor therapy in this group.⁷⁴ Exercise performance has not consistently been shown to improve with ACE inhibitor therapy for all patients with heart failure due to left ventricular systolic dysfunction.^{71,72,74} However, a systematic review and a subsequent randomised controlled trial suggest a greater improvement in patients with more depressed LV ejection fraction.^{71,74} **(Ia)**

High doses of ACE inhibitors lower blood pressure more than lower doses but do not necessarily confer greater benefit in terms of improving symptoms or life expectancy.^{75,76} A higher dose does appear to reduce the risk of hospitalisation due to worsening heart failure more than lower dose.⁷⁵ **(Ib)**

In the absence of any large RCT with mortality as an outcome, the decision was taken not to use surrogate outcomes for intra-class comparisons.

Health economic evidence: Treatment of heart failure with ACE inhibitors is cost effective, largely due to the costs saved from the reduced risk of hospitalisation. Treatment can be cost saving and has very favourable cost effectiveness ratios even when conservative assumptions are employed.

Table 5 Practical recommendations on the use of ACE inhibitors*

Which ACE inhibitor and what dose?

<i>Licensed ACEI</i>	<i>Starting dose (mg)</i>	<i>Target dose (mg)</i>
Captopril	6.25 three times daily	50–100 three times daily
Cilazapril*	0.5 once daily	1–2.5 once daily
Enalapril	2.5 twice daily	10–20 twice daily
Fosinopril*	10 once daily	40 once daily
Lisinopril	2.5–5.0 once daily	30–35 once daily
Perindopril*	2.0 once daily	4 once daily
Quinapril*	2.5–5.0 once daily	10–20 once daily
Ramipril	2.5 once daily	5 twice daily or 10 once daily

*Target dose based on manufacturer’s recommendation rather than large outcome study

How to use?

- Start with a low dose (see above).
- Seek specialist advice where the patient is on a high dose (eg furosemide 80mg) of a loop diuretic.
- Double dose at not less than two weekly intervals.
- Aim for target dose (see above) or, failing that, the highest tolerated dose.
- Remember some ACE inhibitor is better than no ACE inhibitor.
- Monitor blood electrolytes (in particular potassium), urea, creatinine and blood pressure.
- When to stop up-titration/down-titration; see ‘Problem solving’, below.

Advice to patient?

- Explain expected benefits
- Treatment is given to improve symptoms, to prevent worsening of heart failure and to increase survival.
- Symptoms improve within a few weeks to a few months.
- Advise patients to report principal adverse effects, ie dizziness/symptomatic hypotension, cough.

continued

Table 5 Practical recommendations on the use of ACE inhibitors* – *continued***Problem solving**

- Asymptomatic low blood pressure does not usually require any change in therapy.

Symptomatic hypotension

- If dizziness, light-headedness and/or confusion and a low blood pressure consider discontinuing nitrates, calcium channel blockers[†] and other vasodilators.
- If no signs/symptoms of congestion consider reducing diuretic dose.
- If these measures do not solve problem seek specialist advice.

Cough

- Cough is common in patients with chronic heart failure, many of whom have smoking-related lung disease.
- Cough is also a symptom of pulmonary oedema which should be excluded when a new or worsening cough develops.
- ACE inhibitor induced cough rarely requires treatment discontinuation.
- If the patient develops a troublesome dry cough which interferes with sleep and is likely to be caused by an ACE inhibitor, consider substituting an angiotensin-II receptor antagonist for the ACE inhibitor.

Worsening renal function

- Some rise in urea, creatinine and K⁺ is to be expected after initiation of an ACE inhibitor; if the increase is small and asymptomatic no action is necessary.
- An increase in creatinine of up to 50% above baseline, or to 200 µmol/l, whichever is the smaller, is acceptable.
- An increase in K⁺ to ≤ 5.9 mmol/l is acceptable.
- If urea, creatinine or K⁺ do rise excessively consider stopping concomitant nephrotoxic drugs (eg NSAIDs), non-essential vasodilators (eg calcium antagonists, nitrates), K⁺ supplements/retaining agents (triamterene, amiloride) and, if no signs of congestion, reducing the dose of diuretic.
- If greater rises in creatinine or K⁺ than those outlined above persist despite adjustment of concomitant medications the dose of the ACE inhibitor should be halved and blood chemistry rechecked, if there is still an unsatisfactory response specialist advice should be sought.
- If K⁺ rises to ≥ 6.0 mmol/l or creatinine increases by > 100% or to above 350 µmol/l the dose of ACE inhibitor should be stopped and specialist advice sought.
- Blood electrolytes should be monitored closely until K⁺ and creatinine concentrations are stable.

Note: it is very rarely necessary to stop an ACE inhibitor and clinical deterioration is likely if treatment is withdrawn; ideally, specialist advice should be sought before treatment discontinuation.

*Adapted from McMurray *et al.* Practical recommendations for the use of ACE Inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice. *European Journal of Heart Failure* 2001;**3**:495–502.

[†]Calcium channel blockers should be discontinued unless absolutely essential, eg for angina or hypertension.

RECOMMENDATIONS

- | | | |
|-----|---|-----|
| R22 | All patients with heart failure due to left ventricular systolic dysfunction should be considered for treatment with an ACE inhibitor. | A |
| R23 | ACE inhibitor therapy should be instituted in patients with heart failure due to left ventricular systolic dysfunction before beta-blockade is introduced. | A |
| R24 | ACE inhibitor therapy should be initiated at the appropriate dose (see Table 5), and titrated upwards at short intervals (eg every two weeks) until the optimal tolerated or target dose is achieved. | GPP |

- R25** Blood biochemistry (urea, creatinine and electrolytes) should be measured after initiation and at each dose increment. **GPP**

Absolute contraindications to the use of ACE inhibitors include a history of anuria or angioedema with past exposure to the drug, bilateral renal artery stenosis, pregnancy, and cardiogenic shock. Hypotension is not necessarily a contraindication, but consultation with a specialist is advised before use in a patient with a systolic blood pressure less than 80 mmHg. Risk factors for ACE-induced hypotension include hyponatraemia, hypovolaemia, and high dose diuretics. Therefore when ACE inhibitors are introduced in patients who are already taking a high dose of a loop diuretic (eg furosemide 80 mg), the ACE inhibitor may need to be initiated under specialist supervision. ACE inhibitor therapy may be harmful in patients with severe aortic stenosis (see section on valve disease, p 60).

As a general rule, ACE inhibitors should be used with caution in patients with a serum creatinine > 200 µmol/L or a potassium > 5.0 mmol/L. A small rise in serum creatinine is frequently observed in patients with heart failure and is not necessarily a reason for discontinuation. In patients without fluid retention, a reduction in diuretic dose may improve renal function. Risk factors for hyperkalemia during ACE inhibitor therapy include pre-existing renal dysfunction, concomitant use of potassium-sparing diuretics, and diabetes.

7.2.3 Beta-blockers

Many large clinical trials reviewed in four meta-analyses, and one subsequent RCT have shown that several beta-blockers increase life expectancy in patients with heart failure due to LV systolic dysfunction, compared with placebo. This effect has been seen in patients with all functional classes of heart failure (NYHA classes I – IV).^{77–82} (Ia)

In randomised controlled trials, evaluated in three large systematic reviews of long-term outcomes, the use of certain beta-blockers in patients with heart failure significantly reduces hospitalisation compared to placebo, and has an even more marked effect on hospitalisation due to heart failure.^{77,79,81} (Ia)

Beta-blockers may not all have the same efficacy. The best evidence of benefit exists for bucindolol, carvedilol and modified-release metoprolol; there is little evidence of benefit from other beta-blockers.^{77,83,84} (Ia)

There is little evidence to suggest a clinically important difference in the effect on hospitalisation and mortality between selective and non-selective beta-blockers⁷⁷ or those with or without vasodilating properties that have been examined in randomised control trials (carvedilol, metoprolol, bisoprolol).⁸¹ A direct head-to-head comparison of carvedilol with metoprolol in a large randomised trial (COMET) has completed follow-up, and the results will be reported in 2003.⁸⁵ This will provide more robust evidence as to whether there is a clinically important difference in the effect of beta-blockers in patients with heart failure, and may influence future recommendations on the use of this class of drugs in the management of heart failure. (Ia)

There are no randomised clinical trials of atenolol, or some other commonly used beta-blockers, in patients with heart failure. The consensus among the guideline development group was that if a patient with heart failure due to LV systolic dysfunction not already on beta-blockade therapy then they should be commenced on a beta-blocker licensed for the treatment

of heart failure in the UK at the time of issue of this guideline (bisoprolol or carvedilol). Alternatively, if a patient developed heart failure due to LV systolic dysfunction and was already on a beta-blocker for a concomitant condition such as angina or hypertension, then the physician could either decide to change the beta-blocker to one of the beta-blockers licensed for the treatment of heart failure, in the UK at the time of issue of this guideline, or continue with the agent already prescribed. (IV)

Health economic evidence: There is less economic evidence on beta-blockers than ACE inhibitors, but the evidence that does exist consistently shows beta-blockers to be cost effective, largely through the costs saved from the reduced risk of hospitalisation.

In the UK, only carvedilol and bisoprolol are licensed for the treatment of heart failure (at the time of issue of this guideline). No study has made a direct comparison between carvedilol and bisoprolol, and there is no evidence on their relative cost-effectiveness (see Appendix D).

Table 6 Practical recommendations on the use of beta-blockers*

Which beta-blocker and what dose?

Only two beta-blockers are licensed for the treatment of heart failure in the UK at the time of issue of this guideline:

- Bisoprolol (starting dose 1.25 mg once daily; target dose 10 mg once daily)
- Carvedilol (starting dose 3.125 mg twice daily; target dose 25–50 mg twice daily)

NB Carvedilol: maximum dose 25 mg twice daily if severe heart failure. For patients with mild to moderate heart failure maximum dose 50 mg twice daily if weight more than 85 kg – otherwise maximum dose 25 mg twice daily.

How to use?

- Start with a low dose (see above).
- Double dose at not less than two weekly intervals.
- Aim for target dose (see above) or, failing that, the highest tolerated dose.
- Remember some beta-blocker is better than no beta-blocker.
- Monitor heart rate, blood pressure, clinical status (symptoms, signs, especially signs of congestion, body weight).
- Check blood electrolytes, urea and creatinine one to two weeks after initiation and one to two weeks after final dose titration.
- When to down-titrate/stop up-titration, see 'Problem solving', below.

Advice to patient

- Explain expected benefits.
- Emphasise that treatment given as much to prevent worsening of heart failure as to improve symptoms, beta-blockers also increase survival.
- If symptomatic improvement occurs, this may develop slowly – over three to six months or longer.
- Temporary symptomatic deterioration may occur (estimated 20–30% of cases) during initiation/up-titration phase.
- Advise patient to report deterioration (see 'Problem solving', below) and that deterioration (tiredness, fatigue, breathlessness) can usually be easily managed by adjustment of other medication; patients should be advised not to stop beta-blocker therapy without consulting their physician.
- Patients should be encouraged to weigh themselves daily (after waking, before dressing, after voiding, before eating) and to consult their doctor if they have persistent weight gain.

continued

Table 6 Practical recommendations on the use of beta-blockers* – *continued***Problem solving***Worsening symptoms/signs (eg increasing dyspnoea, fatigue, oedema, weight gain)*

- If increasing congestion double dose of diuretic and/or halve dose of beta-blocker (if increasing diuretic does not work).
- If marked fatigue (and/or bradycardia, see below) halve dose of beta-blocker (rarely necessary).
- Review patient in one to two weeks; if not improved seek specialist advice.
- If serious deterioration halve dose of beta-blocker or stop this treatment (rarely necessary); seek specialist advice.

Low heart rate

- If < 50 beats/min and worsening symptoms – halve dose beta-blocker or, if severe deterioration, stop beta-blocker (rarely necessary).
- Consider need to continue treatment with other drugs that slow the heart (eg digoxin, amiodarone, diltiazem) and discontinue if possible.
- Arrange ECG to exclude heart block.
- Seek specialist advice.

Asymptomatic low blood pressure

- Does not usually require any change in therapy.

Symptomatic hypotension

- If low blood pressure causes dizziness, light-headedness or confusion, consider discontinuing drugs such as nitrates, calcium channel blockers and other vasodilators.
- If no signs/symptoms of congestion consider reducing diuretic dose.
- If these measures do not solve problem seek specialist advice.

Note: beta-blockers should not be stopped suddenly unless absolutely necessary (there is a risk of a 'rebound' increase in myocardial ischaemia/infarction and arrhythmias); ideally specialist advice should be sought before treatment discontinuation.

*Adapted from McMurray *et al.* Practical recommendations for the use of ACE Inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice. *European Journal of Heart Failure* 2001;3:495–502.

The BNF recommends that treatment should be initiated by a doctor experienced in the management of heart failure. This may include general practitioners and other clinicians with a special interest in the condition.

Effort should be made to achieve the doses of beta-blockers that have been shown to be of benefit in terms of mortality in large clinical trials (as shown in Table 6). Although beta-blockers can cause fluid retention and fatigue, maximum doses were generally well tolerated in the randomised trials that were included in systematic reviews in this area.^{68,82,86–90} (Ia)

RECOMMENDATIONS

- | | | |
|-----|---|---|
| R26 | Beta-blockers licensed for use in heart failure should be initiated in patients with heart failure due to LV systolic dysfunction after diuretic and ACE inhibitor therapy (regardless of whether or not symptoms persist). | A |
| R27 | Beta-blockade therapy for heart failure should be introduced in a 'start low, go slow' manner, with assessment of heart rate, blood pressure, and clinical status after each titration. | C |

- R28** Patients who develop heart failure due to LV systolic dysfunction and who are already on treatment with a beta-blocker for a concomitant condition (eg angina, hypertension) should continue with a beta-blocker – either their current beta-blocker or an alternative licensed for heart failure treatment. **GPP**

7.2.4 Aldosterone antagonists

These drugs also act as potassium-sparing diuretics. Currently, the only aldosterone antagonist licensed for heart failure in the UK is spironolactone. A more selective aldosterone antagonist, eplerenone, has been developed and a large mortality trial in patients with heart failure after myocardial infarction (EPHESUS) is due to be published in 2003.⁹¹ The results of this trial may influence future recommendations on the use of aldosterone antagonists in patients with heart failure.

▷ Spironolactone

In patients with moderate to severe heart failure (NYHA Class III and IV) due to LV systolic dysfunction, the addition of low-dose spironolactone to therapy with a loop diuretic and ACE inhibitor (\pm digoxin) has been shown in a large randomised controlled trial to increase life expectancy when compared to placebo.⁹² In addition, hospitalisation for cardiac causes is greatly reduced.⁹² **(Ib)**

Use of this drug may increase blood potassium⁹³ but there was no significant clinical problem with hyperkalaemia in the patients included in the RALES trial, which involved close monitoring and titration.⁹² In this trial, patients with raised serum creatinine or potassium concentration were excluded. **(Ib)**

Health economic evidence: No relevant economic evidence relating to spironolactone has been identified.

▷ Eplerenone

Eplerenone is an aldosterone antagonist with fewer side-effects than spironolactone. There is no RCT evidence relating to patients with heart failure currently available to support the use of eplerenone in such patients. The evidence for the clinical effect of eplerenone in patients with heart failure will become clearer when the EPHESUS trial reports.⁹⁴ This drug is not currently licensed for use in the UK. **(IIb)**

RECOMMENDATIONS

- R29** Patients with heart failure due to LV systolic dysfunction who remain moderately to severely symptomatic despite optimal therapy (as outlined in the algorithm) should be prescribed spironolactone at a dose of 12.5 to 50 mg once per day – specialist advice should be sought. **A**
- R30** Patients with heart failure taking spironolactone should have blood potassium and creatinine levels monitored for signs of hyperkalaemia and/or deteriorating renal function (see Table 7 for further details). If hyperkalaemia is a problem then the dose of spironolactone should be halved and biochemistry rechecked. **GPP**

Table 7 Practical recommendations on the use of spironolactone*	
Which dose of spironolactone?	
<input type="checkbox"/>	12.5–25 mg daily, although 50 mg may be advised by a specialist if heart failure deteriorates and no problem with hyperkalaemia.
How to use?	
<input type="checkbox"/>	Start at 25 mg once daily
<input type="checkbox"/>	Check blood chemistry at 1, 4, 8 and 12 weeks; 6, 9 and 12 months, 6 monthly thereafter.
<input type="checkbox"/>	If K ⁺ rises to between 5.5 and 5.9 mmol/litre or creatinine rises to 200 µmol/litre reduce dose to 25 mg on alternate days and monitor blood chemistry closely.
<input type="checkbox"/>	If K ⁺ rises to ≥ 6.0 mmol/litre or creatinine to > 200 µmol/litre stop spironolactone and seek specialist advice.
Advice to patient?	
<input type="checkbox"/>	Explain expected benefits.
<input type="checkbox"/>	Treatment is given to improve symptoms, prevent worsening of heart failure and to increase survival.
<input type="checkbox"/>	Symptom improvement occurs within a few weeks to a few months of starting treatment.
<input type="checkbox"/>	Avoid NSAIDs not prescribed by a physician (self-purchased 'over the counter' treatment, eg ibuprofen).
<input type="checkbox"/>	Temporarily stop spironolactone if diarrhoea and/or vomiting and contact physician.
Problem solving – worsening renal function/hyperkalaemia	
<input type="checkbox"/>	See 'How to use?' section, above.
<input type="checkbox"/>	Major concern is hyperkalaemia (≥ 6.0 mmol/litre) though this was uncommon in the RALES clinical trial; a potassium level at the higher end of the normal range may be desirable in patients with heart failure, particularly if taking digoxin.
<input type="checkbox"/>	Some 'low salt' substitutes have a high K ⁺ content.
<input type="checkbox"/>	Male patients may develop breast discomfort and/or gynaecomastia.
*Adapted from McMurray <i>et al.</i> Practical recommendations for the use of ACE Inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice. <i>European Journal of Heart Failure</i> 2003;3:495–502.	

7.2.5 Digoxin

Despite a small systematic review that suggests that fewer patients withdraw from randomised trials of therapy when on digoxin than on placebo,³⁰⁸ there are no published data from randomised control trials on the effect of digoxin on the signs and symptoms (except for exercise performance)^{95,96} and quality of life⁹⁶ of patients with heart failure. Digoxin reduces the risk of admission to hospital with worsening heart failure in patients with heart failure due to LV systolic dysfunction in sinus rhythm, and may reduce heart failure-specific mortality.⁹⁷ However, a large systematic review and two additional RCTs with medium-term follow up, suggest that it does not increase overall life expectancy.^{95,97} (Ib)

There is some evidence from a medium sized RCT that digoxin therapy may prevent deterioration in maximal exercise performance for patients with heart failure due to LV systolic dysfunction and in sinus rhythm⁹⁵ – and withdrawal may lead to deterioration in maximal, but not sub-maximal, exercise performance.⁹⁶ The clinical effects of the withdrawal of digoxin may be more marked in patients with poorer LV systolic function (eg lower ejection fractions) and more severe symptoms (eg worse NYHA class).⁹⁶ (Ib)

Digoxin has a narrow therapeutic window, with arrhythmias and gastrointestinal side effects being the most common clinical problems. In clinical trials digoxin therapy rarely has to be withdrawn for toxicity reasons.^{95,97} (Ib)

The use of digoxin has an important role in patients with heart failure and atrial fibrillation. Initial treatment with digoxin need not preclude the subsequent use of a beta-blocker.⁹⁸ (IV)

Health economic evidence: There are no economic evaluations of the use of digoxin to treat heart failure in the UK. There is one cost-effectiveness analysis from the United States (based on international RCT evidence) that shows that digoxin may be cost saving in the treatment of patients with heart failure, whether or not they are also receiving ACE Inhibitors (see Appendix D).⁹⁹

The usual daily dose of oral digoxin is 125 to 250 µg if the serum creatinine is within the normal range. Higher doses (> 250 µg) are rarely used for heart failure treatment. Lower doses are used if the patient is elderly (over age 70 years) or has impaired renal function. There is little relationship between digoxin concentration and therapeutic effects.⁶⁸

A number of drugs can alter the pharmacokinetics of digoxin. Those producing the most significant perturbation of digoxin levels are:

- anti-arrhythmic drugs affecting renal clearance and/or volume of distribution (verapamil, amiodarone, propafenone and quinidine)
- drugs *increasing* its absorption (erythromycin, omeprazole and tetracycline)
- drugs *decreasing* its absorption (colestipol, cholestyramine).

A number of drugs can alter the pharmacokinetics of digoxin. See the BNF (<http://bnf.org>) for a comprehensive list.

The role of therapeutic monitoring of serum digoxin concentrations is discussed in the section on monitoring (section 8).

RECOMMENDATIONS

R31 Digoxin is recommended for:

- worsening or severe heart failure due to LV systolic dysfunction despite ACE inhibitor, beta-blocker and diuretic therapy A
- patients with atrial fibrillation and any degree of heart failure. C

7.2.6 Angiotensin-II receptor antagonists

Currently, none of the angiotensin-II receptor antagonists is licensed for use in heart failure in the UK. The clinical evidence for the use of this class of drugs in heart failure is still emerging with several large randomised trials ongoing.

Angiotensin-II receptor antagonists have not been shown to increase life expectancy compared to ACE inhibitor therapy for patients with heart failure due to left ventricular systolic dysfunction in several RCTs.^{100–103} (Ia)

One systematic review of 17 randomised controlled trials demonstrated that the combination of angiotensin-II receptor antagonists and ACEI did not reduce risk of mortality as compared

to ACEI on their own. However, significantly fewer patients required hospitalisation with the dual therapy.¹⁰⁰ (1a)

One large prospective randomised trial, Val-HeFT, showed that the addition of the angiotensin-II receptor antagonist valsartan, at doses of 40 mg to 160 mg twice daily, to standard therapy with a diuretic and ACE inhibitor (with or without digoxin), does not improve life expectancy for patients with heart failure due to left ventricular systolic dysfunction, but reduces hospitalisation with worsening heart failure.¹⁰³ (1b)

Clarification will emerge from ongoing clinical trials as to the possible harm from the ‘triple combination’ of ACE inhibitor, angiotensin-II receptor antagonist and beta-blocker, suggested by *post hoc* subgroup analysis. In the meantime this combination should be avoided.

Therapy with an angiotensin-II receptor antagonist in patients with heart failure due to LV systolic dysfunction who are not on an ACE inhibitor or cannot tolerate an ACE inhibitor (for example, due to a cough) reduces mortality compared with treatment with placebo, as indicated by a systematic review.¹⁰² There are few data on the impact of angiotensin-II receptor antagonists on symptoms, quality of life and exercise performance in patients with heart failure due to LV systolic dysfunction.^{101,103,104} (1a)

In clinical trials, angiotensin-II receptor antagonists are better tolerated than ACE inhibitors.^{101,104} Hypotension and reversible renal dysfunction are the most common serious side effects. (1b)

A large clinical trial examining the effect of candesartan as an addition to ACE inhibition in patients with heart failure due to LV systolic dysfunction, as an alternative to ACE inhibition in patients intolerant of such therapy, and in patients with diastolic heart failure is due to report in 2003 (CHARM).¹⁰⁵ A large randomised outcome trial examining the effects of valsartan monotherapy or as an addition to ACE inhibition in post myocardial infarction patients who have either clinical or radiological signs of heart failure and/or evidence of left ventricular systolic dysfunction is due to report in 2003 (VALIANT). The results of these studies may influence future recommendations on the use of this class of drugs in the management of heart failure.

Health economic evidence: There are no economic evaluations of the use of angiotensin-II receptor antagonists in the treatment of heart failure in the UK. There is one cost effectiveness analysis from the United States, based on international RCT evidence, comparing losartan with the ACE inhibitor, captopril. This shows little difference between the cost effectiveness ratios of these two drugs when used for symptomatic heart failure in older people (see Appendix D).¹⁰⁶

Table 8 Currently available angiotensin-II receptor antagonists*

Drug	Daily dose (mg)
Candesartan	4–16
Eprosartan	400–800
Irbesartan	150–300
Losartan	50–100
Telmisartan	40–80
Valsartan	80–320

*None of these drugs is currently licensed for the treatment of heart failure in the UK.

RECOMMENDATIONS

- R32** At the time of issue of this guideline, angiotensin-II receptor antagonists (see Table 8) are not licensed in the UK for heart failure and studies are ongoing. However, angiotensin-II receptor antagonists may provide an alternative to ACE inhibitors for patients intolerant of ACE inhibitors (for example, because of cough). **A**
- R33** The triple combination of ACE inhibitor, beta-blocker and angiotensin-II receptor antagonist should be avoided, pending the results of further trials. **GPP**

7.2.7 Amiodarone

A small number of RCT and meta-analyses have demonstrated that amiodarone is effective against most ventricular arrhythmias.^{107–109} Evidence from one meta-analysis with long-term outcome assessment suggests a neutral effect on mortality in patients with heart failure.^{107,110,111} **(Ia)**

Amiodarone has numerous side effects. Photosensitivity and asymptomatic corneal micro-deposits are common but other side effects are potentially more serious, eg thyroid dysfunction, pulmonary fibrosis, liver damage, neuropathy.^{107–110} **(Ia)**

Because of the potentially serious side effects from long-term therapy with amiodarone, the guideline development group recommended that the decision to initiate, and to continue, such therapy should be made in consultation with a specialist.

Health economic evidence: No relevant economic evidence relating to amiodarone was identified.

RECOMMENDATIONS

- R34** The decision to prescribe amiodarone should be made in consultation with a specialist. **GPP**
- R35** The need to continue the prescription should be reviewed regularly. **GPP**
- R36** Patients taking amiodarone should have a routine six-monthly clinical review, including liver and thyroid function test, and including a review of side effects. **GPP**

7.2.8 Anticoagulants

Randomised control trials have demonstrated that warfarin reduces the risk of stroke in patients with heart failure with atrial fibrillation. Patients with heart failure were included within these studies.¹¹² **(Ia)**

There is no RCT evidence that patients with heart failure and intracardiac thrombus, left ventricular aneurysm, and/or a history of thromboembolism (in the absence of atrial fibrillation) benefit from oral anticoagulation. The consensus among the guideline development group was that warfarin is likely to be beneficial in such circumstances. **(IV)**

One RCT reported no difference in the risk of death, myocardial infarction and/or stroke for patients with heart failure in sinus rhythm when taking warfarin as opposed to aspirin or no anticoagulant/anti-platelet therapy.¹¹³ There is an ongoing trial (WATCH), which will add to the evidence in this area. **(Ib)**

RECOMMENDATIONS

- R37 Anticoagulation is indicated for patients with the combination of heart failure and atrial fibrillation (see also atrial fibrillation section, p 60). **A**
- R38 In patients with heart failure in sinus rhythm, anticoagulation should be considered for those with a history of thromboembolism, left ventricular aneurysm, or intracardiac thrombus. **GPP**

For guidance on international normalised ratio (INR) levels in atrial fibrillation, please refer to the Haemostasis and Thrombosis Task Force Guidelines on Oral Anticoagulation¹¹⁴ at www.bcshguidelines.com/pdf/bjh715.pdf

7.2.9 Aspirin

There is systematic review evidence that aspirin reduces the risk of vascular events in patients with atherosclerotic arterial disease.¹¹⁵ Aspirin is currently recommended for patients with coronary heart disease,¹¹⁶ although specific RCT evidence for its benefit in patients with heart failure is lacking. **(Ia)**

Concern has been raised from *post hoc* analyses of RCTs that aspirin may reduce the beneficial effect of ACE inhibitors in patients with heart failure or atherosclerotic arterial disease,^{117,118} although not all reports confirm this.^{119,120} In order to provide more robust evidence prospective RCTs to examine this concern are planned. **(IIb)**

The guideline development group discussed the concerns regarding aspirin use in patients with heart failure, many of whom are also prescribed an ACE inhibitor. In the absence of conclusive evidence, and general consensus as to the benefits of aspirin in patients with atherosclerotic arterial disease, the decision was made to continue to support the use of aspirin in patients with heart failure who also had atherosclerotic arterial disease.

RECOMMENDATION

- R39 Aspirin (75–150 mg once daily) should be prescribed for patients with the combination of heart failure and atherosclerotic arterial disease (including coronary heart disease). **B**

7.2.10 Statins (hydroxymethylglutaryl-coenzyme A reductase inhibitors)

In the UK, coronary artery disease (CAD) is the single most common cause of heart failure. Patients with heart failure that subsequently develop myocardial infarction and/or unstable angina have a worse outcome than patients without ischaemic events.^{121,122} **(Ib)**

Several large RCTs report that statins reduce the frequency of ischaemic events and prolong life expectancy in patients with known CAD.^{122–125} The risk of developing heart failure is also reduced.¹²⁶ Although *post hoc* analysis suggests that statins are effective in patients with and without heart failure,¹²² many statin trials have excluded patients with severe heart failure. **(Ib)**

Experimental studies suggest that statins may improve left ventricular function through a variety of mechanisms not linked to the prevention of myocardial ischaemia, but may also

increase the oxidative stress and the effects of endotoxin in patients with heart failure.¹²⁷ The effect of statins on ventricular function and heart failure progression has not been specifically addressed in a randomised controlled trial.

Health economic evidence: There is evidence that statins are a cost effective therapy in patients with cardiovascular disease who are at high risk of CHD events.¹²⁸ However, there is no specific cost-effectiveness information available on the use of statins in patients with heart failure.

RECOMMENDATION

- R40** Patients with the combination of heart failure and known atherosclerotic vascular disease should receive statins only in accordance with current indications. Specific trials in this area are ongoing. **GPP**

7.2.11 Isosorbide/hydralazine combination (specialist initiation only)

Oral isosorbide dinitrate in combination with hydralazine has been shown in one large RCT (which included only men) with long term outcomes to extend life expectancy in patients with heart failure compared with placebo.¹²⁹ It is not, however, as effective as ACE inhibitors.^{130–135} (**Ia**)

Such combination therapy is less well tolerated than ACE inhibitors, with more frequent adverse events than placebo, including gastrointestinal problems and headaches.^{130,132,133,136,137} (**Ib**)

There is evidence that oral isosorbide dinitrate in combination with hydralazine improves exercise capacity and in the one trial that reported on this outcome increases LV ejection fraction.^{129,130} The benefit of hydralazine and dinitrates (in combination) as an additive therapy to ACE inhibitors or beta-blockers remains unclear. (**Ib**)

Health economic evidence: One study in the US considered the cost effectiveness of isosorbide/hydralazine combination in comparison to standard therapy with digoxin and diuretics, using data from the V-HeFT II trial. This was found to be a cost effective therapy in the US context, but the generalisability of this result to the UK is questionable.

RECOMMENDATION

- R41** An isosorbide/hydralazine combination may be used in patients with heart failure who are intolerant of ACE inhibitors or angiotensin-II receptor antagonists. **A**

7.2.12 Inotropic agents (specialist use only)

Inotropic agents are of proven clinical benefit in the short-term treatment of **acute decompensation**. One large and two small RCTs suggest that dobutamine, milrinone and enoximone improve symptoms and exercise performance.^{138–140} However, a large multi-centre randomised controlled trial found no effect of short term inotropic therapy on hospitalisation of patients with acute decompensation of heart failure.¹⁴⁰ (**Ib**)

Intravenous inotropic agents increase mortality when used as **chronic therapy** and no oral inotropic agent has been shown to be of benefit in chronic therapy in terms of increasing life expectancy, although they can improve symptoms.^{139,141–144} (**Ia**)

Randomised control trials of the chronic use of inotropic agents at different dose levels (and of novel inotropic agents) in patients with heart failure are ongoing.

Health economic evidence: No relevant economic evidence relating to inotropic agents was identified.

RECOMMENDATION

- R42** Intravenous inotropic agents (such as dobutamine, milrinone or enoximone) should only be considered for the short-term treatment of acute decompensation of chronic heart failure. This will require specialist advice. **A**

7.2.13 Calcium channel blockers

Three RCTs with medium- to long-term follow up suggest that calcium channel blockers do not improve life expectancy compared with placebo in patients with heart failure who are already receiving an ACE inhibitor.^{145–147} Verapamil, diltiazem and short-acting dihydropyridines such as nifedipine can cause clinical deterioration.^{146,148} (**Ia**)

Amlodipine, a long-acting dihydropyridine, is not harmful in terms of adverse events.^{147,149} (**Ib**)

Health economic evidence: No relevant economic evidence relating to calcium channel blockers was identified.

RECOMMENDATION

- R43** Amlodipine should be considered for the treatment of co-morbid hypertension and/or angina in patients with heart failure, but verapamil, diltiazem or short acting dihydropyridine agents should be avoided. **A**

7.2.14 Others

▷ Nesiritide

Nesiritide is synthetic human BNP. Three medium-term RCTs in patients with heart failure suggest it has short-term haemodynamic benefits in patients with acute decompensation. It is currently not licensed for use in the UK.^{150–152}

▷ Levosimendan

Levosimendan is a calcium sensitiser. Three medium-sized RCTs of patients with heart failure with severely depressed LV ejection fraction suggest this drug may provide short-term haemodynamic benefits in patients with acute decompensation. It is currently not licensed for use in the UK.^{153–155}

▷ Other pharmacological therapies

The guideline development group reviewed both systematic review and small scale RCT evidence for several other drug therapies. The drugs considered were: d-sotalol,¹⁵⁶ epoproserol,^{157,158}

magnesium supplementation, vitamin E supplementation,¹⁵⁹ interferon/thymomodulin,¹⁴⁶ human recombinant growth hormone,¹⁶⁰ L-carnitine,¹⁶¹ pentoxifylline,¹⁶² immunosuppressants.¹⁶³

The group concluded however, that the evidence in non-specialist practice was not robust enough to warrant inclusion in the guideline.

7.2.15 Major co-morbidities that impact on the pharmacological management of heart failure

The presence of certain co-morbidities may affect the drugs that can be used for the treatment of heart failure, or increase the likelihood of side effects. These are summarised in Table 9.

Co-morbidity	Comments
COPD/asthma/reversible airways disease	Beta-blockers are contraindicated in patients with reversible airways disease. The BNF states: 'beta-blockers should be avoided in patients with a history of asthma or chronic obstructive airways disease; if there is no alternative, a cardioselective beta-blocker may be used with extreme caution under specialist supervision'.
Renal dysfunction (eg serum creatinine > 200 µmol/l)	ACE inhibitors and angiotensin-II receptor antagonists may be contraindicated. Patient requires specialist assessment.
Anaemia	Anaemia is common in patients with moderate to severe heart failure and where due to the heart failure (and not other causes) treatment with erythropoietin and iron therapy may improve symptoms and reduce the risk of hospitalisation for worsening heart failure. ^{164,165} The results of several large RCTs addressing this issue are awaited.
Thyroid disease	Severe thyroid dysfunction may cause or precipitate heart failure.
Peripheral vascular disease	Not an absolute contraindication to beta-blocker therapy. High index of suspicion for renal artery stenosis required.
Urinary frequency	Requires appropriate specialist referral. Alpha-blockers may cause hypotension or fluid retention, but are not absolutely contraindicated in patients with heart failure. Diuretics likely to be less well tolerated.
Gout	Avoid non-steroidal anti-inflammatory drugs. Gout can be exacerbated by diuretics and may have an atypical presentation in patients with heart failure. Colchicine may be useful for the treatment of an acute attack of gout. Allopurinol may be useful at reducing the risk of further attacks of gout, but should not be started at the time of an acute episode of gout.

7.2.16 Drugs to be avoided or used with caution in heart failure

Patients with heart failure may have significant renal (and hepatic) impairment. Drugs cleared predominantly by the kidney (and liver) can accumulate in these patients causing drug-related toxicity – these include drugs used to treat heart failure itself, such as ACE inhibitors and digoxin.

Non-prescription drugs (such as herbal remedies) can have important interactions with the prescription drugs taken by patients with heart failure, eg St John's wort can affect the blood

levels of both warfarin and digoxin. Please see the section on anxiety and depression for further details (section 11). Comprehensive details on non-prescription drugs can be found on <http://herbmed.org>

Non steroidal anti inflammatory drugs (NSAIDs) may exacerbate oedema and renal impairment in patients with HF and should be used with caution – this applies to both non-selective agents as well as the newer COX-2 selective agents. Oral and intravenous steroids may also exacerbate oedema. Drugs with a negative inotropic effect should also be avoided – such as verapamil, diltiazem, and Class I anti-arrhythmic drugs.

This guideline can only provide an outline of the relevant issues. Please see the British National Formulary for more complete listings and detail (<http://bnf.org>).

7.2.17 Side effects of drugs commonly used in the treatment of heart failure

All drugs have side effects. The major complications of drugs commonly used for the treatment of heart failure are listed in Table 10. Further details can be found in the ABPI Electronic Medicines Compendium, which can be found at www.emc.vhn.net

Table 10 Major complications of drug therapy in chronic heart failure	
Drugs	Complications
Diuretics	Common: postural hypotension, gout, urinary urgency. Serious: electrolyte imbalance (hypokalaemia, hypomagnesia, hyponatraemia), arrhythmia.
ACE inhibitors	Common: cough, hypotension including postural. Serious: worsening renal function, renal infarction in renal artery stenosis, angio-oedema.
Beta-blockers	Common: tiredness, bradycardia, coldness. Serious: asthmatic attack, exacerbation of heart failure, heart block.
Spironolactone	Common: gynaecomastia, tiredness, rashes. Serious: hyperkalaemia, hyponatraemia.
Digoxin	Common: nausea. Serious: life threatening arrhythmias.
Angiotensin-II receptor antagonists	Common: hypotension including postural. Serious: worsening renal function, renal infarction in renal artery stenosis.
Amiodarone	Common: photosensitivity, nausea, thyroid dysfunction, sleep disturbance, corneal microdeposits. Serious: thyrotoxic storm, pro-arrhythmia, pulmonary/hepatic fibrosis.
Inotropes	Common: nausea, palpitation. Serious: arrhythmia, cardiotoxicity.

It is important that possible side effects are discussed with patients (and carers where appropriate).

7.2.18 Improving adherence to pharmacological therapy

There is evidence to suggest that non-adherence with treatment is a significant cause of readmission in patients with heart failure.^{166,167} There are many causes of non-adherence, which may be accidental or deliberate. There are few studies specific to patients with heart failure but the guideline development group considered that it was reasonable to extrapolate from studies in other chronic conditions.

Simplifying dosing regimens, and educating patients and their carers about their medicines, appear to be important. Three systematic reviews^{168–170} including mixed populations of patients with chronic conditions requiring chronic medication, reported that a simplified dosing regime (reductions in number of medications and frequency of dosing from three times daily to once daily where possible) improved adherence with the number of doses correctly taken. There is, however, mixed evidence for the benefit of reducing twice-daily regimes to once daily. There is no evidence that changing the timing of doses improves adherence. None of these studies demonstrated direct benefits in terms of patient outcome. (Ia)

RECOMMENDATION

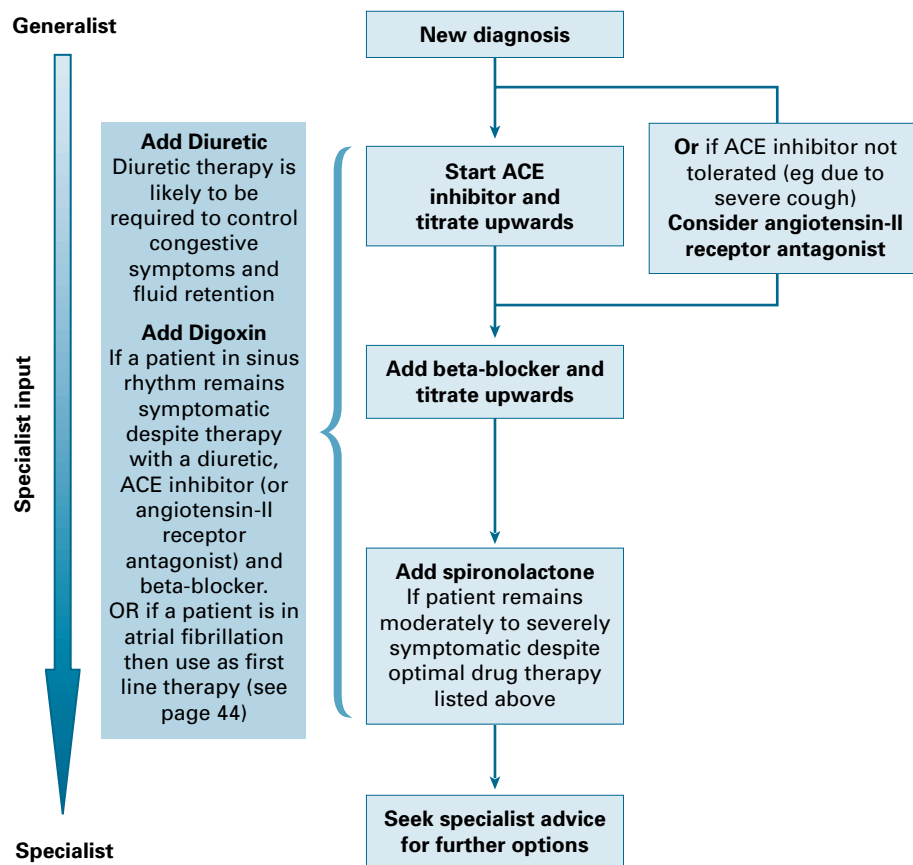
- R44** Dosing regimens should be kept as simple as possible, and the healthcare professional should ensure that the patient and carer are fully informed about their medication. **B**

7.3 Algorithm for the pharmacological treatment of symptomatic heart failure due to LV systolic dysfunction

Patients with symptomatic heart failure due to LV systolic dysfunction should be treated with the following drugs (if tolerated and not contraindicated) and in the sequence indicated. The reader must refer to the text of the main guideline for more detailed discussion and explanation.

Please note:

- Diuretic is first line therapy when a patient presents with acute pulmonary oedema
- Please refer to tables 3–7 (in Section 7) for starting doses of drugs
- The arrow on the left indicates the increasing likelihood of the need for specialist input.



7.4 Invasive procedures

Although drug therapy is the mainstay of treatment of heart failure, some patients will also benefit from diagnostic or interventional invasive procedures. These procedures are normally organised by a specialist. Several RCTs are currently examining the benefit of such procedures, and the evidence base is likely to change substantially in the next 5–10 years. This guideline can only give general advice, and specialist advice is strongly recommended where such procedures might be considered.

7.4.1 Coronary revascularisation

Although ischaemic heart disease is the commonest cause of heart failure due to left ventricular damage in the UK, the benefits of revascularisation in patients with congestive heart failure remain uncertain, with evidence limited to a systematic review of cohort studies of patients with moderate to severe LV systolic dysfunction.¹⁷⁹ Subgroup analyses in large randomised trials of surgical and medical therapy in patients with chronic stable angina¹⁸⁰ have suggested that patients with a low ejection fraction and triple vessel coronary artery disease may have improved survival with surgery. However, left ventricular dysfunction and severe symptoms increase the risks of coronary artery bypass grafting (CABG). Although a number of small studies have suggested that revascularisation may be beneficial in patients with heart failure with large areas of noncontractile but ‘viable’ myocardium, there is an absence of randomised studies of surgery in patients with heart failure. Further data will become available in the near future. This will provide a clearer picture of which patients are likely to benefit from coronary revascularisation. (III)

There are a variety of imaging techniques to detect non-contractile but viable myocardium including nuclear imaging, stress echocardiography and magnetic resonance imaging.

Health economic evidence: Little is known about the health economics of revascularisation in heart failure. A health technology appraisal of interventions for chronic stable angina in 1998 identified no relevant economic evaluations of CABG or PTCA.¹⁸¹

RECOMMENDATION

- R45 Coronary revascularisation should not be **routinely** considered in patients with heart failure due to systolic left ventricular impairment, unless they have refractory angina. C

7.4.2 Cardiac transplantation

Although there are no randomised studies of transplantation in patients with heart failure owing to the intrinsic practical limitations in this field, observational data demonstrate an improved quality of life after transplantation with a 70–80% survival at five years.¹⁸² The major limitations of cardiac transplantation are limited donor organ availability and the fact that most patients do not fulfil current selection criteria (see Table 11). Long-term prognosis is limited by the side effects of immunosuppression (hypertension, malignancy, renal failure and infection) and the development of graft vascular disease. (IV)

Health economic evidence: There are no recent economic evaluations of cardiac transplantation in the UK. While this is a relatively expensive procedure the benefits in terms of both quality and length of life have been shown to be large, resulting in favourable cost effectiveness ratios (see Appendix E).

RECOMMENDATION

- R46** Specialist referral for transplantation should be considered in patients with severe refractory symptoms or refractory cardiogenic shock. **C**

Table 11 Indications for heart transplantation, adapted from ACC/AHA & ESC Guidelines^{16,68}

Indications	Contraindications and cautions
<ul style="list-style-type: none"> <input type="checkbox"/> Patients must be willing and able to withstand the physical and emotional demands of the procedure and its post-operative sequelae. <input type="checkbox"/> Objective evidence of limitation, eg peak oxygen consumption less than 10 ml/min/kg on cardiopulmonary exercise test with evidence for anaerobic metabolism.* <input type="checkbox"/> Patients dependent on intravenous inotropes and mechanical circulatory support. 	<ul style="list-style-type: none"> <input type="checkbox"/> Present alcohol and/or drug abuse. <input type="checkbox"/> Chronic mental illness, which can not be adequately controlled. <input type="checkbox"/> Treated cancer with remission and < 5 years follow-up. <input type="checkbox"/> Systemic disease with multiorgan involvement. <input type="checkbox"/> Uncontrolled infection. <input type="checkbox"/> Severe renal failure (creatinine clearance < 50 ml/min) or creatinine > 200 µmol/l, although some centres accept patients on haemodialysis. <input type="checkbox"/> Fixed high pulmonary vascular resistance (6–8 Wood units and mean transpulmonary gradient > 15 mmHg and pulmonary artery systolic pressure > 60 mmHg). <input type="checkbox"/> Recent thromboembolic complication. <input type="checkbox"/> Unhealed peptic ulcer. <input type="checkbox"/> Evidence of significant liver impairment. <input type="checkbox"/> Other disease with a poor prognosis.
<p>*Patients with significant exercise limitation that have a peak oxygen consumption less than 55% predicted or between 11 and 15 ml/min/kg also warrant consideration for cardiac transplantation if they have recurrent unstable myocardial ischaemia untreatable by other means, or recurrent episodes of congestive heart failure in spite of adherence to optimum medical therapy.</p>	

7.4.3 Ventricular assist devices (VADs)

The worldwide experience of using implantable ventricular assist devices is steadily increasing, with a small number of patients continuing with such mechanical support for more than one year in one prospective trial and in case series.^{183,184} Although some patients appear to recover during VAD therapy, there are insufficient data on the mechanisms of response and the identification of patients in whom devices can be safely removed to justify recommendation of more widespread use of VADs as a bridge to recovery^{185,186} or as chronic therapy. (Ib)

Health economic evidence: These are a relatively new and rapidly evolving technology. At present the cost of the devices is high and the evidence on potential benefits is not of sufficient quality to conduct an economic evaluation. A study of the clinical and cost effectiveness of VADs has recently been funded by the health technology assessment programme and is due to report in 2004 (see Appendix E).

7.4.4 Cardiac resynchronisation therapy

Approximately 30% of patients with heart failure have delayed or incoordinate electrical activation of ventricular contraction. This is manifest on a surface ECG by a bundle branch block pattern and a QRS duration > 120 ms.¹⁸⁷ The presence of left bundle branch block is associated with adverse haemodynamic consequences and reduced survival in patients with heart failure. Two small, short-term RCTs have shown that cardiac function or oxygen uptake can be improved in patients with LBBB by simultaneously pacing the left and right ventricles (referred to as cardiac ‘resynchronisation’).^{188,189} (Ib)

Randomised trials (often employing a cross-over design) of biventricular pacing have demonstrated improvements in symptoms, exercise tolerance and reduced hospitalisations for heart failure. The effect on long-term survival is currently being evaluated in ongoing studies^{189–191} with publication of results expected imminently. (Ib)

Health economic evidence: Implantation and follow-up costs of CRT devices are not significantly dissimilar to those seen with standard dual chamber pacemakers; preliminary results from trials suggest potential cost savings through lower hospitalisation rates coupled with overall benefits in terms of mortality and morbidity.

The results of a large clinical trial examining the impact of cardiac resynchronisation therapy (with or without an implantable cardiac defibrillator) in patients with NYHA Class III or IV heart failure, a QRS duration > 120 mseconds and left ventricular ejection fraction (LVEF) ≤ 35% is due to be published in 2003. This study (COMPANION-CHF)¹⁹² is likely to influence future recommendations on the use of cardiac resynchronisation therapy (with or without an implantable cardiac defibrillator) in patients with heart failure.

RECOMMENDATION

- R47 Resynchronisation therapy should be considered in selected patients with left ventricular systolic dysfunction (LVEF ≤ 35%), drug refractory symptoms, and a QRS duration > 120 ms. The result of ongoing trials will help guide appropriate patient selection. A

7.4.5 Implantable cardioverter-defibrillators (ICDs)

In a large systematic review of CHD patients, ICDs have been shown to prolong life in patients with impaired left ventricular function and a history of sustained ventricular arrhythmia.¹⁹³ There are no large-scale randomised data in unselected patients with heart failure. Ongoing RCTs will help clarify this area.

A NICE health technology appraisal provided guidance on the use of ICDs for arrhythmias,¹⁹⁴ and the recommendations are summarised below.

Health economic evidence: A review of the clinical and cost effectiveness of ICDs for the HTA programme revealed a very wide range of cost effectiveness ratios. The applicability of this evidence to the treatment of heart failure is unclear. As this technology is rapidly evolving the currently high cost of devices is likely to fall and ongoing trials are likely to provide better evidence on potential benefits. The HTA is due to be updated in September 2003.

RECOMMENDATION

R48 Recommendation from NICE Technology Appraisal Guidance No. 11 *Guidance on the use of implantable cardioverter defibrillators for arrhythmias* (www.nice.org.uk/Docref.asp?d=10239): NICE

The use of implantable cardioverter defibrillators (ICDs) should be routinely considered for patients in the following categories:

“Secondary prevention” ie for patients who present, in the absence of a treatable cause, with:

- Cardiac arrest due to either ventricular tachycardia (VT) or ventricular fibrillation (VF).
- Spontaneous sustained VT causing syncope or significant haemodynamic compromise.
- Sustained VT without syncope/cardiac arrest, and who have an associated reduction in ejection fraction (less than 35%) but are no worse than class 3 of the New York Heart Association functional classification of heart failure.

“Primary prevention” for patients (see paragraph 2.5 for definition) with:

- a history of previous myocardial infarction (MI) and all of the following:
 - i) non sustained VT on Holter (24 hour ECG) monitoring;
 - ii) inducible VT on electrophysiological testing;
 - iii) left ventricular dysfunction with an ejection fraction (EF) less than 35% and no worse than class III of the New York Heart Association functional classification of heart failure.
- A familial cardiac condition with a high risk of sudden death, including long QT syndrome, hypertrophic cardiomyopathy, Brugada syndrome, arrhythmogenic right ventricular dysplasia (ARVD) and following repair of Tetralogy of Fallot.

7.4.6 Other invasive therapies

Patients with severe ventricular dilatation often have clinically important mitral regurgitation. Surgical correction of the mitral regurgitation has been suggested as a therapeutic option in such patients from case series but there are no controlled studies.¹⁹⁵

Cardiomyoplasty is possibly of benefit in patients with class III heart failure, however it is currently an experimental procedure, with no RCT evidence to substantiate its use.¹⁹⁶

Health economic evidence: There are no economic evaluations of the use of mitral valve surgery or cardiomyoplasty in the treatment of heart failure.

7.5 Oxygen therapy and continuous positive airways pressure treatment

Patients with heart failure may develop arterial hypoxaemia through mismatches in lung ventilation and perfusion, and disturbances in nocturnal ventilation and respiratory drive (including periodic breathing such as Cheyne-Stokes respiration).^{197,198} This may have acute and chronic deleterious effects on cardiac function.

▷ Domiciliary oxygen therapy

One very small RCT of domiciliary oxygen for seven nights in patients with heart failure and Cheyne-Stokes respiration suggested some improvement in breathing pattern at night, but no improvement in awakenings or daytime sleepiness and functional status.¹⁹⁹ There was a high drop out rate even during the short duration of this study. A working party report of the Royal College of Physicians included recommendations for patients with heart failure.²⁰⁰ Long-term oxygen therapy was recommended if there is daytime hypoxaemia (PaO₂ on air of < 7.3 kPa) or nocturnal hypoxaemia with SaO₂ below 90% for at least 30% of the night. There is a need for further studies in this area. (IV)

▷ Continuous positive airways pressure (CPAP) treatment

Currently the majority of published reports relate to the use of CPAP as therapy for patients with heart failure with Cheyne-Stokes respiration. All the trials are small and may not have a sufficiently long washout period after crossover. Benefit is reported in patients with moderate to severe heart failure in terms of sleep quality,¹⁹⁹ peak oxygen consumption during exercise,¹⁹⁹ maximal inspiratory pressure,²⁰¹ LV ejection fraction,²⁰¹ and cognitive function.¹⁹⁹ No significant differences in arterial oxygen saturations have been reported.²⁰² The findings are mixed in terms of effect on functional status and symptoms.^{201,202} One of the largest RCTs to date included 66 patients with 31 randomised to CPAP at 12.5cm H₂O for at least six hours at night for three months,²⁰³ with unsupervised use thereafter. Patients were stratified by whether they had Cheyne Stokes respiration or not, and for those who had there was a significant increase in LV ejection fraction. There was no significant difference in transplant-free survival to two years, but the study was underpowered to detect this. No adverse effects of CPAP were noted, which was well tolerated. There is a need for further studies in this area. (Ib)

The guideline development group was unable to come to any recommendation on the use of domiciliary oxygen or CPAP therapy for patients with heart failure. Further research is required.

7.6 Treatment of heart failure not due to LV systolic dysfunction

7.6.1 Valve disease

Clinical examination and an echocardiogram should detect valve disease. Detection is important because heart failure due to valve disease is potentially curable, but will require management that differs from that of other causes of heart failure such as LV systolic dysfunction.^{16,68} ACE inhibitor therapy may be harmful in patients with severe aortic stenosis. (III)

RECOMMENDATIONS

- R49** Patients with heart failure due to valve disease should be referred for specialist assessment and advice regarding follow-up. **C**
- R50** ACE inhibitor therapy should not be initiated in a patient with a clinical suspicion of haemodynamically significant valve disease, until the valve disease has been assessed by a specialist. **C**

Patients with valve disease (but no heart failure) should also be assessed by a specialist, as the onset of heart failure increases the risk of surgery and reduces the likelihood of full recovery.

7.6.2 Diastolic dysfunction

The RCT evidence for the treatment of diastolic dysfunction is sparse, but will strengthen in the next few years as the results of ongoing trials become available. The guideline development group agreed the following principles.

RECOMMENDATION

- R51** The diagnosis and treatment of diastolic dysfunction should be made by a specialist, and other conditions that present in a similar way may need to be considered. Patients in whom this diagnosis has been made should usually be treated with a low to medium dose of loop diuretics (eg < 80 mg furosemide per day). Patients who do not respond to this treatment will require further specialist advice. **GPP**

7.6.3 Other causes

The GDG agreed that the management of other causes of heart failure would require specialist input. Such causes include congenital heart disease, cardiomyopathies, and specific heart muscle disease such as amyloid.

7.6.4 Atrial fibrillation (AF)

Atrial fibrillation is common in heart failure and may exacerbate or precipitate heart failure. Management may be directed at either controlling the heart rate or restoring and maintaining sinus rhythm which can improve symptoms, and hence quality of life.

Although there is no randomised trial evidence that restoration of normal sinus rhythm is of clinical benefit to patients with heart failure, it may be appropriate for individual patients. (III)

Amiodarone has been shown in a large scale systematic review of 32 trials to increase the chance of restoring and maintaining sinus rhythm¹⁷¹ although benefits on survival are unproven. (Ia)

Nodal ablation and pacemaker implantation may be of benefit in patients with intractable symptoms and poor heart rate control despite pharmacological intervention¹⁷¹ although more evidence in this field is required. (Ia)

A systematic review of the large RCTs of beta-blockers in patients with heart failure showed that the benefits of beta-blockers are no different in patients with atrial fibrillation than in those without.¹⁷¹ (Ia)

Anticoagulation in patients with heart failure and atrial fibrillation has been discussed in section 7.2.8, p 47. Readers should also see the digoxin section (7.2.5) on p 44.

RECOMMENDATIONS

- | | | |
|-----|---|---|
| R52 | For patients with heart failure and atrial fibrillation, specialist advice should be sought as to whether the aim is improvement of heart rate control or cardioversion (return to sinus rhythm). | C |
| R53 | Anticoagulation is indicated for patients with heart failure and atrial fibrillation (see also anticoagulation section, p 47). | A |

Subgroups of patients with heart failure

7.6.5 Age

The average age of a patient with a new diagnosis of heart failure in the UK is 76 years.¹ In principle, the pharmacological treatment for elderly patients should be similar to that of any other patient with heart failure, but tolerance may be lower, side effects more frequent, and adherence poorer.

One systematic review and five small prospective randomised trials were identified that related to the treatment of older patients, although the definitions of age cut-offs varied between studies. ACE inhibitors have been reported in one systematic review to produce more side effects but improve quality of life in older patients.¹⁷² RCT data have suggested that angiotensin-II receptor antagonists may be initiated in a similar manner in older patients as in other patients with heart failure.¹⁷³ (Ia)

There is no evidence that the dose of beta-blockers should be reduced in older patients, and with low dose initiation and slow titration, trials have indicated benefit.¹⁷⁴ (Ib)

A randomised controlled trial has reported no difference in the clinical response to digoxin compared to placebo in older patients compared with younger patients.¹⁷⁵ More adverse events have been noted in older patients, and low dose initiation of drug therapy is particularly advised where patients have a raised blood creatinine concentration. (Ia)

RECOMMENDATIONS

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| R54 | The management of heart failure should be determined by clinical criteria, irrespective of the age of the patient. | A |
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- R55 Tolerance of drugs may be lower and side-effects require closer and more frequent monitoring in older patients. **GPP**

7.6.6 Gender

Women tend to be under-represented in RCTs of pharmacological therapy in heart failure. The evidence that is available from *post hoc* analysis of randomised trials of most therapy does not suggest that the clinical effects of drugs are different. A post hoc analysis of the DIG trial suggested possible differences in mortality between men and women on digoxin.¹⁷⁶ (IIa)

If a woman of reproductive age has heart failure, there are several important clinical considerations regarding the risk of pregnancy (to mother and child) and the possible teratogenic effects of drugs used to treat heart failure. If the woman has (or has had) peripartum cardiomyopathy (heart muscle disease of no obvious cause developing during or shortly after pregnancy) the risk of further cardiac problems in a subsequent pregnancy is substantial.¹⁷⁷ Drugs such as ACE inhibitors and amiodarone have teratogenic effects. (III)

RECOMMENDATIONS

- R56 The principles of pharmacological management of heart failure should be the same for men and women. **GPP**
- R57 The potential teratogenic effects of drugs should be considered. **GPP**
- R58 **Pregnancy** in women of reproductive age who have heart failure, contraception and pregnancy should be discussed. If pregnancy is being considered or occurs, specialist advice should be sought. Subsequently, specialist care should be shared between the cardiologist and obstetrician. **GPP**

7.6.7 Ethnicity

Non-Caucasian populations are under represented in RCTs, making it difficult to draw firm conclusions. As most evidence available is from *post hoc* analysis of large randomised trials more research in this area is required.¹⁷⁸

RECOMMENDATION

- R59 The principles of pharmacological management should be the same for all patients with heart failure, regardless of ethnicity. **GPP**

8 Monitoring

Heart failure is a chronic condition with a high mortality and a considerable impact on the patient's (and often carer's) quality of life. The clinical condition may fluctuate and repeated admission to hospital is common, particularly for patients with more severe heart failure and other co-morbidities.^{166,204} Treatment usually involves the prescription of several drugs, as outlined in the earlier parts of this guideline. Monitoring of the clinical status is necessary and will involve healthcare professionals in both primary and secondary care. Assessment of cognitive state, such as detecting acute confusion; and monitoring for development of anxiety or depression, is also important. Work with focus groups suggests that many patients and their carers do not know how to access medical advice should the clinical condition deteriorate, thus limiting the possibility of early intervention to reduce the need for readmission to hospital. Patients and their carers are playing an increasing role in monitoring, but this requires appropriate education and support. This section of the guideline gives guidance on the monitoring of patients with heart failure.

8.1 Clinical review

There have been few direct comparisons of the impact of different intensities and frequencies of monitoring of patients with chronic heart failure – although almost all published studies comparing closer, more frequent contact with a healthcare professional who has experience in managing heart failure with 'routine' care report an improvement in quality of life for patients, and a reduction in the need for urgent hospitalisation.^{205–208} (I)

It is not clear which components of these programmes are responsible for the benefit. Authors of trials have commented that more frequent contact with health professionals in itself may have a beneficial clinical effect. Monitoring of patients with chronic heart failure is necessary for a variety of reasons, and the guideline development group agreed a pragmatic approach as suggested below. (IV)

At clinical review the following assessments should be made:

1. **Assessment of functional capacity** Chiefly from history, but more objectively by use of NYHA Class, specific Quality-of-life questionnaires, 6 minute walk test, or maximal exercise test. NB Not all of these tests are likely to be necessary, or appropriate, at each assessment.
2. **Assessment of fluid status** Chiefly by physical examination – changes in body weight, extent of jugular venous distension, lung crackles and hepatomegaly, extent of peripheral oedema, and lying and standing blood pressure (postural drop in blood pressure may indicate hypovolaemia).
3. **Assessment of cardiac rhythm** Chiefly by clinical examination, but may require 12 lead electrocardiogram (ECG) or 24 hour electrocardiographic monitoring ('Holter') if suspicion of arrhythmia.
4. **Laboratory assessment** Checking of serum biochemistry (urea, electrolytes, creatinine) is essential, but other tests (such as thyroid function, haematology, liver function, level of anticoagulation) may also be required depending on the medication prescribed and co-morbidity.

8.2 Review of management plan – including medication

The guideline development group recommended that the assessment of nutritional and cognitive status may also be helpful in determining the overall management plan for the patient with heart failure. Nutritional assessment is not always clear-cut, especially where fluid retention masks malnutrition, so that use of a screening tool²⁰⁹ and referral to a dietitian for assessment (and management) may sometimes be appropriate. (IV)

8.3 Serial cardiac imaging

There is no evidence that *serial* chest radiographs, Doppler echocardiograms or invasive haemodynamic monitoring improve clinical management over and above the items mentioned above. (IV)

8.4 Therapeutic drug monitoring of serum digoxin concentrations

There is no evidence from RCTs that routine monitoring of serum digoxin concentrations improves survival or quality of life for patients with heart failure who are prescribed this therapy. A systematic review of therapeutic drug monitoring suggested that such monitoring may reduce the risk of toxicity.²¹⁰ Several studies have reported a very high proportion of requests for serum digoxin measurement were not acted upon or were inappropriate in terms of timing (which should be 8–12 hours after the last digoxin dose and several days after a change in dosage).^{211–213} The most recent guidelines from the American College of Cardiology and American Heart Association do not advocate the measurement of serum digoxin concentration to assess efficacy of therapy, but rather as an aid to the detection of toxicity.⁶⁸ (IV)

Electrolyte abnormalities (particularly hypokalaemia or hypomagnesaemia) may increase the risk of toxicity, even with serum concentrations of digoxin within the so-called ‘therapeutic range’ of 0.7–2 ng/ml. Deteriorating renal function increases the risk of high serum concentrations of digoxin, as do certain drugs (eg amiodarone, spironolactone). Please see British National Formulary for further details (<http://bnf.org>)

8.5 Serial measurement of circulating natriuretic peptide concentration

Serial measurement of plasma NTproBNP concentrations has been shown in one small RCT to reduce the risk of decompensation,²¹⁴ but further trials are ongoing. Currently it is not possible to give advice on the added value of serial measurement of plasma BNP or NTproBNP in the monitoring of patients with heart failure, but further evidence should be available within the next two years. (Ib)

8.6 Patient self-monitoring and remote monitoring

After appropriate education, some patients may be able to monitor their volume status, usually by regular weighing, with adjustment of their therapies (most typically diuretic dose) in response to changes in weight. To be successful the patient needs to know how to adjust their therapy, and when to access help when their symptoms deteriorate or fail to respond to these first-line measures. More complex remote monitoring (such as telemonitoring) of patients with heart failure is in its infancy, but shows promise for the future. (IV)

RECOMMENDATIONS

R60	All patients with chronic heart failure require monitoring. This monitoring should include:	GPP
	<ul style="list-style-type: none"> ● a clinical assessment of functional capacity, fluid status, cardiac rhythm (minimum of examining the pulse) fluid status, cognitive status and nutritional status ● a review of medication, including need for changes and possible side-effects ● serum urea, electrolytes and creatinine.* 	
R61	More detailed monitoring will be required if the patient has significant co-morbidity or if their condition has deteriorated since the previous review.	GPP
R62	The frequency of monitoring should depend on the clinical status and stability of the patient. Monitoring interval should be short (days to two weeks) if the clinical condition or medication has changed, but is required at least six-monthly for stable patients with proven heart failure.	GPP
R63	Patients who wish to be involved in monitoring of their condition should be provided with sufficient education and support from their healthcare professional to do this, with clear guidelines as to what to do in the event of deterioration.	GPP
R64	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.	GPP
R65	The serum digoxin concentration should be interpreted in the clinical context as toxicity may occur even when the concentration is within the ‘therapeutic range’.	GPP

*This is a minimum. Patients with co-morbidities or co-prescribed medications will require further monitoring – please see relevant section above. Monitoring serum potassium is particularly important if a patient is taking digoxin or spironolactone.

9 Referral and approach to care

The management of heart failure is likely to be shared between healthcare professionals in both primary and secondary care. Patients and their carers are increasingly involved in management decisions. Work with patient focus groups suggests that the major failings of management relate to poor communication between healthcare professionals, and between healthcare professionals and the patients they care for. It is one of the aims of high-quality care that patient preference is sought and considered.

The guideline development group recommended that referral from one healthcare professional to another (and to and from primary/secondary/tertiary care) should be guided by the level of expertise of the healthcare professional and the need for further investigation, intervention or support. This is particularly important for patients in whom the diagnosis is not clear, where invasive interventions may be considered, and where a patient fails to respond adequately to initial therapy. A clear management plan that is reviewed regularly and known by the patient and all the healthcare professionals involved with their care is likely to optimise outcome.

Of necessity, many of the recommendations in this section of the guideline are based on expert opinion rather than on the result of RCTs. This does not undermine the value or importance of these recommendations, which may have a large impact on the quality of care and outcome for the person with heart failure and their carers.

9.1 Referral for more specialist advice

None of the trials identified by the systematic literature search was able to demonstrate that certain criteria for referral were better than others.^{215,216} Most studies that were identified included multiple interventions, making the efficacy of any one intervention in isolation difficult to assess. The guideline development group recommended referral in certain clinical situations listed below, but healthcare professionals should always use their judgement in deciding when such a course of action is appropriate. Specialist advice may be obtained without the need for the patient to see the specialist. (IV)

RECOMMENDATIONS

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| R66 | Patients with heart failure require specialist advice in the following situations: | GPP |
| | <ul style="list-style-type: none">● heart failure due to valve disease, diastolic dysfunction or any other cause except LV systolic dysfunction● one or more of the co-morbidities outlined in Table 9 (p 51)● angina, atrial fibrillation or other symptomatic arrhythmia● women who are planning a pregnancy or who are pregnant. | |
| R67 | The following situations also require specialist advice: | GPP |
| | <ul style="list-style-type: none">● severe heart failure● heart failure that does not respond to treatment as discussed in this guideline and outlined in the algorithm (p 54)● heart failure that can no longer be managed effectively in the home setting. | |

9.2 Discharge planning

There is no specific evidence to support formalised discharge planning in patients with heart failure.^{206,208} A recent meta-analysis comparing discharge planning with usual care for a range of medical conditions could not demonstrate a difference in hospital length of stay between these two management methods.^{206,208}

The guideline development group agreed that good communication between primary and secondary care is extremely important for effective discharge planning. A consensus recommendation was agreed. (IV)

RECOMMENDATIONS

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| R68 | Patients with heart failure should generally be discharged from hospital only when their clinical condition is stable and the management plan is optimised. Timing of discharge should take into account patient and carer wishes, and the level of care and support that can be provided in the community. | GPP |
| R69 | The primary care team, patient and carer must be aware of the management plan. | GPP |
| R70 | Clear instructions should be given as to how the patient/carer can access advice particularly in the high risk period immediately following discharge. | GPP |

9.3 Multidisciplinary team approach to heart failure management

Multidisciplinary care programmes improve patients' quality of life, satisfaction with care, and the risk of unplanned hospitalisation for heart failure, compared with conventional care.^{207,217,218} There is no convincing evidence that such programmes improve survival.^{205,217,219} (Ib)

Good communication and team working between disciplines, with close contact with patients, was seen by the guideline development group as key for effective heart failure management. (IV)

Health economic evidence: There is very little economic evidence available on the potential costs and benefits of multidisciplinary teams in the management of heart failure. Most formal evaluations have taken place in the United States and have little relevance to the UK healthcare system. A systematic review of nine RCTs comparing a multidisciplinary team approach to more 'usual' care²²⁰ showed that these teams can have beneficial effects on mortality, hospitalisation and length of stay for patients with heart failure. Of the seven RCTs that considered costs all but one trial showed the teams to be cost saving largely via reduced hospitalisation (see Appendix F).

RECOMMENDATION

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| R71 | Heart failure care should be delivered by a multidisciplinary team with an integrated approach across the healthcare community. | A |
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9.4 Care pathways

None of the trials of care pathways identified by the systematic literature search included patients with heart failure. The evidence from trials in other chronic conditions have failed to demonstrate any consistent benefit in terms of quality of life or readmission rates.^{68,221} (Ib)

The guideline development group considered the evidence for the impact of care pathways for patients with heart failure to be lacking, and recommended further research in this area.

9.5 Non-NHS agencies

‘Non-NHS agencies’ includes home carers, private nursing homes, residential homes and ‘mental health of older people’ homes.

Heart failure is one of the most common reasons for admission to nursing home care. 25% of patients admitted to nursing homes are hospitalised within a six-month period, and this percentage is higher for patients with heart failure.

Research suggests that poor adherence with medication regimes is common in nursing home residents and under prescription and under dosing of recommended heart failure treatment is also common in nursing home populations.

Regular assessment of patients with heart failure in residential and nursing homes, including regular review of medications, improves quality of care and reduces readmission rates.

RECOMMENDATIONS

R72	Standard one of The Older People National Service Framework states that ‘social care services will not use age in their eligibility criteria or policies to restrict access to available services. This applies to patients with heart failure.’ www.doh.gov.uk/nsf/olderpeople.htm	GPP
R73	Management plans for patients with heart failure should be discussed with non-NHS agencies where they are involved in or responsible for the care of a person with heart failure.	GPP
R74	The principles of pharmacological management for a patient cared for in a non-NHS institution should be similar to those for any other patient with heart failure.	GPP
R75	The education needs of non-NHS agency carers should be considered.	GPP

10 Supporting patients and carers

Understanding the information needs of patients and carers is vital. During the development of this guideline, the NCC-CC commissioned a patient and carer focus group to identify issues that are important to patients with heart failure regarding their experiences and perceptions of heart failure care. Consensus guidelines for good communication have been produced by a Royal College of Physicians working party.²²² These were reviewed and discussed by the guideline development group along with the findings of the patient and carer focus groups, and it was agreed to include the key recommendations in this guideline.

10.1 Communication

The focus group reported a variety of positive and negative experiences, but all agreed that honesty and accuracy of information were paramount. There was a strong feeling amongst the group that the attitude of the healthcare professional and their willingness to spend time explaining the condition and the process of care was very important, as this inspires feelings of confidence and ability to cope with the illness. (IV)

Many of the people who participated in the focus group felt the provision of information relating to their diagnosis, condition and care had been inadequate. Several group members reported that consultations had been very short, and that information was often fractured, out of context and only offered when demanded by the patient. (IV)

There is no specific literature on communication between healthcare professionals and patients with heart failure, however generic studies of communication^{223–228} between healthcare professionals and patients suggest that communication is most effective when the content, style and timing of information is tailored to the needs of the individual patient.^{229–232} (III)

The guideline development group emphasised the importance of considering the cognitive ability of the patients with heart failure when sharing information. Cognitive impairment is common in patients with heart failure either as a result of their condition or due to co-existing disease. In these circumstances it is particularly important that carers and relatives are made aware of treatment regimes for the patients they care for and be encouraged to identify any need for clinical support (please also see Section 8 on monitoring). (IV)

Healthcare professionals often perceive a disparity in the information needs of caregivers and patients. This is seldom the case.^{233–235} (III)

Breaking the news of a diagnosis can be made easier for the patient (and doctor) by improved training in this area.^{236,237} It is important to convey hope and provide the patient with choices by detailing the therapeutic options that are available.^{230,238} (III)

The informed patient is more likely to adhere to treatment than an uninformed patient.^{231,239–241} (Ia)

Health economic evidence: It is not possible to say anything certain about the economic implications of improved information provision and communication. Improvements in coordination of information could potentially result in savings through increased efficiency,

and this is particularly true at the interface between primary and secondary care and between the NHS and social services. Good information provision may directly improve patient well-being by reducing uncertainty, relieving stress and contributing to empowerment if the patient is more involved in decisions about care. This may also have subsequent effects in terms of functional status. In addition, information may change the pattern of service use and this will also have the potential to benefit patients, carers and their families. However, if current provision is very poor, then substantial resource increases may be required in order to improve the situation. A significant part of this resource will be required to equip health professionals with the necessary skills to assess individual patient needs for information.

RECOMMENDATIONS

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| R76 | Good communication between healthcare professionals and patients and carers is essential for the best management of heart failure. | GPP |
| R77 | <p>Guidelines for good communication:</p> <ul style="list-style-type: none"> ● Listen to patients and respect their views and beliefs ● Give patients the information they ask for or need about their condition, its treatment and prognosis, in a way they can understand including information about any serious side effects of drugs to be prescribed ● Provide the most important information first ● Explain how each item will affect patients personally ● Present information in separate categories ● Make advice specific, detailed and concrete ● Use words the patients will understand; confirm understanding by questions; define unfamiliar words; write down key words; draw diagrams and keep a copy in the medical notes ● Repeat the information using the same words each time ● Prepare material, written or taped, to back up handwritten notes ● Share information with patients' partners, close relatives or carers if they ask you to do so. When patients cannot indicate their consent for such sharing of information, it is advisable to share the information that those close to the patient need or want to know, except where you have reason to believe that the patient would object if able to do so. | C |
| R78 | The content, style and timing of information provision should be tailored to the needs of the individual patient. | C |
| R79 | Healthcare professionals should assess cognitive ability when sharing information. | GPP |
| R80 | Carers and relatives of patients who are cognitively impaired should be made aware of treatment regimes for the patients they care for and be encouraged to identify any need for clinical support. | GPP |
| R81 | Management of heart failure should be seen as a shared responsibility between patient and healthcare professional. | GPP |
| R82 | Unless specifically excluded by the patient, carers and relatives should be involved in the management of the patient, particularly where the patient cannot look after him or herself. | GPP |

10.2 Prognosis

Doctors perceive themselves as bad or unrealistic prognosticators,^{222,242–245} and communication between patients and doctors may be poor regarding the advance planning associated with the specific end of life issues of prognosis, or death and dying. The undulating clinical course and the difficulty of predicting prognosis in heart failure are well recognised. These create barriers to open communication and advance planning.

The guideline development group found it difficult to recommend which clinical and laboratory features of patients with heart failure should be used to estimate prognosis in routine practice. Much of the evidence is from small series of highly selected patients, and the additional value of routine use of more sophisticated tests such as cardiopulmonary exercise testing is not clear.²⁴⁶ Severity of symptoms, aetiology of heart failure, blood pressure, left ventricular function, renal function, neuroendocrine activation, and exercise performance are the variables most consistently reported as being associated with survival in patients with heart failure^{5,246} although the integration of these data into an estimate of prognosis is not straightforward. (IV)

In most clinical circumstances, the need is to identify patients who require referral for more specialist advice or more intensive therapy. This will depend on whether the patient is in primary or secondary care, the aims of therapy, and the patient's wishes. This guideline gives advice regarding which patients are most likely to benefit from referral for more specialist advice, and when patients should be admitted and discharged from hospital.

Further research is required before recommendations can be made as to the best timing and method of estimating prognosis for patients with chronic heart failure. This is likely to vary depending on clinical circumstances.

RECOMMENDATION

R83 Prognosis should be discussed with patients and carers in a sensitive, open and honest manner. **GPP**

10.3 Support groups

All members of the focus group thought that support groups had contributed a large amount to their understanding of their condition and entitlements. Many members reported feelings of isolation and uncertainty when discharged from hospital, and none of the focus group had ever been offered psychological support, either in hospital or following discharge. (IV)

No specific trials regarding support groups for patients with heart failure were identified in the systematic literature search.

Support groups provide a social network for patients and carers and are a valuable source of information and emotional support.^{247–249} They are available for patients with cardiac problems in general, and often include patients with heart failure. (III)

RECOMMENDATION

R84 Healthcare professionals should be aware of local cardiac support networks and provide this information to patients and carers. **GPP**

11 Anxiety and depression

Depression tends to be more common in patients with heart failure than in the general population.²⁵⁰ There is little specific evidence on which to base therapy for depression for patients with heart failure. Drug therapy with antidepressants may lead to complications such as fluid retention, hypotension and arrhythmias. Readers should consult the forthcoming NICE guideline on depression for generic advice (www.nice.org.uk) or the Joint Royal Colleges report *The psychological care of medical patients* (www.rcplondon.ac.uk/pubs/wp_pcomp.pdf) (IV)

A Cochrane review across patients with a range of medical illnesses provides evidence that antidepressants, significantly more frequently than either placebo or no treatment, cause improvement in depression. Antidepressants are commonly acceptable to patients and should at least be considered in those with both physical illness and depression.²⁵¹ (Ia)

St John's wort (*Hypericum perforatum*) is popular as an over-the-counter remedy for depression. It induces drug-metabolising enzymes and a transport protein leading to several drug interactions. It acts to reduce the efficacy of co-administered digoxin and warfarin. The amount of active ingredient can vary from one preparation to another and patients often switch between preparations, leading to variable enzyme induction. Importantly, when patients stop taking St John's wort the blood levels of interacting medicines may rise, leading to toxicity. For further information please visit www.mca.gov.uk/ourwork/monitorsafeequalmed/currentproblems/cpmay2000.pdf

RECOMMENDATIONS

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| R85 | The diagnosis of depression should be considered in all patients with heart failure. | C |
| R86 | Where depression is likely to have been precipitated by heart failure symptoms then reassessment of psychological status should be undertaken once the physical condition has stabilised following treatment for heart failure. If the symptoms have improved no further specific treatment for depression is required. | C |
| R87 | Where it is apparent that depression is co-existing with heart failure, then the patient should be treated for depression following the NICE guideline (<i>Depression: the management of depression in primary and secondary care</i>), scheduled for publication in February 2004. | C |
| R88 | For patients with heart failure, the potential risks and benefits of drug therapies for depression should be considered carefully. | GPP |
| R89 | Patients with heart failure should consult a healthcare professional before using over the counter therapies for depression such as St John's Wort (<i>Hypericum perforatum</i>). Healthcare professionals should be aware of the potential interaction with prescribed medication, and always ask about self-medication, including the use of herbal products. | GPP |

12 End of life

The aim of palliative care is to improve the quality of life for patients with incurable disease. It also aims to improve the quality of dying and to ameliorate the potentially devastating effects of dying on the family and carers. There is substantial evidence for considerable unmet palliative needs of patients and informal carers in heart failure.^{244,252–254} The main areas of need include symptom control, psychological and social support, planning for the future and end of life care.^{244,245,252–258}

General palliative care is delivered by the **usual** professional carers of the patient and family where the palliative need is of low to moderate complexity. Specialist palliative care services are provided for patients and their families with palliative need of moderate to high complexity. There is only anecdotal evidence that general or specialist palliative care improves the care of patients with heart failure specifically. There is some evidence that specialist palliative care in cancer improves symptom control, reduces time spent in hospital, improves patient and carer choice and satisfaction and reduces overall cost.^{259,260} (IV)

It is not known when, how and by whom supportive and palliative care is best provided during the patient's journey from diagnosis of heart failure to death. The provision of this type of care is complex because it must respond to a broad range of needs and is likely to be provided in a variety of different settings. There is no good evidence on the effects of palliative care on quality of life of patients with heart failure.

Owing to the significant risk of sudden death at all stages of the disease, there may be a role for 'prospective' management of uncertainty in all patients. This might include planning for the future and discussion of resuscitation preferences.

NICE has commissioned supportive and palliative care guidance to be published 2003/4. While it will focus on commissioning services for patients with cancer and their carers, it is anticipated that the guidance may inform the development of effective service models for other groups of patients with similar needs. This guidance will focus on service configuration and not clinical care; no similar guidance has been commissioned for other diseases.

Health economic evidence: Little is known about the health economics of palliative care but it is important to bear in mind that a significant proportion of the cost burden of this care will fall on the patient and their carers.

Further research in this area is recommended by the guideline development group.

RECOMMENDATIONS

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| R90 | Issues of sudden death and living with uncertainty are pertinent to all patients with heart failure. The opportunity to discuss these issues should be available at all stages of care. | GPP |
| R91 | The palliative needs of patients and carers should be identified, assessed and managed at the earliest opportunity. | GPP |
| R92 | Patients with heart failure and their carers should have access to professionals with palliative care skills within the heart failure team. | GPP |

13 Prevention

The prevention of cardiac damage leading to heart failure lies outside the scope of this guideline and can only be dealt with in outline. The GDG felt that this area was of sufficient importance to warrant inclusion, with principles of good practice. Many potential causes of cardiac damage can be prevented or treated, and the extent of any damage reduced. Aspects of lifestyle such as diet, smoking, alcohol consumption, and exercise affect cardiac risk. Accurate identification and appropriate treatment of hypertension, hyperlipidaemia, and diabetes will reduce the risk of cardiac (and vascular) damage. The relevant clinical guidelines should be consulted.^{16,68,116,261–268} (IV)

Rapid treatment of acute myocardial infarction, prevention of reinfarction, and the treatment of myocardial ischaemia, can reduce the extent of cardiac damage. (IV)

If the underlying cause of cardiac damage or abnormality cannot be removed, attempts should be made to delay the progression to heart failure. This includes timely correction of valve disorders and congenital heart disease. (IV)

There is evidence that ACE inhibitors and beta-blockers can delay the progression to heart failure in patients with a history of myocardial infarction,⁶⁸ and in those with asymptomatic LV systolic dysfunction.⁶⁸ There is evidence that ACE inhibitors are cost-effective in this clinical situation.^{269–272} (IV)

Screening for asymptomatic cardiac abnormalities that may progress to heart failure is outside the scope of this guideline.

PRINCIPLES OF GOOD PRACTICE

- ❑ To help prevent heart failure, healthcare professionals should encourage and support people to make healthy lifestyle choices such as not smoking, exercising regularly, avoiding excessive alcohol intake and controlling their weight.
- ❑ Patients with hypertension, hyperlipidaemia, diabetes, and coronary artery disease (including acute myocardial infarction) should be treated according to current guidelines.
- ❑ Patients with heart valve disease should be assessed by a specialist.

14 Audit criteria

The audit criteria listed in the following pages reflect the key recommendations of the NICE clinical guideline on the management of chronic heart failure in adults in primary and secondary care. Whilst one of the criteria (pre-discharge management plan) relates to hospital care, and one (disease register) relates mainly to primary care, the remainder should be applied to both primary and secondary care settings. It is anticipated that the standards will be detailed in local development plans. Year-on-year improvement in the results of the audit criteria is important, and comparison with other local health care communities may be helpful in setting realistic milestones towards the target standard. The 'exception' boxes list the circumstances where applying the standard would be inappropriate for an individual patient. It is recognised that there will be other situations where a clinical decision may be taken not to follow the guideline (for example taking into account the informed patient's wishes), and interpretation of performance should take these factors into account. Heart failure registers are a necessary pre-requisite to performing these audits. They are needed to establish the denominator, and to facilitate accurate data collection.

The criteria are all process criteria. It is also recommended that consideration should be given to setting up audit of re-admission rates for heart failure within 30 days of discharge. It is difficult to set a 'standard' for such an outcome measure, since it would be unrealistic to expect a routine audit to be able to differentiate between 'avoidable' and 'unavoidable' admissions.

A potential problem with the criteria proposed is that general practices that have low identification rates of heart failure (perhaps because of poor coding, or under-investigation) may apparently perform very well against these criteria. Therefore, we would propose that an additional data item that should be reported in general practice is age-specific prevalence of heart failure. This would allow the standards achieved to be interpreted against the practice-specific prevalence.

Table 12 Audit criteria			
Key recommendations	Criterion	Other relevant recommendations	Definition of terms
The basis for historical diagnoses of heart failure should be reviewed, and only patients whose diagnosis is confirmed should be managed in accordance with this guideline.	1. 'Disease register' % of patients on general practice heart failure registers who have had this diagnosis confirmed.	Where the diagnosis of heart failure is still suspected, but confirmation of the underlying cardiac abnormality has not occurred then the patient should have appropriate further investigation.	The diagnostic algorithm (see page 29) summarises how a diagnosis of heart failure should be confirmed.
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.	2. Echocardiography % of patients with a new diagnosis of heart failure (in the previous 12 months) who have had an echocardiogram.		Patient choice; or where this would be inappropriate (eg terminal illness).
All patients with heart failure due to left ventricular systolic dysfunction should be considered for treatment with an ACE inhibitor.	3. ACE inhibitors % of patients with heart failure due to left ventricular systolic dysfunction who are prescribed an ACE inhibitor or an angiotensin-II receptor antagonist, if ACE inhibitors are not tolerated (eg because of cough).	At the time of issue of this guideline angiotensin II receptor antagonists (see Table 8) are not licensed in the UK for heart failure and studies are ongoing. However, angiotensin-II receptor antagonists may provide an alternative to ACE inhibitors for patients intolerant of ACE inhibitors (for example, because of cough).	Patient choice; contraindications (see guideline text); or documented adverse events led to withdrawal of ACE inhibitor; heart failure not due to LV systolic dysfunction.
Beta blockers licensed for use in heart failure should be initiated in patients with heart failure due to LV systolic dysfunction after diuretic and ACE inhibitor therapy (regardless of whether or not symptoms persist).	4. Beta-blockers % of patients with heart failure due to left ventricular systolic dysfunction who are prescribed a beta-blocker.	Patients who develop heart failure due to LV systolic dysfunction and who are already on treatment with a beta-blocker for a concomitant condition should continue with a beta-blocker – either their current beta-blocker or an alternative licensed for heart failure treatment.	Patient choice; contraindications (see guideline text); or documented adverse events led to withdrawal of beta-blocker; heart failure not due to LV systolic dysfunction.

Table 12 Audit criteria – continued

Key recommendations	Criterion	Other relevant recommendations	Exceptions	Definition of terms
<p>All patients with chronic heart failure require monitoring. This monitoring should include:</p> <ul style="list-style-type: none"> 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. 	<p>5. Monitoring % of patients with proven heart failure who are reviewed on a six-monthly* basis. * – this is a minimum</p>	<p>The frequency of monitoring should depend on the clinical status and stability of the patient. Monitoring interval should be short (days to weeks) if the clinical condition or medication has changed, but is required at least six monthly for stable patients with proven heart failure.</p>	<p>Patient choice.</p>	
<p>Patients with heart failure should generally be discharged from hospital only when their clinical condition is stable and the management plan is optimised. The primary care team, patient and carer must be aware of the management plan.</p>	<p>6. Discharge planning a. % of patients with heart failure who have a pre-discharge management plan in place. b. % of patients discharged from hospital with a (primary or secondary) diagnosis of heart failure for whom a management plan has been rapidly communicated to the primary care team.</p>		<p>Patient choice.</p>	<p>b. 'Rapidly' will need to be defined and agreed at a local level, for audit purposes.</p>
<p>Management of heart failure should be seen as a shared responsibility between patient and health care professional.</p>	<p>7. Patient understanding All patients with heart failure receive a copy of the public version of the guideline.</p>		<p>Patient choice.</p>	

15 Areas for future research

The Guideline Development Group recognise that there is a huge amount of ongoing research activity in many aspects of the management of heart failure. Several key studies of drug therapy and other interventions are due to report in the near future, and these will undoubtedly influence the recommendations made in future versions of this guideline. However, the Guideline Development Group wish to draw attention to several specific areas that would benefit from further research. Heart failure trials have not generally recruited typical heart failure patients or conducted health economic evaluations. This would usefully add to the evidence base for future recommendations.

Table 13 Areas for future research

Guideline section	Page	Research recommendation
6 Diagnosis – symptoms, signs and non-cardiac investigation	25	Validity and repeatability of signs, symptoms and tests for heart failure diagnosis.
6 Diagnosis – diastolic heart failure	27	Confirming a diagnosis of ‘diastolic’ heart failure.
7.1 Treating heart failure – lifestyle	32	The benefits of rehabilitation for patients with heart failure.
7.1 Treating heart failure – lifestyle	32	The optimum lifestyle advice on diet and nutrition. The benefits of interventions aimed at improving diet and nutrition.
7.2 Treating heart failure – pharmacological therapy	36	The benefits of pharmacological treatments specific to non-Caucasian patients with heart failure.
7.5 Treating heart failure – oxygen therapy	59	The benefits of domiciliary oxygen for patients with heart failure. The benefits of continuous positive airways pressure for patients with heart failure.
7 Treating heart failure – adherence to therapy	52	The optimum method to improve adherence to therapy.
9.4 Care pathways	69	The benefits of a care pathway approach for patients with heart failure.
10.2 Prognosis	73	The optimum method of estimating prognosis for patients with heart failure.
11 Anxiety and depression	75	The treatment of mental health problems arising co-morbidly with chronic heart failure.
12 End of life	77	The optimum method of meeting the palliative care needs of patients with heart failure.
General	–	The psychological effects of treatment on patients with heart failure (including interventions such as implantable defibrillators).

APPENDICES

Appendix A: Clinical questions

Please note: An asterisk denotes a question to be answered by expert opinion, and confirmed by consensus, rather than by full systematic review, owing to nature of question or paucity of evidence on initial search.

Q1. What is the accepted definition for heart failure?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q2. What is the current burden of heart failure in the UK, and trends in prevalence, and what do we know about prognosis and how is it being affected by current management?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q3. What is the burden of heart failure for the patient?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q4. What is best practice for communication at the initial diagnosis of heart failure, and in ongoing management to improve quality of life?

Addressed by systematic search and review.

Q5. Does a fully informed patient impact on concordance with treatment, and outcome?

Addressed by systematic search and review.

Q6. What are the aims of heart failure treatment for the patient and the healthcare professional, in terms of morbidity and mortality?*

Addressed by an expert discussion paper, drafted by Audrey Alimo.

Q7. Is there evidence that support and education for carers and relatives of heart failure improves patient quality of life, and clinical outcomes?

Addressed by systematic search and review.

Q8. What are the most appropriate tests in a patient with suspected heart failure to confirm diagnosis?

This was linked with the following sub-questions.

What clinical signs of heart failure are useful? Is an echocardiogram essential for the diagnosis of heart failure? What is the role of BNP (or NT proBNP) in diagnosing heart failure? Can a normal ECG rule out heart failure?

Addressed by systematic search and review.

Which patients with suspected heart failure should be referred for specialist diagnosis?*
What are the symptoms of heart failure?* What other conditions may present with similar symptoms?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q9. What are the key elements for interpreting the results of cardiac imaging, to confirm a diagnosis of heart failure?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q10. What is the best method for diagnosis of isolated diastolic dysfunction?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q11. How should the initial management plan be determined? In what circumstances should a previous diagnosis of heart failure be reassessed?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q12. What are the causes of heart failure and how do these affect prognosis and treatment? What tests are indicated to establish underlying cause of heart failure?

Addressed by systematic search and review.

Q13. How are patients with heart failure affected by anxiety and depression? How best is such anxiety and depression diagnosed and treated, and what is the role of pharmacological and non-pharmacological interventions?

Addressed by systematic search and review.

Q14. What licensed drug therapy can be used to modify the outcome of heart failure in terms of quality of life, morbidity and mortality? (Including acute decompensation of chronic heart failure.)

Addressed by systematic search and review.

Q15. What is the best sequence for pharmacological therapy, and how should it be initiated?

Addressed by systematic search and review.

Q16. What drugs are to be avoided in patients with heart failure?*

Addressed by an expert discussion paper, Kevin O'Shaughnessy, Mojgan Sani and Bibi Greenwood.

Q17. What is the evidence of benefit of lifestyle advice and other therapies (homeopathy, reflexology, hydrotherapy, crystal therapy and acupuncture) in terms of morbidity, mortality, and quality of life?

Addressed by systematic search and review.

Q17a. What is the evidence for recommending rehabilitation and/or a period of exercise training for patients with chronic heart failure?

Addressed by systematic search and review.

Q18. What invasive procedures have a role in the treatment of patients with heart failure? How and when should patients best be identified for invasive interventions?

Addressed by systematic search and review.

Q19. Other than communication, what is the best way to facilitate concordance with drug and lifestyle prescriptions?

Addressed by systematic search and review.

Q20. In what circumstances should a patient with an established diagnosis of heart failure be referred back to primary care, referred to secondary care, including criteria for hospitalisation, to ensure best possible treatment?*

Addressed by an expert discussion paper, drafted by Jonathan Richards.

Q21. What considerations need to be met prior to discharge from hospital after an episode of acute decompensation?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q22. What evidence is there that a dedicated multidisciplinary team improves care of those diagnosed with heart failure above the standard approach?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q23. Are there sub groups of heart failure patients that should be treated differently?

Addressed by systematic search and review.

Q24. What evidence is there that palliative care improves the care of patients with Heart Failure? When should a patient be referred to such care?*

Addressed by an expert discussion paper, drafted by Louise Gibbs.

Q25. At what stage is it appropriate to consider end of life issues for heart failure patients?*

Addressed by an expert discussion paper, drafted by Louise Gibbs.

Q26. Under what circumstances should the optimal treatment of heart failure patients involve the work of non-NHS agencies?*

Addressed by an expert discussion paper, drafted by Graham Archard and Rose Anne Kenny.

Q27. What support groups help patients and families to cope with heart failure?*

Addressed by an expert discussion paper, drafted by Derrick Masters.

Q28. Should patients with heart failure be given advice on nutrition to improve morbidity and mortality?

Addressed by systematic search and review.

Q29. What advice should be given to patients with, or at risk of, heart failure to promote prevention?*

Addressed by an expert discussion paper, drafted by Martin Cowie.

Q30. Can monitoring of digoxin levels facilitate improved therapeutic care for individuals with heart failure (including acute decompensation)?

Addressed by systematic search and review.

Q31. Can domiciliary oxygen therapy be used to modify the outcome of heart failure in terms of quality of life, morbidity and mortality (including acute decompensation)?

Addressed by systematic search and review.

Q32. Can CPAP therapy be used to modify the outcome of heart failure in terms of quality of life, morbidity and mortality (including acute decompensation)?

Addressed by systematic search and review.

Appendix B: Search strategy

Table B1 Mapping exercise

Question	Population	Study type	Database	Year
All questions	Heart failure	Guideline	Guideline websites	–
		Systematic review	Cochrane Library	–
			Medline	1966 – 2002
			Embase	1980 – 2002
			CINAHL	1982 – 2002
			PsycINFO	1887 – 2002
			AMED	1985 – 2002
		Economics	Cochrane Library	–
			Medline	1993 – 2002
			Embase	1993 – 2002
		EconLit	1993 – 2002	

Table B2 Searches for individual questions

Question	Population	Study type	Database	Year
Q1 What is the accepted definition of HF?	Heart failure	Expert review	Cochrane Library	–
Q2 What is the current burden of HF in the UK, and trends in prevalence, and what do we know about prognosis and how is it being affected by current management?	Heart failure	Expert review	Cochrane Library	–
Q3 What is the burden of HF for the patient?	Heart failure	Expert review	Cochrane Library	–
Q4 What is best practice for communication at the initial diagnosis of HF, and in ongoing management to improve quality of life?	Heart failure	Systematic review	Medline	1966 – 2002
		RCT	Embase	1980 – 2002
		Any type of study		

continued

Table B2 Searches for individual questions – continued

Question	Population	Study type	Database	Year	
Q5 Does a fully informed patient impact on concordance with treatment and outcome?	Heart failure	Any type of study	Medline	1966 – 2002	
			Embase	1980 – 2002	
Q6 What are the aims of HF treatment for the patient and the healthcare professional, in terms of morbidity and mortality?	In any condition	Systematic review	Cochrane Library	–	
			Heart failure	Expert review	–
Q7 Is there evidence that support and education for carers and relatives of HF improves patient quality of life and clinical outcomes?	Heart failure	Systematic review	Cochrane Library	–	
			RCT	Medline	1966 – 2002
			Observational study	Embase	1980 – 2002
			Author search	Medline	1966 – 2002
			Embase	1980 – 2002	
Q8 What are the most appropriate tests in a patient with suspected HF to confirm diagnosis?	Heart failure	Systematic review	Cochrane Library	–	
			RCT	Medline	1992 – 2002
			Embase	1992 – 2002	
Q9 What are the key elements for interpreting the results of cardiac imaging, to confirm a diagnosis of HF?	Heart failure	Cohort study	Medline	1992 – 2002	
			Embase	1992 – 2002	
Q10 What is the best method for diagnosis of isolated diastolic dysfunction?	Heart failure	Expert review	Cochrane Library	–	
			Heart failure	Expert review	–
Q11 How should the initial management plan be determined?	Heart failure	Expert review	Cochrane Library	–	
			Heart failure	Expert review	–
Q11a In what circumstances should a previous diagnosis of HF be reassessed?	Heart failure	Expert review	Cochrane Library	–	
			Heart failure	Expert review	–
Q12 What are the causes of HF and how do these affect prognosis and treatment?	Heart failure	Systematic review	Cochrane Library	–	
			Observational study	Medline	1980 – 2002
			Embase	1980 – 2002	

continued

Table B2 Searches for individual questions – continued					
Question	Population	Study type	Database	Year	
Q13 How are patients with HF affected by anxiety and depression? How best is such anxiety and depression diagnosed and treated, and what is the role of pharmacological and non-pharmacological interventions?	Heart failure	Systematic review	Cochrane Library	–	
		RCT	Medline	1966 – 2002	
		Observational study	Embase	1980 – 2002	
			CINAHL	1982 – 2002	
			PsycINFO	1887 – 2002	
	AMED	1985 – 2002			
Q14 What licensed drug therapy can be used to modify the outcome of HF in terms of quality of life, morbidity and mortality (including acute decompensation of chronic HF)?	Heart failure	Systematic review	Cochrane Library	–	
		RCT	Medline	1966 – 2002	
			Embase	1980 – 2002	
Q15 What is the best sequence for pharmacological therapy, and how should it be initiated?	Heart failure	Systematic review	Cochrane Library	–	
		RCT	Medline	2002 – 2002	
			Embase	2002 – 2002	
		Cohort study	Medline	1980 – 2002	
			Embase	1980 – 2002	
Q16 What drugs are to be avoided in patients with HF?	Heart failure	Expert review	Cochrane Library	–	
Q17 What is the evidence of benefit of lifestyle advice and other therapies (homeopathy, reflexology, hydrotherapy, crystal therapy and acupuncture) in terms of morbidity, mortality, and quality of life?	Heart failure	Systematic review	Cochrane Library	–	
		RCT	Medline	1966 – 2002	
			Embase	1980 – 2002	
			CINAHL	1982 – 2002	
			AMED	1985 – 2002	
Q17a What is the evidence for recommending rehabilitation and/or a period of exercise training for patients with chronic HF?	Heart failure	Systematic review	Cochrane Library	–	
		RCT	Medline	1966 – 2002	
		Cohort study	Embase	1980 – 2002	
Q18 What invasive procedures have a role in the treatment of patients with HF? How and when should patients best identified for invasive interventions?	Heart transplantation Artificial heart	Systematic review	Cochrane Library	–	
		RCT	Medline	1993 – 2002	
			Embase	1993 – 2002	

continued

Table B2 Searches for individual questions – continued

Question	Population	Study type	Database	Year
Q19 Other than communication, what is the best way to facilitate compliance / concordance with drug and lifestyle prescriptions?	Heart failure	Systematic review	Cochrane Library	–
		RCT	Medline	2001 – 2002
			Embase	2001 – 2002
	In any condition	Any type of study	Medline	1980 – 2002
			Embase	1980 – 2002
Q20 In what circumstances should a patient with an established diagnosis of HF be referred back to primary care, referred to secondary care, including criteria for hospitalisation, to ensure best possible treatment?		Systematic review	Cochrane Library	–
	Heart failure	Systematic review	Cochrane Library	–
		RCT	Medline	1966 – 2002
	In any condition	Cohort study	Embase	1980 – 2002
		Systematic review	Cochrane Library	–
Q21 Are there sub groups of HF patients that should be treated differently?	Congenital heart defect	Systematic review	Cochrane Library	–
	Angina pectoris	RCT	Medline	2001 – 2002
	Diastole		Embase	2001 – 2002
	Atrial fibrillation	Cohort study	Medline	1980 – 2002
	Heart transplantation		Embase	1980 – 2002
	Sleep apnoea syndrome			
	Anaemia			
	Diabetes mellitus			
	Cognition disorder			
	Older people			
	Ethnic groups			
	Heart failure	Expert review	Cochrane Library	–
Q22 What evidence is there that palliative care improves the care of patients with HF? When should a patient be referred to such care?	Heart failure	Expert review	Cochrane Library	–
Q23 At what stage is it appropriate to consider end of life issues for HF patients?	Heart failure	Expert review	Cochrane Library	–
Q24 Under what circumstances should the optimal treatment of HF patients involve the work of non-NHS agencies?	Heart failure	Expert review	Cochrane Library	–
Q25 What support groups help patients and families to cope with HF?	Heart failure	Expert review	Cochrane Library	–

continued

Table B2 Searches for individual questions – continued					
Question	Population	Study type	Database	Year	
Q26 Should patients with HF be given advice on nutrition to improve morbidity and mortality?	Heart failure	Systematic review	Cochrane Library	–	
			Medline	1966 – 2002	
			Embase	1980 – 2002	
			CINAHL	1982 – 2002	
Q27 What advice should be given to patients with, or at risk of HF to promote prevention?	Heart failure	Expert review	Cochrane Library	–	
Q28 Can monitoring of digoxin levels facilitate improved therapeutic care for individuals with HF (including acute decompensation)?	Heart failure	Systematic review	Cochrane Library	–	
			Medline	1966 – 2002	
			Embase	1980 – 2002	
Q29 Can domiciliary oxygen therapy be used to modify the outcome of HF in terms of quality of life, morbidity and mortality (including acute decompensation)?	Heart failure	Systematic review	Cochrane Library	–	
			Medline	1966 – 2002	
			Embase	1980 – 2002	
Q30 Can CPAP be used to modify the outcome of HF in terms of quality of life, morbidity and mortality (including acute decompensation)?	Heart failure Obstructive sleep apnoea	Systematic review	Cochrane Library	–	
			Medline	1966 – 2002	
			Embase	1980 – 2002	

Appendix C: Searching for health economics evidence

Searches and data sources

No study design criteria were imposed *a priori* as it was already known that little economic evidence was available, and it was thought best not to restrict the searches at this stage. The search strategies were designed by the information scientist with guidance on search terms from the health economist. All reviewing was carried out by the health economist. The following databases were searched from 1993 to 2002: CRD (including DARE, NHS EED, HTA), OHE HEED, Cochrane Library, Medline, Embase and Econlit. In addition key review papers were checked for useful references.

Inclusion assessment

The titles, and where available the abstracts, were screened to assess whether the study met the following inclusion criteria.

▷ Patients

At least some of the patients had heart failure. After the initial searches, supplementary searches in relation to specific questions were carried out, without the requirement that some patients had heart failure.

▷ Economic evidence

The study was an **economic evaluation** or included information on **resources, costs** or specific **quality of life** measures.

▷ Study design

No criteria for study design were imposed *a priori*.

Summary results

After reviewing titles, abstracts and CRD/OHE HEED commentaries (where available) a database of 259 potentially useful items was assembled. Very few of these were good quality formal economic evaluations and where these existed they were largely studies of ACE inhibitors or beta-blockers. In general the economic information came from studies that considered either costs or outcomes but not both.

There were 25 cost effectiveness analyses based on RCTs. Seventeen of these were on ACE inhibitors, four on beta-blockers, two on general management programs, one on revascularisation and one on exercise training.

Eleven systematic reviews were identified but only two of these contained formal economic analysis. Of the 35 other (non-systematic) reviews, 27 were on pharmacological treatments, five on general management and three on invasive procedures. Fourteen of these reviews contained formal cost effectiveness analyses of varying quality, and the majority of these considered the use of ACE inhibitors.

Appendix D: Health economics of pharmacological therapies

Comparing the results of cost-effectiveness studies

There are numerous difficulties in comparing the results of studies that employ heterogeneous data and methods. All of the studies reported here are reasonably explicit about the data and methods used, and this eases comparisons. Studies with insufficient detail were omitted from consideration.

In relation to the clinical data the trials vary greatly in the characteristics of the patients studied in terms of: age, sex, symptoms of heart failure, duration and degree of heart failure, association with myocardial infarction, and in the end points of hospitalisation, death and progression to heart failure.

Economic analyses vary for a number of reasons including:

- ❑ **Source of cost and benefit data** While efficacy data is usually taken from the named trials, the sources of resource use (and cost) data vary; some are prospective trial data and some are collected retrospectively. Either method can be collected for the whole trial sample or a sub-sample. In some analyses resource use data from an observational source is combined with trial data on effectiveness. In all cases the validity of comparisons from different countries is also an issue.
- ❑ **Which costs and benefits are included?** The studies reported all take the health service of the country in question as the relevant perspective. Therefore they focus on direct costs (largely medication and hospitalisation) and direct benefits (life years gained).
- ❑ **Period of analysis** This can be restricted to the trial period or extended beyond the trial.

If analysis is extended beyond the trial period, costs and benefits can be projected in a number of ways. This will usually involve a decision analytic model that follows a hypothetical cohort of patients (usually with characteristics similar to the trial sample) through time. Various assumptions are necessary about disease progression, resource use and the flow of benefits over time. These are subject to varying degrees of uncertainty and a good economic analysis will include sensible sensitivity analyses to reflect this uncertainty.

▷ Location of study

While much of the effectiveness data on pharmacological therapies is obtained from multinational trials, the economic analyses usually adopt the perspective of one particular healthcare system. The costs of providing an intervention are specific to the healthcare system in question and non-UK results may be of limited use in informing this guideline. In particular different healthcare systems will have different policies and practice on length of stay, the criteria for hospitalisation, outpatient arrangements, the relative distribution of care between primary and secondary services etc. Nevertheless, all good quality cost effectiveness studies are reported here for completeness and to inform discussion. It is important to note that where cost figures have been converted into sterling, this is for guidance only. The figures are not directly comparable due to the different years in which the source data was collected.

▷ Discounting of costs and benefits

When costs and benefits accrue over a number of years these are usually discounted to convert future values into current values. The base case figures in the tables usually report figures for costs discounted at 5% or 6%. Some 'best' and 'worst' figures include varying assumptions relating to the discounting of costs and benefits. In all of the studies reported, variations in the discount rate make no substantive difference to the results presented.

General economic considerations

▷ Potential cost savings

- These are likely to occur if a treatment improves QoL and slows disease progression
- The magnitude of *direct costs* (and hence potential savings) will depend on:
 - the morbidity burden relating to the condition,
 - the specific costs related to this morbidity (for example, GP visits are relative cheap and hospitalisation is relatively expensive),
 - the efficacy of treatment in relation to morbidity (for example, how big the impact is on hospitalisation).
- The slowing of the progression of CHF from mild (NYHA I and II) to more severe states (NYHA III and IV) will reduce all forms of healthcare utilisation including hospitalisation.

▷ Potential additional costs

- Direct costs of the treatment itself (drugs and related, eg monitoring, treating adverse effects).
- If the treatment extends life, survivors will continue to utilise healthcare resources.

The studies reviewed here concentrate largely on *direct costs* (those arising from provision of treatment). *Indirect costs* (loss of earnings and pension payments for those who survive) are not likely to be as great as in some other chronic conditions since CHF is concentrated in older people. *Intangible costs*, that reflect the drawbacks of CHF such as pain, depression and reduced QoL, are very difficult to quantify. If indirect and intangible costs were included in the economic analyses of pharmacological therapies such as ACE inhibitors and beta-blockers they would be likely to produce even more favourable cost effectiveness ratios.

Increasing the use of effective pharmacological therapies in eligible patients will increase treatment costs but some, or all, of these will be offset, largely by reduced hospitalisation. If the savings are not large enough to offset the increase in cost, the net increase in costs has to be considered against benefits such as life years gained (LYG), or quality adjusted life years (QALYs).

The focus here is on LYG, as there is little data on QoL in CHF that can be used in economic evaluation (for example SF-36 or EQ-5D scores) to apply a quality weighting to LYG. The years of life saved are still associated with significant disability. This is important when comparing the cost-effectiveness of beta-blockers and ACE inhibitors with treatments, like statins, that prevent the transition from full health to disease.

1. Ace inhibitors

Summary

- ❑ Evidence shows that ACE inhibitors in CHF reduce hospitalisation by slowing disease progression, improving quality of life (QoL) and extending length of life.
- ❑ ACE inhibitors appear to be *cost effective*. They can be *cost saving* and have very favourable cost effectiveness ratios even when conservative assumptions are employed.
- ❑ ACE inhibitors are under prescribed and doses in clinical practice are lower than in trials and therefore may be too low to achieve optimum benefits in terms of cost effectiveness.^{273–275}
- ❑ A recent survey²⁷³ suggests that while more than 90% of doctors believe there is strong evidence for mortality benefits of ACE inhibitors in CHF, only 47–62% of doctors actually prescribe them. The recent BHF Heart Failure Supplement¹ reports that around 53% of patients with heart failure receive ACE inhibitors.
- ❑ Under prescribing may be due to (i) an exaggerated perception of risk, especially renal failure and hypotension;²⁷⁶ (ii) the incorrect perception that lower doses retain mortality benefits while reducing risk of side effects²⁷⁷ (the ATLAS study shows this to be false; with higher doses of lisinoprol being more effective and cost effective than lower doses);²⁷⁸ (iii) diagnostic uncertainty.
- ❑ Guidelines may have important role in encouraging the use of ACE inhibitors in primary care.

▷ Note

- ❑ The clinical evidence in this paper has been taken primarily from two systematic reviews^{70,279} and the summaries of trials provided in the economics literature.
- ❑ The economic analysis is largely based on three trials: SOLVD, SAVE and AIRE.
- ❑ Due to time constraints the use of ACE inhibitors across different patient groups has not been specifically considered. There appears to be little evidence on this area.

Existing guidance that has considered economic implications

- 1) *Trent Working Group on Acute Purchasing guidance note for purchasers on ACE inhibitors in heart failure.*²⁸⁰ This report took the cost effectiveness of ACE inhibitors as given and focused on the effects of increased ACEI use on hospitalisation. It concluded that the effects on reduced hospitalisation mean that the health gain associated with the use of ACE inhibitors can be achieved with potential resource savings.
- 2) Inherited NICE guideline on *Prophylaxis for patients who have experienced a MI.*²⁸¹ This considers the use of ACE inhibitors in patients with prior MI and CHF. The economic analysis used a ‘profiling’ approach to list the potential costs and consequences of ACEI use. The relevant recommendation for patients with prior MI and CHF is that ‘all patients should be offered long term treatment with an ACEI and then a beta-blocker ... All of these treatments are cost effective.’ (A)
- 3) North of England Evidence Based Development Project (1997) guideline on *ACE inhibitors in primary care management of adults with symptomatic heart failure.*²⁸² The economic analysis used a ‘profiling’ approach to list the potential costs and consequences of ACEI use. The relevant recommendations are:

- All patients with symptomatic heart failure and evidence of impaired left ventricular function should be treated with an ACE inhibitor. (A)
- Patients with recent myocardial infarction and evidence of left ventricular dysfunction should be treated with an ACE inhibitor. (A)
- Treatment of heart failure with ACE inhibitors is cost-effective. (A)
- Statement: ACE inhibitors appear to be a cost effective use of resources when compared with other common health service interventions. (III)

▷ Drug costs

Eight ACE inhibitors are licensed for the treatment of CHF in the UK. There are large differences in prices across drugs and between branded and generic versions.

There does not seem to be any evidence to suggest that one ACEI is better than another;²⁷⁹ although most clinical evidence comes from trials of enalapril. In addition a recent study by Schneeweiss *et al*²⁸³ found no adverse effects resulting from the introduction of reference pricing for ACE inhibitors in British Columbia, which encourages switching from more expensive to cheaper drugs.

▷ Existing evidence of the cost effectiveness of ace inhibitors

Fifty-two papers considering the economics of ACE inhibitors in the treatment of heart failure were identified by the economic review. Of these, only 12 were cost-effectiveness analyses of sufficient quality to report in the evidence tables; three were UK studies (Table D1) and the remainder were from other countries (Table D2).

▷ The weight of evidence of the cost effectiveness of ACEIs

- The cost effectiveness results cover a broad range. One UK study shows ACE inhibitors in the treatment of CHF to be *cost saving* in the base case scenario (as do four of the international studies); in other words ACE inhibitors represent a *dominant technology* in cost-effectiveness terms producing greater benefits than the comparator (usual care) at lower cost.
- The majority of cost effectiveness ratios calculated on UK data are well within the boundaries of what would normally be considered a cost effective treatment.
- The one very high (non-UK) C/QALY figure (£149,000)²⁷¹ reflects very conservative assumptions about benefits and drug costs and is the figure estimated for patients in the youngest age group, who benefit the least from treatment (as shown in the SAVE trial).
- The evidence therefore suggests that ACE inhibitors are cost effective in the treatment of CHF. However it should be noted that evidence from the UK context is limited.

Hospitalisation in more detail

- Hospitalisation accounts for 60–70% of all expenditure on CHF in the UK.^{8,284,285}
- Of the major ACE inhibitor trials seven have included data on hospitalisation for CHF. These trials consistently show a reduction in admissions to hospital for progressive heart disease in patients taking ACE inhibitors. On average a GP would expect four patients

with CHF to be admitted to hospital each year. The SOLVD results suggest that one of these admissions might be prevented (or delayed) through the use of ACE inhibitors.

- ❑ Since hospitalisation is most frequent in the latter stages of the disease, treatment with ACE inhibitors may simply postpone hospitalisation, beyond trial follow-up (maximum four years). McMurray and Davie²⁸⁴ argue that this is probably not a justifiable concern since ACE inhibitors extend life for a relatively short period (eg 0.16 LYs in SOLVD Treatment Trial). Also the economic analysis of the SOLVD data shows no evidence of ‘catch-up’ costs in the later stages of the trial period.²⁸⁶
 - ❑ While HF hospitalisations decrease, it may be that other causes of morbidity mean that overall hospitalisation rates are not reduced. This does not seem to be reflected in the trial data, with ACE inhibitors appearing to reduce (but not significantly) other-cause hospitalisation in symptomatic patients.
 - ❑ Will the reductions in hospitalisation found in trials convert to clinical practice? The admission rate in the SOLVD control arm matches that found in general practice in England. Also McMurray *et al*²⁸⁵ compare hospitalisation rates from official data sources, primary care surveys hospital survey and clinical trials and find them broadly in agreement.
 - ❑ Reductions in hospitalisation will not automatically translate to financial savings. However, with 90% occupancy Cornell *et al*²⁸⁰ estimate that reductions in hospitalisation amount to around 13.3 beds (about half an average ward) in a typical district.
- ▶ Other concerns about the generalisability of trial data
- ❑ The trials are all ‘intention to treat’ analyses, therefore the calculations do take into account those who withdraw due to adverse effects or intolerance. However they do not take into account those excluded at the screening stage.
 - ❑ Patients tend to be younger in trials (early 60s). CHF is more common in older patients who have shorter life expectancy and are more susceptible to side effects.
 - ❑ Doses in clinical practice tend to be lower than in trials.^{287–290} There are estimates that only 14–22% of patients in clinical practice met the target doses suggested by the large trials.

Side effects and risks

- ❑ Evidence suggests that ACE inhibitors are low in side effects with few people unable to tolerate them, including the elderly though doses may need to be reduced. Less than 2% of patients in SOLVD (both treatment and prevention trials) had side effects severe enough to stop treatment.
- ❑ Increased use of ACE inhibitors may lead to increased incidence of renal failure in the elderly resulting from combination therapy of ACE inhibitors with NSAIDS. This could have considerable resource consequences.

Different groups of patients

- ❑ This has not been explicitly considered. Evidence from the studies reviewed here suggests:
 - Reduction in mortality is greater in higher risk groups. In severe CHF, treating six patients for one year would prevent one death, whereas in less severe disease it would be necessary to treat 62 patients.²⁹¹ Even in patients with less severe disease it is only necessary to treat nine patients for one year to prevent one admission to hospital.

Table D1 Existing evidence on cost-effectiveness of ACE inhibitors in the treatment of CHF in the UK							
Reference	Trial and drug	Period of economic analysis	Comments	Costs included and year	Quality	Cost/LYG	
						Base Case	Sensitivity analysis
						Best	Worst
Hart <i>et al</i> (1993) ³⁰⁷	SOLVD enalapril	4 years	Initiation assumptions: (i) all patients three days (ii) all patients one day (iii) 40% for one day (iv) all in GP.	Direct	Good sensitivity analysis. Applicable to guideline context.	Net saving.	£2,508
Hummel <i>et al</i> (1997) ²⁶⁹	SAVE captopril	4 years	Considered reduced need for revascularisation in treatment group.	Direct 1994	Limited sensitivity analysis. Question on applicability of patient group.	£10,128	
Martinez and Ball (1995) ³⁰⁹	AIRE ramipril	(i) 1 (ii) 2 (iii) 3.8 years	Separate analysis for differing follow-up periods.	Direct 1993	Good sensitivity analysis. Applicable to guideline context. Question on applicability of patient group.	(i) £426 (ii) £142 (iii) £255	Net saving. £3,500

Cost-effectiveness is usually represented using a cost-effectiveness ratio (CER), eg cost per LYG. If an intervention is found to produce net savings, it is not usual to present CERs because of the negative numerator. No attempt has been made to convert cost figures to the same base year. Base case figures are for discounted costs (at 5% or 6%). In many cases a variety of discount rates on costs and benefits are included in the sensitivity analysis.

SOLVD – use of enalapril for treatment of CHF. Four year follow-up.

SAVE – use of captopril as a preventative measure post acute MI. ie selective use of prevention strategy in asymptomatic, high risk patients. Four year follow-up.

AIRE – use of ramipril in patients who were thought clinically to have developed CHF at time of acute MI. 15 month follow-up.

Table D2 Existing international evidence on cost-effectiveness of ACE inhibitors in the treatment of CHF

Reference	Trial data	Period of analysis	Comments	Costs included and year	Quality	Cost/LYG		
						Base Case	Best	Worst
Butler and Fletcher (1996) Australia ³¹⁰	SOLVD enalapril	4 years		Direct 1993	Good.	Net saving.	Net saving.	£8,377
van Hout <i>et al</i> (1993) Netherlands ³¹¹	SOLVD enalapril	10 years		Direct	Long extrapolation.	Net saving.	Net saving.	Net saving.
Paul <i>et al</i> (1994) US ³¹²	SOLVD enalapril	10 years	Benefits assumed: (i) constant (ii) linear decline (iii) cut-off at 4 years.	Direct 1992	Long extrapolation.	(i) £6,644 (ii) £7,193 (iii) £8,426.	£1,370	£19,181
Scott and Scott (1996) New Zealand ³¹³	SOLVD enalapril	4 years		Direct 1993	Good.	Net saving.	Net saving.	Not quantified.
Glick <i>et al</i> (1995) US ²⁸⁶	SOLVD enalapril	(i) 4 years (ii) lifetime	Attempted QALY calculation.		Some details unclear.	(i) Net saving (ii) < £70.		
Tsevat <i>et al</i> (1995) US ²⁷¹	SAVE captopril	Lifetime	Separate models by age 50, 60, 70, 80 Also benefits assumed: (i) continue beyond 4 years (ii) limited to 4 years.	Direct 1991	Very good range of SA. Applicability of patient group?	(80 years)* £2,535 (50 years) £41,650	(80 years)* £2,466 (50 years) £7,125	(60–80 years)* £5,960–£20,000 (50 years) £149,078
Erhardt <i>et al</i> (1997) Sweden ³¹⁴	AIRE ramipril	(i) 1 (ii) 2 (iii) 3.8 years	Separate analysis for differing follow-up periods.	Direct 1993	Question on applicability of patient group.	(i) £2,307 (ii) £1,086 (iii) £680	£350	£7,195
Schadlich <i>et al</i> (1998) Germany ³¹⁵	AIRE ramipril	(i) 1 (ii) 2 (iii) 3.8 years	Separate analysis for differing follow-up periods.	Direct 1993	Question on applicability of patient group.	(i) £2,697 (ii) £1,308 (iii) £800	Net saving.	£4,442
Andersson <i>et al</i> (1999) Sweden ³¹⁶	SOLVD AIRE SAVE	Not clear	Patients split into: (i) symptomatic CHF (ii) post MI asymptomatic (iii) post MI CHF.	Direct 1996	Some details unclear.	(i) £1,767 (ii) £3,370 (iii) £3,350	Net saving.	Less than £7,000

See notes to Table D1. All cost figures have been converted to pounds sterling using current exchange rates (29/05/02). NOTE: These figures are not comparable but are for guidance only. *Figures in Tsevat *et al* (1995) are for C/QALY. Utility values derived by time trade-off from a sub-sample (n = 82). Given that one year in less than full health is <1, C/QALY > C/LYG for the same LYG.

- Analysis of the SAVE data showed that ACE inhibitors can be cost effective as a preventative measure in post acute MI, ie selective use of a prevention strategy in a high-risk asymptomatic group.^{269,271}
- Analysis of SAVE data also showed that in this group, cost effectiveness was greatest in the older age groups, and the CER may be high (> £30k) for patients of 50yrs at MI.²⁷¹

Trent WGAP report: Guidance note for purchasers on ace inhibitors in heart failure

This report is concerned specifically with the economics of the use ACE inhibitors for the treatment CHF in a 'typical' English health district with a population of 500,000. It starts from the premise that ACE inhibitors are cost effective, and focuses on modelling potential cost savings in the form of reduced hospitalisation.

Key assumptions of the model:

- a simple (non-age specific) prevalence rate for the whole population
- a proportion of these patients are assumed to be prescribed ACE inhibitors already
- of the remaining population, a proportion will be assumed to be unsuitable for treatment with ACE inhibitors, due to contraindications
- the *identified marginal population* are the CHF patients who are suitable for treatment with ACE inhibitors, but who currently do not take the drug
- the cost of treating these patients with ACE inhibitors is estimated by estimating the annual drug treatment cost and making assumptions about the additional number of GP consultations required to undertake U&E tests at initiation and during monitoring
- each patient to be considered for treatment with an ACE inhibitor is also assumed to require an echocardiogram to confirm the diagnosis of heart failure
- the model requires an assumption about the proportion of heart failure patients who require hospitalisation for ACE initiation
- the model assumes that cost savings result only from reduced demand for secondary sector in-patient hospitalisation. Any reduced demand for GP consultations, outpatient visits, non-ACE drug costs etc, is excluded
- in this respect, the model will underestimate the potential cost savings of ACE inhibitor treatment for the given population
- the model examines only the 'year one' costs and savings, which are expected to be higher than in subsequent years.

▷ Results

The model parameters, assumptions and results for the base case scenario are described in Table D3. This suggests that in the base case, extending the use of ACE inhibitors could result in net cost savings of £418,762. Using the evidence on effectiveness from SOLVD, for a population of 500,000, an additional 42 premature deaths could be prevented per annum.

The right hand column reports more recent evidence enabling an updating of some of the parameters. The figures in bold denote changes to the original estimates, and the results in the right hand column are produced when the model is run with these updated parameters. In most cases the revised parameter estimates are within the ranges considered in the original sensitivity analysis (see below). Two issues warrant further consideration.

Table D3 Central scenario from WGAP report and updated information

Key variables	WGAP parameters and sources	Updated parameters and sources
Additional costs of treatment		
Prevalence of CHF	1% (Hart <i>et al.</i> , 1993 ³¹⁷)	1.5% (McDonagh <i>et al.</i> , 1997, ³¹⁸ cited in McMurray <i>et al.</i> 1998 ³¹⁹)
Proportion CHF patients already on ACE inhibitors	40% (North Derbs HA, PACE 1997)	20–30%, (Mair <i>et al.</i> , 1996; ³²⁰ Clark <i>et al.</i> , 1994 ³²¹), 54% (Hobbs <i>et al.</i> 2000 ³²²), 10–60% (McMurray 1998 ³¹⁹)
Proportion CHF patients <i>not</i> suitable for ACEIs	10% (Mair <i>et al.</i> 1996 ³²⁰)	5–20% cited in Andersson <i>et al.</i> (1999) ³¹⁶
Marginal population	2,500 [2700]*	2700
ACE inhibitor drug costs	£98.19 Ramipril (cheapest) av. Dose 2.5mg	£52–£339 (BNF43, 2002)
Echocardiograms per ACE inhibitor patient	1	Some may already have diagnosis confirmed by echo.
Echocardiography test costs	£40 (North Derbs HA)	£53 (Northern General Hospital, Sheffield)
Additional GP visits	3	Mason <i>et al.</i> (2000) ³²³ four GP visits and four nurse visits.
Cost of GP visit	£10.30 Netten and Dennett (1997) ³²⁴	£19 (Netten, Rees and Harrison, 2001) ³²⁵
Additional U&E tests	3	Recent survey (Kaira <i>et al.</i> , 1999) ³²⁶ suggests that renal monitoring is not carried out as often as it should be.
Cost of U&E test	£4.20 (Central Sheffield Uni. Hospitals Trust)	
Proportion of ACE inhibitor patients initiated in hospital	2% (SOLVD and later estimates unclear)	
Cost of generic one day inpatient stay (or GP consultation)	£201.05 Netten and Dennett (1997) ³²⁴	£198 (av. CHF IP stay, 2001 NHS Ref. Costs)
Total marginal cost	£489,513 [£528,674]	£532,386
Cost savings from treatment		
IP rate per patient per year (no-treatment group)	0.65 (WGAP analysis of SOLVD) ²⁸⁰	
RRR of hospitalisation from ACE inhibitors	18% (SOLVD) ¹²¹	
ARR of hospitalisation from ACE inhibitors (per patient/yr)	0.12 (SOLVD) ¹²¹	
Average inpatient LoS for CHF	12.15 (North Derbs HA, PACE)	9 (2001 NHS Ref. Costs)
Average reduction in LoS from ACE inhibitors	5% (North Derbs HA, PACE)	
Cost per inpatient day	£201.05	£198 (av. CHF IP stay, 2001 NHS Ref. Costs)
Net inpatient cost	-£877,255 [-£947,436]	-£691,158
Net inpatient cost	-£387,743 [-£418,762]	-£158,772

Source: Adapted from Cornell *et al.* (1998)

*Arithmetic error is original. Figures in [] are corrected.

Length of stay – The revised base case scenario suggests a cost saving but this is substantially reduced from the original. The main reason is the shorter mean length of stay for CHF suggested by the 2001 NHS Reference Costs database www.doh.gov.uk/nhsexec/refcosts.htm

Revising all other parameters and leaving LoS at 12 days, results in a net saving of £389,157, very similar to the original. The reference costs database distinguishes between mean length of stay for those aged under 70 (seven days), and those of 70 and older (11 days). For the younger age group the net saving is small at around £5,000.

Drug costs – The model is run assuming the cheapest ACE inhibitor (currently captopril at £52/year) is used. However, drugs costing up to £339/year are available. At this cost the model estimates a net cost increase of £616,000.

Sensitivity analysis indicates that the assumptions of the central case scenario would have to change substantially in order to eliminate the net saving result of the central scenario.

▷ Discussion of the WGAP model and results

- ❑ Modelling has indicated that managing heart failure patients according to good clinical practice, that is, using echocardiographic investigation and treatment using ACE inhibitors, can be achieved with potential marginal cost savings.
- ❑ The updated central case scenario implies that, for a population of 500,000, an additional 42 premature deaths could be prevented per annum with a potential net cost saving of around £160,000 in ‘year one’.
- ❑ The exclusion of potential savings from reduced demand for out-patient and GP attendances through the use of ACE inhibitors implies that the modelled savings are under-estimated in the central case.
- ❑ The demand and costs for U&E tests and echocardiography have been ‘front loaded’ into ‘year one’, which means that the actual net costs could be even lower than those indicated by the results of the modelled central scenario.
- ❑ The model does not allow for the possibility of induced extra demand for echocardiography for patients subsequently confirmed not to have heart failure. This induced demand will mean increased costs of echocardiography per patient with heart failure detected.
- ❑ The increased use of echocardiography could result in potential savings from the reduction or avoidance of inappropriate or over-prescribing of diuretics and ACE inhibitors for misdiagnosed patients.
- ❑ Recent work on screening out the need for echocardiography with pre-tests using electrocardiography and BNP testing may have implications for the assumptions relating to echocardiography employed here (see Appendix G).
- ❑ The analysis has been confined to the ‘year one’ costs and benefits of treating heart failure patients with ACE inhibitors. The model does not fully address issues associated with treatment over the lifetime of the patient, eg changes in the reduction in risk of hospitalisation over time, costs of treating patients who live longer because of their improved health state.

- ❑ The studies reported in tables D1 and D2, some of which do model the lifetime effects of ACE inhibitor treatment, indicate that the cost-effectiveness of ACE inhibitors, in terms of discounted LYG, is very favourable. Life years may even be gained with cost savings.
- ❑ The SOLVD study¹²¹ excluded frail elderly patients and patients with severe heart failure. If the hospitalisation gains from treatment with ACE inhibitors are lower for these groups of patients than those found in the SOLVD sample, then the hospitalisation savings indicated by the model have been overestimated.
- ❑ Modelled bed day savings, whilst a true opportunity for cost saving, will not automatically accrue to the purchasers as cash savings. The benefits are more likely to manifest themselves in the form of reduced waiting times and increased bed capacity in wards no longer occupied by heart failure patients.

2. Beta-blockers

Summary

- Trial evidence suggests that beta-blockers can improve symptoms, prolong survival and reduce hospitalisation.
- Therefore, while increasing the use of beta-blockers in eligible patients will increase treatment costs some, or all, of these will be offset, largely by reduced hospitalisation.
- The majority of patients in beta-blocker trials are also being treated with ACE inhibitors, so the benefits of beta-blocker therapy can be considered as additional to those achieved with first line use of ACE inhibitors.
- The existing economic evidence suggests that the use of beta-blockers is cost effective, or may be cost saving.
- Trial follow-up is relatively short so we know little about the longer-term cost and benefit profiles of beta-blockers.
- Recently published BHF statistics¹ suggest that in 1998 only 11% of heart failure patients were receiving beta-blockers in England and Wales. However, this had increased from around 8% in 1994. A number of papers suggest that low prescribing rates are caused by concerns on tolerability, but no evidence is presented to support this claim.

Drug costs

Only two beta-blockers are licensed for the treatment of CHF in the UK.*

Both convenience of administration and cost are important factors in determining the appropriate drug to use.

There may be differences in therapeutic efficiency, symptomatic benefit and adverse effects between these two drugs, but no trial has carried out a direct comparison.

Existing guidance that has considered economic implications.

The inherited NICE guideline on *Prophylaxis for patients who have experienced a MI* (North of England Guidelines Group, 2001)²⁶⁵ states:

- beta-blockers are associated with a substantial reduction in all cause mortality in patients with symptoms of heart failure being treated with an ACE inhibitor, who may or may not have experienced an MI.

The relevant recommendation for patients with prior MI and CHF is:

- ‘All patients should be offered long term treatment with an ACE inhibitor and then a beta-blocker... All of these treatments are cost effective.’ (A)

*A substantial number of people with heart failure are treated with the β -blocker atenolol for CHD, but this is not licensed for the treatment of heart failure.

Existing economic evidence on the use of beta-blockers

- ❑ Only six studies of adequate quality were identified by the economic review; these are summarised in Table D4. Five are based on data from the CIBIS trials (bisoprolol) and one employs data from the Carvedilol Heart Failure Trials Program.
 - ❑ Four of the studies are cost-effectiveness analyses; two of the studies look only at costs. Only three of the studies consider the UK context.
 - ❑ The studies by Varney²⁹² and Delea *et al*²⁹³ attempt to extrapolate the cost and benefits profile beyond the end of the trial by using decision analytic models. These are subject to a large degree of uncertainty. For the UK study (Varney) all CERs are well within acceptable limits of cost-effectiveness. For the US study (Delea *et al*) the worst case CERs are relatively high (close to £30,000) but this may reflect the high cost of Carvedilol in comparison with bisoprolol and a very conservative benefits scenario where benefits persist for six months only.
 - ❑ Like ACE inhibitors, there is some concern that treatment with beta-blockers may simply delay resource utilisation, or even increase it due to increased survival. There is no evidence to inform this view and trial follow-up is short.
- ▶ Initiation and up-titration
- ❑ In clinical practice achieving and maintaining dose is more difficult than in a trial.
 - ❑ Achievement of maintenance dose may be protracted, so considerable resource burden occurs early during initiation and up-titration.
 - ❑ Both beta-blockers are licensed for initiation in a community setting.
 - ❑ The proportion of patients dealt with in the community rather than the hospital may be an important determinant of costs.
 - ❑ The Varney study suggests that initiation by a specialist nurse in the community will be more expensive than initiation in hospital as the nurse is expected to spend more time with the patient.

Table D4 Existing evidence on cost-effectiveness of beta-blockers in the treatment of CHF								
Reference	Trial and drug	Country	Period of economic analysis	Details	Costs included and year	Quality	Cost/LYG	
							Base Case	Sensitivity analysis
							Best	Worst
Varney (2001) ²⁹²	CIBIS I&II bisoprolol	UK	(i) 1.3 years (ii) 5 years.	Consider variations in: (a) management (community based v. hospital shared) (b) rates and costs of all-cause hospitalisation (c) drug costs. As well as a limited and extended (beyond 1.3 yrs) benefits scenario.	Direct 2000	Good SA.* Extrapolation beyond trial follow-up.	None reported (majority of scenarios show small cost/LYG).	Net saving. £2,761
CIBIS II investigators (2001) ⁸⁶	CIBIS II bisoprolol	France Germany UK	1.3	Costs calc, using per diem and DRG in France and UK.	Direct 1998	SA on LoS, initiation and titration.	Net saving.	Net saving. £5,500 (UK)
Schadlich et al (1998) ³²⁷	CIBIS I bisoprolol	Germany	2 years	Considers patient cost burden (this increases with treatment).	Direct 1994	SA not explicit. Results only applicable in Germany.	Net saving.	Net saving.
Delea et al (1999) ²⁹³	Carvedilol HF Trials program	US	10 years	Consider two benefit scenarios: (i) limited – persist for six months then end abruptly (ii) extended – persist for six months then taper off over three years.	Direct 1997	Good SA. Extrapolation beyond trial follow-up.	(i) £20,208 (ii) £8,774	(i) £28,242 (ii) £12,637
Costing studies							Costs (bisoprolol v. placebo)	
Malek et al (1999) ³²⁸	CIBIS I bisoprolol	UK	1.9 years	Careful consideration of applying trial results to UK context.	Direct 1997	Poor SA, simply varying each parameter by ±10%.	£717 v. £726 £860 v. £965	£594 v. £517
Levy et al (1998) ³²⁹	CIBIS I bisoprolol	France	2 years	Includes sub-group analysis of patients without previous history of MI (nonischaemic).	Direct 1995	Poor SA; only on hospital and drug costs. All: £1,870 v. £2,297. Nonischaemic: £2,149 v. £2,678.	Net saving.	Net saving.

*SA = sensitivity analysis. Cost-effectiveness is usually represented using a cost-effectiveness ratio (CER), eg cost per LYG. If an intervention is found to produce net savings, it is not usual to present CERs because of the negative numerator. No attempt has been made to convert cost figures to the same base year. All figures are from 1991-96. All cost figures have been converted to pounds sterling using current exchange rates (10/06/02). These figures are not comparable and are for guidance only. Most cost and benefit figures presented here are not discounted due to the relatively short analysis periods. Exceptions are the five-year extrapolation in Varney where both costs and benefits are discounted at 6%, and the lifetime extrapolation in Delea et al where both costs and benefits are discounted at 3%.
CIBIS I: Bisoprolol v. conventional treatment. Average follow-up 1.9 years. CIBIS II: Bisoprolol v. conventional treatment. Average follow-up 1.3 years.
Carvedilol HF Trials Program: Carvedilol four concurrent RCTs, n = 1094, NYHA II to IV, LVEF < = 0.35. six months follow-up.

Table D5 Existing economic evidence on diuretics in the treatment of CHF

Reference	Economic analysis	Data sources	Patients	Period of economic analysis	Details	Costs included and year	Quality	Results
Mosher and Abrahamson (1995) US ³³⁰	Decision model torasemide v. furosemide	Published sources, expert panel	Hypothetical male 65–70 yrs, NYHA II-III with long term hypertension and mild to moderate renal impairment	1 year following diagnosis	Health events modelled: resistance to treatment, adverse effects of, diuretics symptoms of CHF, addition of ACE inhibitor and digoxin, hospitalisation CABG, angioplasty, MI	Direct 1994/5	No statistical evaluation of the difference between the two groups. No details on SA. Heavy use of expert opinion.	Costs per patient (drug costs as % of total costs) Torasemide: \$1,624 (12%) Furosemide: \$1,738 (1%)
Heaton <i>et al</i> (1996) US ³³¹	Retrospective cost analysis, torasemide and furosemide	Claims database	Patients continuously enrolled in a pharmacy benefit plan, Sept 93–March 95 Furosemide, n = 1118, Torasemide, n = 75	6 months before, 12 months after for furosemide, 5 months after for torasemide	No formal comparison of the two groups is made given differences in the pre-study period. Torasemide patients appeared to be sicker (higher claims) but NYHA not available. Before and after comparisons are made for each group.	Direct 1993/95	Difference in baseline is a major weakness.	Costs per patient per month Torasemide: before \$1,897, after \$823* Furosemide: before \$227, after \$261
Spannheimer <i>et al</i> (1998) Germany ³³²	Retrospective cost analysis and cost effectiveness. Torasemide v. furosemide	Patient records and questionnaire	Patients selected by GPs and specialist physicians. NYHA II-III, receiving drug for at least 1 year. n=200 each drug group	1 year	Only those costs deemed by the physicians to be related to CHF or use of diuretics are included.	Direct and indirect 1996	Patient groups were well matched. Bias towards more stable patients. Little SA reported. Average costs distorted by small no. of patients with long and costly hospitalisations.	Total costs Torasemide: DEM1,502 Furosemide: DEM1,863 Cost effectiveness: Torasemide: Annual cost per patient with improved NYHA class: DEM3,954 Furosemide: DEM7,605

continued

Table D5 Existing economic evidence on diuretics in the treatment of CHF – continued								
Reference	Economic analysis	Data sources	Patients	Period of economic analysis	Details	Costs included and year	Quality	Results
Noe <i>et al</i> (1999) US ²⁹⁴	Prospective cost analysis, torasemide v. furosemide	Medicare payment data	Patients from five managed care organisations with NYHA II-III randomised to torasemide (n = 103) or furosemide (n = 137).	6 months		Direct 1996	Patients had a relatively low rate of hospitalisation. No SA reported. Randomised but open label.	Total costs per patient Torasemide: \$1,520 Furosemide: \$1,503
Stroupe <i>et al</i> (2000) ³³³	Prospective cost analysis, torasemide v. furosemide		Patients from a public acute care hospital, randomised to torasemide (n = 93) or furosemide (n = 100).	1 year		Direct 1998	NYHA class not specified. Randomised but open label.	Total costs per patient Torasemide: \$13,899 Furosemide: \$16,023

SA = sensitivity analysis
 * An extended analysis for the torasemide group including an 'after' period of 11 months gave a cost PPPM of \$471. No attempt has been made to convert costs to standard base years or currencies. The figures cannot be directly compared and are for guidance only.

3. Digoxin

- ❑ Only one US-based study⁹⁹ was identified, which presents an economic analysis of data from the PROVED and RADIANCE trials.
- ❑ This study estimates costs and outcomes of continuation *v.* withdrawal of digoxin therapy in patients with normal sinus rhythm, NYHA II-III and LVEF $\leq 35\%$.
- ❑ Trial data is supplemented with epidemiological information from published reports and expert opinion.
- ❑ The trials suggest that digoxin may reduce the rate of heart failure related hospitalisation in patients who are (RADIANCE) and are not (PROVED) receiving ACE inhibitors.
- ❑ The trials find no effect on life expectancy.
- ❑ Continuation of digoxin therapy involves risks from toxicity, hence monitoring costs are an important component of resource use along with the costs of the drug itself, and the costs of treating side effects.
- ❑ The base case scenario suggests that digoxin therapy is cost saving, that is the extra costs of the drug, drug administration, monitoring and toxicity are more than outweighed by savings from reduced hospitalisation.
- ❑ Extensive sensitivity analysis was performed and the vast majority of cases showed digoxin to be cost saving.
- ❑ This is a relatively old study and is based in the US, hence applicability to the UK context is unclear.

4. Diuretics

- ❑ Five studies were identified but none consider the UK context (four US, one Germany), these are summarised in Table D5.
- ❑ All of the studies compare torasemide (the newer, more expensive drug) with furosemide.
- ❑ None of the studies constitute a formal economic evaluation although one does attempt a cost effectiveness calculation using improvement in NYHA class as the outcome measure.
- ❑ None of the studies are of very high quality, in particular because they report very little sensitivity analysis of the results and they only consider costs over a relatively short time period.
- ❑ Most of the studies show that the higher drug acquisition costs of torasemide are more than outweighed by lower healthcare resource use as a result of reduced hospitalisation.
- ❑ However, in one of the prospective US community-based studies²⁹⁴ the total costs of treatment with torasemide and furosemide are shown to be very similar. The benefits from torasemide treatment are greater but no formal QoL outcomes or comparison between costs and benefits is undertaken.
- ❑ The potential cost savings associated with torasemide are solely derived from reduced hospital admissions and readmissions, therefore these savings could only be realised if hospitals can capitalise on this reduction in demand for beds.

Quality of life and side effects

- ❑ Evidence suggests that these drugs are most effective at relieving symptoms, hence we would expect the QoL benefits to be substantial.
- ❑ Relatively small numbers of adverse events have been reported, and the majority are mild or transitory and do not require discontinuation of treatment.

Information for the UK

Diuretics are generally much cheaper than ACE inhibitors and beta-blockers.

- ❑ Evidence from the General Practice Research Database suggests that most patients with heart failure (>90%) are already being treated with diuretics, but there appears to be no readily available information on the distribution of molecules used.
- ❑ Diuretics are rarely used in heart failure as a monotherapy but there is no evidence on their incremental benefit or cost effectiveness when used alongside ACE inhibitors and beta-blockers.

Appendix E: Health economics of invasive procedures

The diagnosis of heart failure

- ❑ The systematic review revealed virtually no economic information in this area. Invasive procedures are rarely used in diagnosis in the UK – in contrast with the US.
- ❑ One paper was identified with a UK setting.²⁹⁵ This compares echocardiography *v.* cardiac catheterisation (CC) in the **evaluation** of patients with valvular heart disease. The findings may be relevant for the approx 10% of new patients with HF, with valve disease as an underlying cause.
- ❑ The paper is relatively old and is of poor quality. It is **not** a formal economic evaluation.
- ❑ Cardiac catheterisation is most commonly used in the UK to provide further information on aetiology, prior to surgery; hence the assumption of equivalent outcomes from echo and CC would **not** seem to be valid.

Table E1 Summary of Channer and Robertson (1991)

Cardiac catheterisation:	Echocardiography:
<ul style="list-style-type: none"> ❑ is invasive ❑ associated with a number of potential adverse effects ❑ these may be a particular problem in patients with HF ❑ involves exposure to X-rays with associated dangers ❑ imaging quality assumed to be equivalent ❑ no discussion of heart failure with respect to specific indications ❑ Conclusion: 'CC should be reserved for patients in whom details of coronary anatomy are necessary in planning surgery, and in cases where echocardiography fails, technically, to provide the quality of data necessary to make the clinical decision'. 	<ul style="list-style-type: none"> ❑ is non-invasive ❑ uses ultrasound, which has no known deleterious biological effects.

Estimated costs of CC and echo in 1988/89

▷ Capital costs

Capital costs of CC are much higher than echo. However, these are not central to the cost comparison since CC cannot be completely replaced by echo, therefore savings in terms of reduced numbers of CCs are made via savings in staff costs, consumables etc. Capital savings may be made if enough CCs are avoided to render replacement equipment unnecessary.

Variable costs

Table E2 Variable costs: costs per examination (1988/89 original estimates)	
R&L heart catheter examination	
With inpatient stay	£283
No inpatient stay	£143
R only (no inpatient stay)	£54
Echocardiography	£13
Note: These costs include all staff, ward and equipment and consumable costs (they exclude capital costs). See updated cost estimates below.	

- ▷ How many CC procedures need to be displaced to make an investment into echocardiography equipment worthwhile?
 - In brief, they estimate that if 100 CC procedures can be displaced then the acquisition of a new echocardiography service pays for itself. The more CCs are displaced, the greater the cost savings.
 - **But**, the paper gives no indication of how many CCs **could** be displaced by echo.
 - This comparison does **not** appear to include the costs of staff training involved in offering a new service.

Invasive treatments for heart failure

1. Left ventricular assist devices (LVADs)

- ❑ These are a relatively new and rapidly evolving technology. They were originally developed as a bridge to heart transplant, but increasing experience suggests that they may also be useful as a bridge to cardiac recovery or as a long-term alternative to transplant.^{*296}
 - ❑ The shortage of organs for transplantation is one incentive for increased use of LVADs as a treatment in their own right.[†]
 - ❑ Most evidence on benefits and costs is from the US, and comes from cohort studies of small numbers of patients in individual units; most have no control group. Resource use and cost information is of limited relevance to a UK setting.
 - ❑ Only a small number of patients have had LVADs implanted in the UK. It is not possible to say exactly how many LVAD procedures are carried out, as these are not recorded separately in the Hospital Episode Statistics. Agreement to provide treatment has been on an ad hoc basis with individual health authorities.²⁹⁷
 - ❑ One good UK systematic review with economic modelling was identified (Christopher and Clegg, 1999).^{334,‡} The study makes good use of available data **but** available data were very scarce.
- ▷ Summary of Development Evaluation Committee Report on LVADs for end stage heart failure (Christopher and Clegg, 1999)
- ❑ ‘... although there was some suggestion of potential benefits ... the evidence was not of sufficient quality to reach a decision. The committee noted a need for high quality evaluative research in this area, with duration and quality of life being a primary outcome, and taking into account UK practice and costs.’
- ▷ Potential numbers of patients who could benefit
- ❑ It is difficult to estimate the number of patients who could benefit from LVADs. In general, patients who may receive LVAD as a *bridge to transplant* have end-stage heart failure without irreversible end-organ failure (Goldstein *et al*, 1998²⁹⁶).
 - ❑ Statistics from the National Transplant Database (www.uktransplant.org.uk) can provide some idea of the potential numbers of LVAD recipients.
 - In the 12 months to March 2003, 147 heart transplants were carried out in the UK. This is not expected to increase significantly in the near future.
 - ❑ As of 9 March 2003, 99 people were on the waiting list. As a *bridge to recovery*, the number of deaths from myocarditis and cardiomyopathy give some indication of the potential numbers of patients who could benefit.

*The results of the Randomised Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial, which includes an economic analysis, are expected during 2003.

†Fewer than half of potential recipients receive a heart transplant, even when patients aged over 60 years are excluded from consideration (Taggart and Westaby, 1997³³⁵).

‡One more recent Canadian study (McGregor, 2000³³⁶) was also found, but its findings are of limited applicability in a UK setting.

- In 1997 there were 57 deaths from myocarditis (five of which were in those aged 75 or above), and 1,594 deaths from cardiomyopathy (376 of which were in those aged 75 or above).*
 - The DEC systematic review identified 10 cohort studies; five of these had control groups; all 10 judged to be of ‘poor’ design.
- ▷ Cost utility analysis of LVADs as a bridge to transplant
- Devices considered: HeartMate 1000 IP; HeartMate IV; Novacor; Jarvik 2000; AB-180. The last two are in their early developmental stages, with no available evidence to evaluate their use.
 - Utility (preference) estimates are taken from a US study (Moskowitz *et al*, 1997³³⁷).
 - This study obtained utilities (using standard gamble) from LVAD patients at three points in time: before LVAD implantation, during LVAD support and after heart transplantation.
 - The sample consisted of all 29 patients who underwent LVAD implantation at Columbia-Presbyterian medical centre during December 1993 to June 1995.

Table E3 Mean utilities associated with the three states of health

Health state	Sample (of 29)	Mean utility score	Range
End stage HF immediately before LVAD implantation	14	0.548	0.050 to 0.875
During LVAD support	20	0.809	0.550 to 0.990
After cardiac transplantation	11	0.964	0.700 to 1.000

Patients not interviewed were either too ill or had died.

- Main potential benefits:
 - increased QoL whilst on LVAD
 - increased functional capacity in terms of NYHA
 - faster improvement of QoL post-transplant.
- If 100 patients are treated with LVADs they gain approximately 218 QALYs (sensitivity range 98 to 361) more than an equivalent group of 100 patients not treated, over 20 years.
- Estimates of cost data were extremely difficult to obtain and were taken from a variety of sources, summarised below.
- Costs are broken down into:
 - LVAD (device, procedure and follow-up)
 - transplant (transplant procedure, follow-up and follow-up drug costs).
- Costs are dominated by the LVAD device and the transplant procedure.
- Discounted cost per QALY is estimated at £39,800 (sensitivity range £28,500 to £74,000).
- To achieve a more cost-effective ratio, the costs of the device and procedure would have to fall substantially.

*HMSO Mortality Statistics cited in Christopher and Clegg (1999).

Table E4 Cost estimates in Christopher and Clegg (1999), in pounds sterling				
	NHS Ref Costs	NHS Trusts Finance Depts	Clinician estimate	BNF and Trust Protocol
LVAD				
Device		52,875	55,000	
Procedure		9,604		
Follow up (annual)		750		
Transplant				
Procedure	23,949	21,600/18,949		
Follow-up (annual)		3,500		
Follow-up drug costs (year 1)				2,890
Follow-up drug costs (after year 1)				3,161
Adapted from Christopher and Clegg (1999), Appendix 11. Costs in bold were used in base case estimates.				

- ▶ Potential savings from LVAD treatment
 - ❑ Reduction in drugs for end-stage heart failure.
 - ❑ Decreased ICU use.
 - ❑ Reduction in transplant follow-up costs.

- ▶ Disbenefits of LVAD treatment
 - ❑ The adverse events recorded in the cohort study judged by the DEC report to be of the best methodological quality,²⁹⁸ are:
 - device related bleeding, haemolysis, infection, right ventricular failure, thromboembolism, septic embolism, renal dysfunction.
 - ❑ Of these only infection was significantly different between the LVAD (n = 75) and the control (n = 33) group, but the potential disbenefits are not trivial.

- ▶ Further issues
 - ❑ Data in the DEC report date back to 1997 and it is likely that both clinical and economic factors have changed significantly since that time. As LVADs are an emerging technology, costs are likely to fall, especially via reduced LoS and readmission.
 - ❑ A major resource use factor associated with LVAD use is hospitalisation.
 - ❑ Morales²⁹⁹ cites a 103-day average bridge to transplant time (in one unit in the US). It is preferable, for cost and QoL reasons, if the patient can be discharged during this time.

2. Heart transplant

- ❑ The shortage of organs and strict eligibility criteria mean that this is only available to a small number of patients.
- ❑ QALY estimates for heart transplant have been published but these are relatively old.³⁰⁰
- ❑ One paper³⁰¹ developed a model to investigate the costs of care **following** heart transplantation (the costs of transplant procedure itself are not assessed).

- ❑ Data from all cardiac transplant recipients who underwent a first transplant between 1986 and 1993 at the Papworth Hospital, and who were maintained using a triple-drug immunosuppression regimen. 387 patients, age range 6 to 63 years (94% between 20 and 60 years). Main indications for surgery were ischaemic heart disease (54%) and dilated cardiomyopathy (42%).
- ❑ Expected cost per transplantation patient £26,000 (£2,000–£57,600) over five years (discounted at 6%). The 95% range of cost estimates is wide:
 - patients who die early after transplantation have relatively little cost implication for the transplant service
 - patients who survive in the longer-term with a problematic post-operative course incur the greatest resource use.
- ❑ Routine hospital visits account for the largest proportion of costs in the early period after transplant. Maintenance of immunosuppression accounts for the largest proportion of costs after the first three months.
- ❑ QoL as well as length of life is extremely important in evaluating benefits of transplant. There is one good systematic review of QoL benefits after transplantation, which reviews information from 218 studies and 14,750 patients.³⁰² Of these, 2,826 were heart recipients.
- ❑ There is little heart transplant-specific information in the review but it does find that of all organ recipients, heart and heart and lung transplant patients are the most likely to show significant improvement across all dimensions of QoL.

3. Biventricular pacing

- ❑ The economic searches identified the 2001 report on ventricular pacing and resynchronisation for heart failure from the National Horizon Scanning Centre.³³⁸
- ❑ There are a number of on-going trials, mainly comparing biventricular pacing with single ventricle pacing. Preliminary results suggest a potential benefit in terms of morbidity and mortality.
- ❑ One economic analysis (see below) suggests savings in terms of hospitalisation, and estimates that 4,200 to 8,400 patients with heart failure (NYHA III-IV) in England and Wales could be eligible.
- ❑ Implantation and follow up costs for 1,000 patients are in the region of £5m–£7.5m.
- ❑ Economic modelling of the likely costs and benefits is required.
- ❑ One Swedish study (Braunschweig *et al*, 2000⁶⁶) aimed to assess total and heart failure related hospital days, as well as safety and efficacy of biventricular pacing in 16 patients with severe heart failure.
- ❑ This is a small sample with no control.
- ❑ Patients had heart failure due to ischemic heart disease or dilated cardiomyopathy with NYHA class III-IV, despite optimised drug treatment including ACEIs or beta-blockers. Mean follow-up 120 to 365 days. Thirteen patients improved by at least one NYHA class.

Table E5 Summary of results of Braunschweig *et al* 2000

	Year before pacing	Year after pacing	P (difference)
Total hospital days	253	45	< 0.01
HF related hospital days	183	39	< 0.01

Appendix F: Health economics of other non-pharmacological therapies

Exercise training

- ❑ Only one economic study was identified by the systematic review (Georgiou *et al*, 2001³³⁹). This is based on the results from the largest RCT of exercise training, and has a US setting.
- ❑ The study shows exercise training to be cost effective. However, a major element of patient-borne costs (travel time and expenses) are excluded from the analysis.

Summary of Georgiou *et al* (2001): cost-effectiveness analysis of long-term moderate exercise training

- ❑ The study uses efficacy results from Belardinelli *et al*.³⁰³ Ninety-nine patients were randomised to exercise program and control. All had stable CHF, NYHA II-IV, 90% were on ACEIs, age range 55–64. Only NYHA class II and III patients considered in the analysis.
- ❑ Exercise training (ET) was performed in two phases over 14 months:
 - three times 1 hr/wk for eight weeks
 - two times 1 hr/wk for 12 months
 - a total of 128 hours per person.
- ❑ Effectiveness was measured as the increment in life expectancy.
- ❑ Modelling was used to estimate the cost and benefit scenarios beyond the 14-month trial follow-up period.
- ❑ Efficacy results for the 14-month trial period were taken from the trial itself.

Table F1 Summary of results of Georgiou *et al* 2001

	ET group	Control group
Mortality rates	18%	41%
Hospitalisation rates (all cause)	10%	29%

- ❑ Age and sex specific estimates of survival for the next 10 years were taken from a national epidemiological study.³⁰⁴
 - ❑ These were adjusted upwards to reflect improvements in CHF survival with ACEIs.
- ▶ Costs of ET and monitoring
- ❑ ET was carried out in hospital, by a trainer hired by hospital, who supervised patients in groups of four.
 - ❑ Costs included: salary of trainer, equipment, space rental, cardiopulmonary test. The main cost drivers were salary and space rental. Other costs considered were: wages lost

due to attendance at ET (assumed all are full-time workers), hospitalisation (adapted from Delea *et al.*).²⁹³

- ❑ Travel costs of attendance at ET (a major patient burden) were excluded.

Table F2 Cost effectiveness of ET		
	ET group	Control Group
Cost of ET per patient	\$2,054	\$0
Wage lost from ET per patient	\$2,509	\$0
Hospitalisation rate*	10%	29%
Averaged cost of hospitalisation per patient	\$719	\$2,055
Total cost per patient	\$5,282	\$2,055
Incremental cost of ET per patient	\$3,227	N/A
Incremental life expectancy (yrs)	1.82	N/A
Cost effectiveness ratio (\$/LYG)	\$1,773	N/A
Sensitivity analysis of CER		
Upper limit	\$8,274	
Lower limit	\$1,012	
<p>* Hospitalisation rates were assumed to be the same for both groups after the follow-up period. The common rate was taken from Delea <i>et al.</i>²⁹³</p> <p>A discount rate of 3% is applied to costs and benefits. Sensitivity analysis varied survival probabilities (trial and post follow-up), rate of improvement provided by ACEIs, hospitalisation rates).</p>		

▷ Comments

- ❑ The methods and results are reported with sufficient detail. The sensitivity analysis is appropriate.
- ❑ The results cannot be extrapolated to patients outside the 55–64 years age group, and the resource use and costs are US specific.
- ❑ Improved survival is not adjusted by QoL as there are no suitable QoL data.
- ❑ Qualitative data suggest that ET improves QoL, hence calculating QALYs would be likely to weight the CER more heavily in favour in ET.
- ❑ The assumption of common hospitalisation rates after the 14 month follow-up period is very conservative.
- ❑ This only quality economic study identified shows exercise training to be cost-effective. However, it is very specific to the location and specific exercise programme in question. In addition, its relevance to the UK context is questionable.

Multi-disciplinary teams

- ❑ The searches identified very little economic evidence available. It is difficult to compare the costs and outcomes from different programs. Most evaluated interventions are based in the US.

McAlister *et al* (2001)²²⁰

- ❑ Systematic review of nine RCTs comparing multidisciplinary teams providing specialised follow-up with usual care. Follow-up length varied from 3–12 months.

Table F3 Summary of results of McAlister *et al* (2001)

Outcome	No of RCTs	Results
Mortality	6	None found a significant difference initially, but one found a significant benefit in favour of the intervention after 18 months follow-up.
Hospitalisation	9	All found fewer hospitalisations in intervention group. Only significant in two cases. Significant reduction in risk of hospitalisation overall. Suggests that for every eight patients with HF treated by a multidisciplinary team rather than usual care, there will be one fewer hospital admission over about six months.
Length of stay	7	Six found significantly reduced LoS or total no. of hospital days in intervention group.
Use of medications	2	Both showed significantly greater use in intervention patients.
QoL and/or functional status	3	Only one found significantly better outcomes in intervention arm.
Costs	7	All but one reported that the intervention was cost saving.

Capomolla *et al* (2002)³⁰⁵

- ❑ RCT comparison between HF management program delivered by a day-hospital and usual care.
- ❑ Setting is Italy. 234 patients, 112 randomised to intervention arm. Average follow-up is 12 months.

Table F4 Summary of results of Capomolla *et al* (2002)

Outcome	Results
Mortality	Significantly fewer deaths in intervention group.
Hospitalisation	Significantly fewer hospitalisations in intervention group.
Use of medications	Significantly higher doses of ACEIs, beta-blockers and nitrates in intervention group; lower doses of diuretics and digitalis.
QoL and/or functional status	Significant improvement in NYHA class in intervention group; not significant in control group.
Costs	After one year, annual drug costs per patient were significantly higher in the intervention group, but this was more than compensated for by savings in costs of hospitalisations.

Appendix G: A cost effectiveness model for the appropriate use of echocardiography in the diagnosis of heart failure

Summary

This paper represents a rapid attempt to use economic modelling to inform the recommendations on the most efficient use of echocardiography facilities in the diagnosis of heart failure. The question studied is:

*Should all patients presenting to a GP with suspected heart failure get BNP & ECG & echocardiography as a matter of course, or should they **initially** undergo an ECG and BNP and only get an echocardiogram if the first two tests suggest an abnormality?*

This question is considered by calculating the additional cost per life year gained of the first strategy on the assumption that a diagnosis of heart failure provides access to treatment not otherwise available to the patient (in this case ACE inhibitors).

Using our best estimates from UK data, the baseline cost per life year gained of immediate echocardiography is around £16,000. This would normally be considered cost effective in the context of NICE's historical decisions regarding **drug** therapies. However, the cost effectiveness of **diagnostic** technologies, especially in chronic conditions, is rarely investigated and therefore it is difficult to compare this figure with anything else.

The issue of appropriate referral to echocardiography is key. If the proportion of patients being sent for echocardiography who actually turn out to have heart failure is low, then immediate use of echo does not look cost effective. If we can use other tests (in this case ECG and BNP) to filter out patients who do not require an echocardiogram, this could result in more efficient use of echo facilities.

Evidence from open access services should give us a reasonable estimate of the 'prevalence' in this population if echocardiography is made more readily available. If this proportion falls below 25%, the cost per LYG shoots up. For example, the Davie *et al*³⁰⁶ study in Edinburgh suggests that 18% of patients referred by GPs for echocardiography actually turned out to have heart failure. This would result in a cost effectiveness ratio of > £30,000 using the model developed here.

In addition the sensitivity of BNP and ECG (combined) is also important; the higher the sensitivity the higher the cost per LYG of immediate echocardiography. The results are sensitive to key model parameters (see table opposite).

Table G1		
Proportion of people referred for echo who actually have HF	Sensitivity of BNP and ECG	Cost per LYG
Baseline		
0.29	97%	£16k
Sensitivity analyses		
0.20	98%	£40k
0.30	96%	£11k

Introduction

In developing recommendations for the diagnosis of heart failure the guideline development group were aware that a policy of referring all cases of suspected heart failure for echocardiography would have substantial service implications, and create problems for GPs who do not have open access to echocardiography.

While it was generally agreed that an echocardiogram was necessary to confirm a diagnosis of heart failure and provide information on the underlying functional abnormality of the heart, it was also suggested that a diagnosis of heart failure could, in many cases, be ruled out by carrying out a full clinical examination and tests including a chest X-ray, 12 lead electrocardiogram and natriuretic peptide (BNP or NT proBNP) testing. If these tests do not reveal any abnormality then a diagnosis of heart failure is very unlikely.

In order to aid the guideline development process a model has been constructed to investigate the possible costs and benefits of two alternative recommendations relating to the use of echocardiography in the diagnosis of heart failure; on the one hand echocardiography could be carried out on all patients who present to the GP with possible symptoms of heart failure, or on the other hand echocardiography could be reserved for those patients who have an abnormality revealed by the other three diagnostic tests described above.

The model is a simplified version of the real clinical situation and is characterised by much uncertainty around some of the key parameters. However, no attempt at modelling the cost effectiveness of echocardiography in diagnosing heart failure has been attempted before, so the model represents a step forward in that respect. It is hoped that the model can provide some useful information to help formulate the guidelines on diagnosis.

A brief description of the modelling choices

The diagnosis modelling exercise is necessarily a simplified version of the real clinical situation. It is based on the assumption that there are three main diagnostic tests for heart failure; ECG, BNP and echocardiogram.*

One key question is formulated: Should all patients presenting to a GP with suspected heart failure get *all three* tests (including echocardiography) as a matter of course, or should they *initially* undergo an ECG and BNP and only get an echocardiogram if the first two tests suggest an abnormality?

*Following discussion at the CRG, chest X-ray was omitted from the list of initial tests.

Considering a person with suspected heart failure, there are four possible scenarios relating to the tests and their results:

- 1) Carry out two tests (ECG, BNP), neither are abnormal.
- 2) Carry out two tests, one is abnormal therefore carry out an echocardiogram.
- 3) Carry out two tests, two are abnormal therefore carry out an echocardiogram.
- 4) Carry out two tests plus an echocardiogram as a matter of course.

Scenarios 2, 3, and 4 all have the same costs (of the three tests) and detection rate, suggesting only two important alternative strategies:

- A) carry out ECG and BNP initially and only refer to echocardiography if an abnormality is identified by the two tests; *or*
- B) carry out all three tests initially.

If the problem is set up in this way the key issue becomes:

How many cases of heart failure would carrying out only ECG and BNP miss? That is, if these two tests show no abnormality but echocardiography would have picked up an abnormality? The answer to this rests on the sensitivity and specificity ECG and BNP in diagnosing heart failure. To simplify the model it is assumed that echocardiography is the diagnostic gold standard with both sensitivity and specificity of 100%. (The appropriateness of this assumption is discussed below.) We also assume that missed diagnoses are not 'caught' within the four-year period considered.

Costs of each strategy include the costs of the tests, the costs of treating heart failure with drugs and the hospitalisation costs for treated and untreated heart failure. The benefits will be expressed in terms of life years gained (LYG) from heart failure treatment, assuming that a diagnosis of heart failure means access to treatment that has positive effects in terms of life years gained and reduced hospitalisation. No attempt is made to adjust the life years gained with quality weights since there is no adequate source of information on quality of life in treated and untreated heart failure patients.

A simplified representation of the model

A simple schematic of the two strategies is shown in Figure 1: strategy A in which a patient only receives an echocardiogram if there is an abnormality on either or both of the first two tests; strategy B where all three tests are carried out as a matter of course.

In a very simple example, for 100 patients, say that strategy A (ECG and BNP) finds no abnormality, but strategy B detects heart failure in two patients via echocardiography. Then if strategy A is carried out two diagnoses will be 'missed', that is those patients will not have access to treatment for heart failure, whereas they would have done under strategy B.

The relative costs and benefits of these two strategies are summarised in Table G2 overleaf.

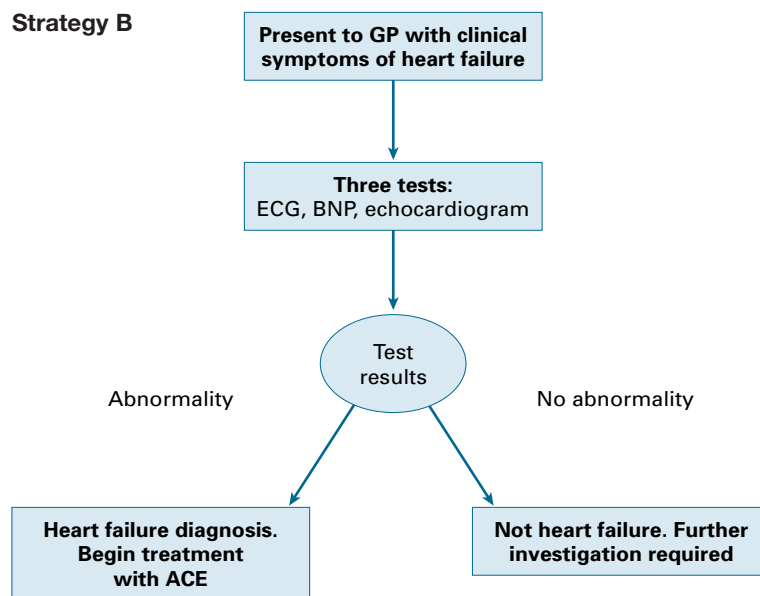
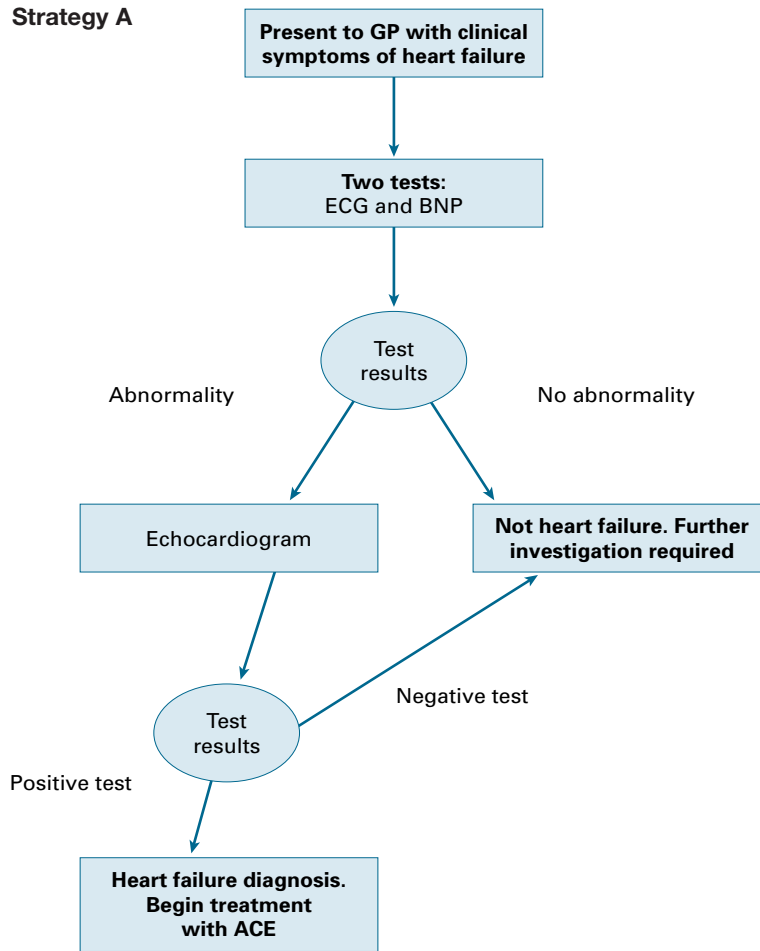


Figure 1: Strategies for the diagnosis of heart failure.

Table G2 Relative costs and benefits of strategies A and B		
	Diagnostic strategy	
	A	B
Tests	BNP + ECG. 100 patients. No abnormality detected. 2 diagnoses missed.	BNP + ECG + echo. 100 patients. 2 abnormalities detected. No diagnoses missed.
Costs	Costs of tests 1 and 2. 2 × costs of untreated HF.	Costs of tests 1 and 2. Cost of test 3 (echo). 2 × costs of <i>treated</i> HF.
Life years gained	Negative (relative to B) due to untreated HF.	LYG from treatment (assume baseline of 0).

The model in more detail

The model traces a hypothetical cohort of 100 adults who present to the GP with possible symptoms of heart failure. The model traces this cohort for a period of four years. The time period is limited to four years as this is the maximum follow-up time available to compare outcomes for treated and untreated heart failure using data from the SOLVD trial.¹²¹ No attempt has been made, at this stage, to extrapolate findings beyond trial follow-up.

The parameter values and evidence sources for the baseline scenario show (Table G3) that the additional costs of carrying out an echocardiogram on all 100 patients as a matter of course, as opposed to using ECG and BNP as a filter, is £2,062. However the life years gained from this strategy are very small at only 0.13 life years for 100 patients. This results in a baseline cost per life year gained of £15,928.

Model parameters, baseline values and one-way sensitivity analysis

▷ Prevalence of heart failure in this population

This is an estimate of the number of patients referred by a GP with possible heart failure who actually receive a diagnosis of heart failure after further investigation. The baseline estimate of 29% comes from the Hillingdon Heart Failure Study (Cowie *et al* 1999³⁴⁰). This study identified incident cases of clinical heart failure developing in a population of 151,000 people served by 81 GPs in 31 practices in the Hillingdon district, west London. The GPs agreed to refer all suspected cases of new heart failure to a rapid access study clinic, preferably before the patient had started treatment. Between April 1995 and July 1996, 122 patients were referred.

There is a large amount of uncertainty surrounding this parameter and estimates in the range 18% to 50% have been obtained in other studies on similar populations. In particular, the GPs in the Hillingdon study may have had higher than average awareness of heart failure. In one-way sensitivity analysis increasing the prevalence estimate results in a reduction in the cost per LYG. The cost per LYG is very sensitive to this parameter especially at high values (see below for more detail on key parameters).

In the simple model the patient cohort is assumed to be approximately 50% male and prevalence rates are assumed to be equal between men and women. However, there is evidence

from the Hillingdon study and a study in Finland (Remes *et al*)²⁷ that prevalence rates may differ substantially between men and women. In the Hillingdon study only 17% of the women referred had a diagnosis of heart failure confirmed by further investigation, whereas this figure was 41% for men. A possible extension to the model would be to divide the cohort into men and women with different prevalence rates and possible different mortality rates.

Survival probabilities

Treated heart failure – The baseline values for the cumulative survival probabilities for treated heart failure over the four-year period are taken from the treatment arm of the SOLVD trial, which assessed the effect of the ACE inhibitor enalapril on mortality in patients with mild to moderate heart failure.

Untreated heart failure – The baseline values for the cumulative survival probabilities for untreated heart failure come from the control arm of the SOLVD trial.

Table G3 Baseline scenario		
Parameter	Baseline value	Source
Epidemiology		
Prevalence	29%	Hillingdon study ³⁴⁰
Cumulative survival probabilities	(yrs 1,2,3,4)	
Treated heart failure	0.88, 0.78, 0.68, 0.62	SOLVD trial ¹²¹
Untreated heart failure	0.84, 0.73, 0.64, 0.57	SOLVD trial ¹²¹
Non-heart failure	0.80, 0.75, 0.70, 0.67	Hillingdon study ³⁴⁰
Diagnostic accuracy		
Echocardiography		
Sensitivity	100%	Assumed gold standard
Specificity	100%	Assumed gold standard
Three tests		
Sensitivity	97%	Hillingdon study ³⁴⁰
Specificity	61%	Davie <i>et al</i> (1996) ³⁰⁶
Cost of tests		
Echocardiography	£53	NGH, Sheffield
ECG	£9.30	McMurray <i>et al</i> (1993) inflated ²⁸⁵
BNP	£12.50	Martin Cowie
Cost of drugs	£139	BNF (generic enalapril)
Hospitalisation Rate	0.65 patient/yr	SOLVD ¹²¹
Reduction from treatment	0.82	SOLVD ¹²¹
Length of stay	9	NHS Reference Costs
Reduction from treatment	0.95	SOLVD ¹²¹
Results		
Total Costs		
Strategy A	£88,138	
Strategy B	£90,200	
Life Years Gained		
Strategy A	299.51	
Strategy B	299.64	
Cost per life year gained	£15,928	

Cumulative survival probabilities for both treated and untreated heart failure were estimated from the SOLVD data using the actuarial method.³⁰⁷ Both sets of probabilities may be higher than those seen in clinical practice due to the strict protocols adhered to in a clinical trial.

In one-way sensitivity analysis as the mortality differential between treated and untreated heart failure increases, that is as the gains from treatment increase, the cost per LYG is reduced. However, the cost per life year gained is not very sensitive to changes in the mortality differential. Increasing the mortality gains from treatment by 10% (in each of the four years) reduces the cost per life year gained to £6,459.

Non-heart failure, but with clinical symptoms

The cumulative survival probabilities for patients who present with possible symptoms of heart failure but who do not receive a diagnosis of heart failure after further investigation were taken from the Hillingdon study (de Giuli, personal communication).

The mortality rate in the first 12 months is higher than for the untreated arm of the SOLVD trial,¹²¹ but it is lower in subsequent years. This may reflect the unrealistic context of the trial compared to the Hillingdon study that more closely reflected normal clinical practice.

Changes in the cumulative survival probabilities for this group have no effect on the cost per life year gained.

In this model, given that echo is assumed to be the gold standard with sensitivity and specificity of 100% no one will receive a confirmed diagnosis of heart failure who does not have the disease. Any abnormality in the first two tests will be referred for echocardiogram and this is assumed to give a definitive diagnosis. This is not a true reflection of the clinical situation and a possible extension to the model would be to reduce the sensitivity and specificity of echocardiography to below 100%. One implication of this is that some patients will have a diagnosis of heart failure confirmed when in fact they do not have the disease and this will result in them receiving inappropriate treatment.

Sensitivity of the tests

The *sensitivity* of a diagnostic test for heart failure refers to the proportion of patients correctly identified with heart failure by the test, ie the proportion of patients with the disease who also get a positive test result.

The *specificity* of a diagnostic test refers to the proportion of patients who do not have the disease who also get a negative test result.

The assumption employed here is that echocardiography is the diagnostic gold standard with both sensitivity and specificity of 100%.

For ECG and BNP there are a number of studies that estimate the sensitivity and specificity of the individual tests in patient groups similar to that considered here. However, there is little information on the combined diagnostic sensitivity and specificity of these two tests. A literature search for studies that reported sensitivity and specificity of ECG and/or BNP in diagnosing heart failure in a relevant patient group produced six papers in relation to BNP and seven for ECG; these are summarised in tables G4 and G5 (at the end of this appendix).

Given that in this model an abnormality on any test would mean referral for echocardiography, a key issue is the lowest estimate of specificity on any one test, as it is this that will determine the number of ‘unnecessary’ referrals for echocardiography. In fact the combined specificity will be lower than the lowest specificity of any one test given that not all tests will identify the same patients as having (or not having) the disease.

The baseline figure for sensitivity (0.97) is taken from the BNP study by Cowie *et al.*²⁸ This sensitivity figure was found using a cut-off value for BNP level of 22.2 pmol/L chosen to give a negative predictive value of 98% in the study.

The baseline figure for specificity (0.61) is taken from a large study (n = 534) of patients sent by their GPs to an open access echocardiography service.³⁰⁶ The figure refers to the specificity of ECG in diagnosing heart failure, where a major abnormality on ECG was taken as a sign of left ventricular systolic dysfunction.*

In one-way sensitivity analysis increases in sensitivity and specificity of the three tests increase the cost per LYG (see below for more detail on key parameters).

Costs

▷ Tests

The baseline cost for an echocardiogram (£53) is taken from the Finance Department at the Northern General Hospital, Sheffield. It is a full cost estimate including hospital overheads.

The baseline cost for ECG is taken from McMurray *et al.*²⁸⁵ and inflated to 2002 figures using the GDP market price index of inflation.

The costs for BNP testing were obtained from Martin Cowie (Clinical Adviser).

In one-way sensitivity analysis changes in the costs of BNP and ECG have no effect on the cost per LYG since these are included in both scenarios. As the cost of echocardiography increases the cost per LYG also increases and this relationship is linear. If the cost of an echocardiogram was only £25 the cost per life year gained would be £6,914. Doubling the cost of echocardiography to £106 results in a cost per life year gained of £32,989.

▷ Drugs

In the baseline analysis it is assumed that ACE inhibitors form the only treatment available to patients with a confirmed diagnosis of heart failure that are not available to patients who do not have a confirmed diagnosis (see below).

The dosage and costs of treatment with ACE inhibitors are taken from the BNF (March 2002). The baseline cost estimate is £139 per year for the generic version of enalapril.

In one-way sensitivity analysis increases in the cost of treatment with ACE increase the cost per LYG. However, the cost per life year gained is not that responsive to changes in the cost of ACE

*The Davie *et al* study³⁰⁶ classifies ECG results as normal, minor abnormality or major abnormality. *Minor* abnormality is: atrial enlargement, bradycardia, tachycardia, broadening of QRS complex, poor R wave progression, right axis deviation, myocardial ischaemia, first degree atrioventricular block, non-specific ST-T wave changes. *Major* abnormality is: atrial fibrillation, previous MI, LV hypertrophy, bundle branch block, left axis deviation.

inhibitors. Using the cheapest ACE (generic captopril at £52 per patient per year) gives a cost per life year gained of £14,318, whereas the most expensive ACE (fosinopril at £339) gives a cost per life year gained of £19,628.

Similarly if the additional cost of drug initiation and titration were included as well as the annual drug costs this would only result in small increases in the cost per life year gained.

▷ Hospitalisation

In the baseline analysis the estimated hospitalisation rates for treated and untreated heart failure are taken from the SOLVD trial.¹²¹ This gives a hospitalisation rate for untreated heart failure of 0.65 admissions per patient per year with a reduction from ACE treatment of 18%. The average length of stay for a heart failure related admission (nine days) is taken from the NHS Reference Costs database, and the SOLVD trial suggests a reduction in LoS of 5% resulting from treatment with ACE. The average cost of an inpatient bed day (£198) is taken from the NHS Reference Costs database.

A simplifying assumption is made that hospitalisation rates and average length of stay are the same in each of the four years.

In one-way sensitivity analysis if the gains from ACE treatment in terms of hospitalisation are increased the cost per LYG is reduced, and these relationships are linear. Hence, the cost per life year gained is not very sensitive to changes in any of the hospitalisation parameters.

▷ Life years gained

The assumption is that a confirmed diagnosis of heart failure means the patient has access to treatment that is not available to people who do not have a confirmed diagnosis despite presenting to the GP with possible symptoms of heart failure. In the baseline analysis it is assumed that ACE inhibitors are available to patients with a confirmed diagnosis of heart failure. A further assumption is that everyone who has a confirmed diagnosis is eligible for treatment with ACE inhibitors. Treatment with diuretics is assumed to be available to patients with clinical symptoms regardless of their diagnosis, therefore the cost of diuretic treatment is not included in the model. Estimates of the mortality gains from treatment with ACE inhibitors are taken from the treatment arm of the SOLVD trial.

The weight of evidence from the literature suggests that ACE inhibitors are a cost effective treatment for heart failure (see Appendix D). As explained above as the mortality differential between treated and untreated heart failure increases the cost per life year gained is reduced.

The assumption that ACE inhibitors are the only treatment available to patients with a confirmed diagnosis of heart failure that may have mortality gains and benefits in terms of reduced hospitalisation is not realistic. Clinical trials on the use of beta-blockers to treat heart failure have largely included people who are already being treated with ACE inhibitors. These trials have demonstrated an additional benefit from the use of beta-blockers over and above treatment with ACE inhibitors. A possible extension to the model would be the inclusion of the benefits of treatment with beta-blockers. This is likely to reduce the cost per LYG since, like ACE inhibitors, studies have shown beta-blockers to be a cost-effective treatment for heart failure. However, the results are not expected to be very sensitive to this modification.

Discounting

As the cost and benefits in this model accrue over four years they are discounted to current values using the rates recommended by NICE – 6% for costs and 1.5% for benefits. In one-way sensitivity analysis increases in either discount rate reduce the cost per LYG. As the time period is relatively short changes to the discount rate make little difference to the result.

▷ Key parameters

There is a large amount of uncertainty around many of the parameters in this model but some are more important than others in terms of the sensitivity of the cost per life year gained to changes in these parameters.

The key parameters are discussed below.

Prevalence – Figure 2 shows the non-linear relationship between prevalence rate and cost per life year gained holding all the other parameters at their baseline values.

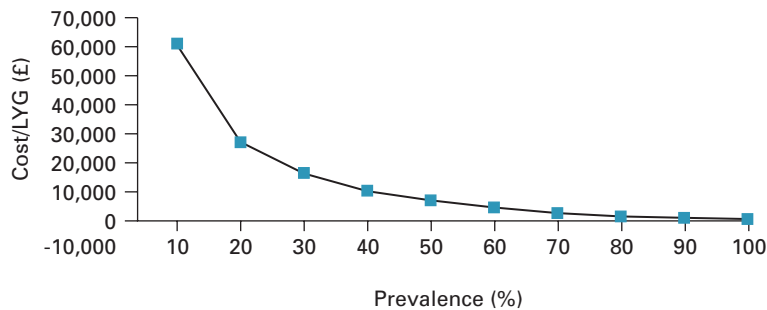


Figure 2: Prevalence

If the proportion of patients referred by the GP for echocardiography who actually obtain a diagnosis of heart failure falls below 20% the cost per life year gained increases very quickly. If the prevalence in this population was as low as 18% (as shown in the open access study by Davie *et al*),³⁰⁶ the estimate of the cost per LYG increases to just over £30,000.

Sensitivity and specificity – Figures 3 (below) and 4 (overleaf) show the relationship between the sensitivity and specificity of BNP and ECG and cost per LYG if all other parameters are held at their baseline values. It is important to note that the sensitivity plot assumes that specificity remains constant at 0.61, and the specificity plot assumes sensitivity remains constant at 0.97.

As the sensitivity of ECG and BNP increases to above 0.97 the cost per life year gained is increased rapidly.

The relationship is not as steep for specificity, but a specificity of larger than 0.75 results in a high cost per life year gained.

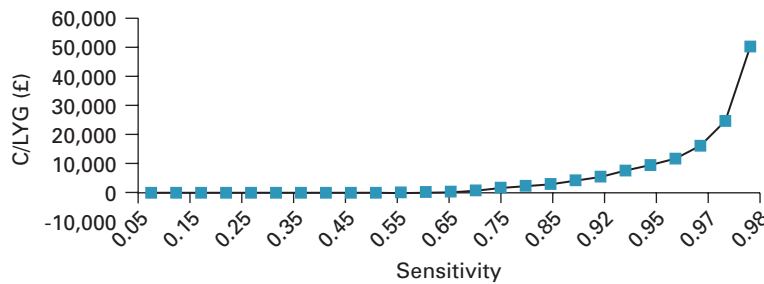


Figure 3: Sensitivity

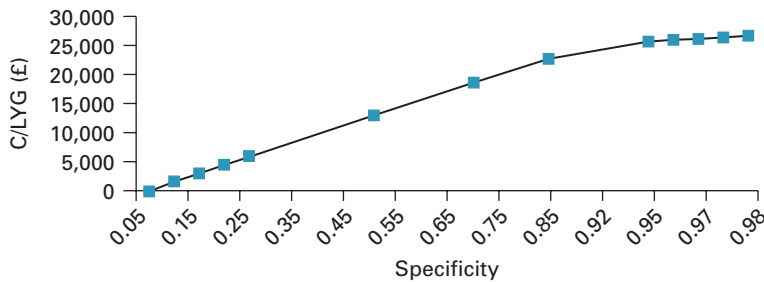


Figure 4: Specificity

▷ Other issues

The model assumes that the only value of echocardiography is in diagnosing heart failure and this is not realistic. Echocardiography can provide information on the underlying functional abnormality of the heart, and can therefore have a value in detecting other conditions that present with symptoms similar to heart failure. Echocardiography can also provide additional information that may affect the care pathway for heart failure.¹⁵ In addition, a more certain diagnosis can also provide an additional utility to the patient.

Where are the tests done and who interprets the results will both have implications for cost. This is particularly important in relation to echocardiography.* Similarly the process of accessing echocardiography may also affect the cost and the appropriateness of doing the echo alongside the other tests or not – specialist clinic, cardiology outpatients, directly to echo from PC.

*The structure of the model means that, in relation to BNP and ECG, this will not affect C/LYG, although the issues may still be important in terms of the appropriateness of doing the echo alongside the other tests.

Table G4 Statistics for BNP in the diagnosis of heart failure

Reference	Patient group	Sample	Condition	Cut off pmol/L (pg/ml)	Sens. (%)	Spec. (%)	- pred val (%)	+ pred val (%)
Cowie <i>et al</i> 1997 ²⁸	Referred by GPs for suspected HF Hillingdon Study	n = 122 D+ = 35	HF	≥ 22 (≥ 76)	97	84	98	70
Landray <i>et al</i> 2000 ³⁴¹	Referred by GPs for suspected HF	n = 126 D+ = 40	LVSD	(≥ 17.9)* (≥ 10) (≥ 76)	88 92 66	34 18 87	15	38
Campbell <i>et al</i> 2001 ³⁴²	Diabetic patients at one GP	n = 38 D+ = 4	LVSD		75	91	97	50
Smith <i>et al</i> 2000 ³⁴	Community based study of elderly patients from GP lists	n = 155	LVSD	≥ 18.7 ≥ 19.8 ≥ 26.7	92 83 75	65 70 80	99 98 98	18 19 24
McDonagh <i>et al</i> 1998 ³⁴³	Community based study from GP lists	n = 1653 D+ =	LVSD	≥ 5.2 (≥ 17.9)	all 76 with IHD 84	87 76	97.5 97.5	16 30
	Sub-sample aged > 55			≥ 5.2 (≥ 17.9)	all 89 with IHD 92	71 72	99.2 98.5	18 32
Luchner <i>et al</i> 2000 ³⁴⁴	Population based sample	n = 610	severe LV impairment	≥ 9.9 (≥ 34)			99.5	7

Table G5 Statistics for ECG in the diagnosis of heart failure							
Reference	Patient group	Sample	Condition	Abnormality	Sens. (%)	Spec. (%)	- pred val (%) + pred val (%)
Landray <i>et al</i> 2000 ³⁴¹	Referred by GPs for suspected HF	n = 126 D+ = 40	LVSD	Q waves, bundle branch block, T wave inversions, LV hypertrophy	41	87	24 60
Houghton <i>et al</i> 1997 ²⁶	Referred by GPs for suspected HF	n = 200 D+ = 165	LVSD	Any abnormality	89	46	
Davie <i>et al</i> 1996 ³⁰⁶	Patients sent by GP to open access echo service	n = 534 D+ = 96	LVSD	Normal or minor v. major abnormality	94	61	98† 35*
Rihal <i>et al</i> 1995 ³⁴⁵	Patients enrolled in CASS study who presented with chest pain	n = 14,507	depressed LVEF	Abnormality	90	34	92 29
Mosterd <i>et al</i> 1997 ³⁴⁶	Population sample (Rotterdam study)	n = 1980 D+ = 59	LVSD	Abnormality	54 (41-67)	79 (77-81)	98 (97-99) 7 (5-10)
Ditto	Sub-sample aged > 70	n = 522 D+ = 21			67 (43-85)	64 (60-69)	98 (96-99) 7 (4-12)
Ditto	Sub-sample at high risk of HF	n = 865 D+ = 39			64 (47-79)	73 (70-76)	98 (96-99) 10 (7-15)
Nielsen <i>et al</i> 2000 ³⁴⁷	Patients from pc with current or past signs or symptoms of heart disease	n = 126 D+ = 15	LVSD	QRS and/or ST-T changes	56	87	97 21
Campbell <i>et al</i> 2001 ³⁴²	Diabetic patients at one GP	n = 38 D+ = 4	LVSD		75	79	96 30

D+ = confirmed diagnosis (D+ / n = prevalence). *This is much lower than recommended for test cut-off. IHD = ischaemic heart disease.

† Sanderson recalculates the statistics for the Davie *et al* study on the basis of population prevalence of 1%. +ve pred val = 2.4%, -ve pred val = 99%.

Appendix H: Patient focus groups: patients' views and experiences*

Background

The National Collaborating Centre for Chronic Conditions worked with the Patient Involvement Unit for NICE and the two patient representatives on the Heart Failure GDG to supplement the existing research evidence with focus group work to obtain more detailed information on patient and carer experiences.

▷ The focus group

Eleven men and one woman (aged between their early forties and their late seventies) with diagnoses of heart failure, all at different stages of treatment were recruited through a cardiac support group in south-east England, affiliated to the British Heart Foundation. The focus group was held in a district general hospital in Essex and was facilitated by the Patient Involvement Unit in collaboration with two members of the NCC.

In advance of the group, participants were sent a brief information sheet that listed key topic areas to be addressed by the guideline (diagnosis; communication issues; drug treatment; non-pharmacological treatments; secondary prevention; depression and anxiety; psychological support; complementary therapies; the role of carers, relatives and support groups). Participants were asked to consider their own experiences of care in relation to the major topic areas as well as general issues about treatment and management that they would like to see reflected in the guideline. It was emphasised that issues of primary concern to participants would take priority in any discussion. In fact patients' priority issues closely reflected those of the developers, although not all guideline topic areas were identified as important.

Findings

▷ Diagnosis and prognosis

Many participants were very happy with the care and information they had received but were unanimous about the importance of receiving an appropriate diagnosis.

'It's incredibly important to receive a proper diagnosis. If you've got a car, you don't just accept that there's something wrong with it – it's the petrol gauge, it's the big end etc – why would you do it with your body?'

Most patients wanted a 'named' disease to help them cope better with their illness. Many had never been given a formal diagnosis and felt frustrated that terminology used meant that the health professionals were unable to identify specifically what was wrong with them. The term 'idiopathic dilated cardiomyopathy' was cited as a phrase used in place of a categorical diagnosis. There were also concerns that some health professionals would rather give any diagnosis than none, resulting in a patient's diagnosis constantly changing.

*Written by Victoria Thomas, Assistant Director of The Patient Involvement Unit for NICE.

‘If they keep changing your diagnosis gradually, you feel like you’ve been conned.’

Participants expressed concerns that specialists will not admit that they have made a wrong diagnosis – patients would prefer honesty about any mistakes made. Patients wanted detailed and speedy information about their prognosis but felt that health professionals were often unwilling to give prognostic information, leading to uncertainty about the future.

‘No-one said that I would not recover completely.’

▷ Communication with health professionals

Some patients expressed frustration at both the quality and extent of communication between consultants and patients, with particular concerns about the apparent insensitivity that some consultants displayed, in particular when speaking to patients in front of relatives.

‘The cardiologist said, “Well, there’s no more I can do for you. Why are you wasting my time?” This was bad enough for me, but for my wife who was there with me, she was absolutely devastated.’

The importance of good communication was stressed, as insensitive comments may have far-reaching implications for the psychological health of the patient. However, participants, including some of those who had expressed misgivings about professionals’ communication skills, could not praise the compassion and care of nursing and medical staff highly enough.

▷ Communication between health professionals

Many participants felt that the various health professionals involved in their care did little to communicate with one another appropriately. This was exemplified by one patient who had experienced delays in referral to specialist services owing to internal mail problems. Several patients talked about the frustration of having to re-explain their case history at each consultation, even with their notes sitting in front of the consultant.

‘I couldn’t fault them [the health professionals] it was just the fact that they couldn’t communicate with each other.’

▷ Role of GPs

Some people were very positive about the attentiveness shown by their GP. However, there was general dissatisfaction that the patients themselves felt more knowledgeable and expert about their treatments than their GPs.

‘I feel more in touch with the drugs and side-effects than my GP. I wish that wasn’t the case. I wish there was a process for keeping GPs more up to date.’

Participants felt that ‘out of hours’ or locum GPs were often more knowledgeable than the patient’s usual family doctor. Many people also expressed the wish that GPs were more willing to refer them on to specialists.

▷ Drug treatment

Many patients were happy with the drug treatment that they were receiving (particularly those also receiving cardiac rehabilitation). There were concerns about taking combinations of different pills without knowing how these might be interacting:

‘I’m never really sure whether I should be taking all of my pills or not.’

People felt that medication was not reviewed often enough – and that perhaps consultants were reluctant to reconsider once a potential solution had been identified.

▷ Cardiac rehabilitation

The focus group patients in cardiac rehabilitation programmes were extremely positive about the experience.

‘It makes you mentally and physically more able to cope.’

There was some cynicism however that only those guaranteed to show a beneficial result were referred to for rehabilitation, exasperation that so few places were available (also reflected by a recent paper*) and a perception that many people were rejected for not being fit enough.

‘Because of the limited places available, they tend to only take people who are almost guaranteed to show a good result.’

▷ Psychological support

Participants felt that psychological support is not available to those patients who are not on a rehabilitation programme, despite an acknowledgement by health professionals that the right attitude is crucial to making a good recovery. The patients related stories about people with similar case histories to themselves who, identifying themselves as ‘invalids’ had far worse prognoses.

‘He just accepted that he would be an invalid for life, that there was no point in trying, and he died within six months. He’d got it so fixed in his mind that he had a fatal disease.’

Some people stated that they would find having a counsellor useful, to help them correlate the diverse information that they receive.

▷ Follow-up and after-care

All participants expressed frustration at ‘falling out’ of the system following discharge from a consultant’s care with no easy route back in to the system if they needed help or support. They expressed a wish for clear management plans and for their carers to be actively involved in these plans.

‘Once you’ve been discharged, you don’t belong anywhere.’

*Tod AM, Lacey EA, McNeill F. ‘I’m still waiting...’: barriers to accessing cardiac rehabilitation services. *Journal of Advanced Nursing* 2002;40(4):421.

▷ Mutual support

All participants reported benefits from mutual support, eg at a support group – especially from other patients at the same stage of treatment, diagnosis or rehabilitation.

‘Now I’ve been discharged from my consultant, I don’t have anyone. If it weren’t for the support group, I’d have no-one.’

The need for mutual support from the outset of their condition was stated as an important therapeutic tool.

▷ Private healthcare

Many participants had opted for private health care as they were genuinely concerned for their health and lives whilst on NHS waiting lists. However, most chose to return to the NHS, describing the care as ‘far superior’.

‘I elected to go private at one stage but it just doesn’t compare to the NHS. I changed back.’

Conclusions

Participants made a number of proposals that they felt would significantly improve a patient’s experience of care, and would like to see reflected in the guideline:

- early and accurate diagnosis;
- willingness of health professionals to admit mistakes in diagnosis or prognosis if they occur, or if unable to come to a definitive conclusion;
- sensitive and open communication with patients and their families;
- communication between health professionals (eg at the primary/secondary care interface);
- GPs to be more informed about the therapies that their patients receive;
- patients’ drug regimens to be reviewed more frequently;
- the value and importance of cardiac rehabilitation, psychological support and mutual support;
- clear management plans with active carer involvement; and
- development of strategies to provide a consistent, easily accessible and high quality service to patients with heart failure.

The participants had positive things to say about the care they had received, and the health professionals who provided it but found certain aspects of care, particularly those over which they had little control, very frustrating. They welcomed the production of national guidelines identifying benefits in trying to standardise the quality and level of NHS care.

Appendix I: Registered stakeholders consulted via NICE process

Abbott Laboratories Limited (BASF/Knoll)
Age Concern England
Ambulance Service Association
Association of British Clinical Diabetologists
Association of British Health-Care Industries
Association of the British Pharmaceuticals Industry (ABPI)
AstraZeneca UK Ltd
Aventis Pasteur MSD
Aventis Pharma
Bayer plc
BioSyn Diagnostics UK Ltd
Bristol-Myers Squibb Pharmaceuticals Ltd
British Association for Accident and Emergency Medicine
British Association for Nursing in Cardiac Care
British Association for the Study of Community Dentistry (BASCD)
British Cardiac Patients Association
British Cardiac Society
British Dietetic Association
British Geriatrics Society
British Geriatrics Society's Special Interest Group in Diabetes
British Heart Foundation
British Hypertension Society
British In Vitro Diagnostics Association
British Medical Association
British National Formulary
British Pacing and Electrophysiology Group
British Psychological Society
British Society for Heart Failure
British Society of Echocardiography
Cardiomyopathy Association
Cardiothoracic Centre Liverpool NHS Trust
Chartered Society of Physiotherapy
Community District Nurses Association
Conwy and Denbighshire NHS Trust
Department of Health
Exeter Primary Care Trust
Faculty of Public Health Medicine
General Medical Council
Guidant Corporation
Havering Primary Care Trust
Heart UK
Long Term Medical Conditions Alliance
Medtronic Limited
Merck Sharp & Dohme
National Council for Hospice and Specialist Palliative Care Services
Newcastle upon Tyne NHS Trust
NHS Information Authority (PHSMI Programme)
NHS Quality Improvement Scotland
Norfolk and Norwich Healthcare NHS Trust
North Tees Primary Care Trust
Novartis Pharmaceuticals UK Ltd
Ortho Biotech
Patient Involvement Unit for NICE
Pfizer Limited
Pharmacia Limited
Primary Care Cardiovascular Society
Prodigy
Relatives and Residents Association
Roche Products Limited
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Nursing
Royal College of Pathologists
Royal College of Physicians of London
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society of Great Britain
Royal Society of Medicine
Royal United Hospitals Bath NHS Trust
Sanofi-Synthelabo
Scottish Intercollegiate Guidelines Network (SIGN)
Servier Laboratories Limited
Society of Cardiothoracic Surgeons
Takeda UK Ltd
UK Pain Society
UK Thalassaemia Society
Welsh Assembly Government (formerly National Assembly for Wales)
Wolverhampton City Primary Care Trust

Appendix J: Evidence tables

These are available at www.rcplondon.ac.uk/pubs/books/chf/

The evidence tables provide full details of the studies identified and critically appraised as part of the formal systematic review. They are organised according to guideline section, clinical question and study design.

Appendix K: Inclusion and exclusion of literature

These are available at www.rcplondon.ac.uk/pubs/books/chf/

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