DOCTOR OF PHILOSOPHY

How do older heart failure patients manage their medication? A multi-methods study

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A multi-methods study

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List of Abbreviations

ACC	American College of Cardiology
ACEi:	Angiotensin-converting-enzyme inhibitor
AHA	American Heart Association
ANP	Advanced Nurse Practitioner
ARB	Angiotensin receptor blocker
BMQ	Beliefs about Medication Questionnaire
BNP	B-type Natriuretic Peptide
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CASP	Critical Appraisal Skills Programme
CCI	Charlson Comorbidity Index
CHD	Coronary heart disease
CHF	Congestive Heart Failure
CHI	Community Health Index
CHFQ	Chronic Heart Failure Questionnaire
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CRD	Centre for Reviews and Dissemination
CRF	Case Report Form
CSES	Cardiac Self-Efficacy Scale
CSM	Common Sense Model
CSQ	Consultation Satisfaction Scale

DUP	Drug use profiles
ECG	Electrocardiogram
EF	Ejection fraction
ESC	European Society of Cardiology
EoSRES	East of Scotland Research Ethics Service
GDS	Geriatric Depression Scale
GCP	Good Clinical Practice
GP	General Practitioner
HADS	Hospital Anxiety & Depression Scale
HBM	Health Belief Model
HF	Heart Failure
HFPEF	Heart Failure with preserved ejection fraction
HFREF	Heart Failure with reduced ejection fraction
HFSN	Heart Failure Specialist Nurse
HRQoL	Health Related Quality of Life
ICF	Informed Consent Form
IPQ-R	Revised Illness Perception Questionnaire
IQR	Inter quartile range
JVP	Jugular venous pressure
KCCQ	Kansas City Cardiomyopathy questionnaire
LV	Left ventricular
LVH	Left ventricular hypertrophy
LVEF	Left ventricular ejection fraction

LVSD	Left Ventricular Systolic Dysfunction
MCI	Mild cognitive impairment
MCS	Mechanical Circulatory Support
MDT	Multidisciplinary Team
MEMS	Medication event monitoring system
MI	Myocardial Infarction
MISS-21	Medical Interview Satisfaction Scale
MLHFQ	Minnesota Living Heart Failure Questionnaire
MMAS	Morisky Medication Adherence Scale
MMSE	Mini-mental Status Examination
MoCA	Montreal Cognitive Assessment
MRC	Medical Research Council
NHANES	National Health and Nutrition Examination Survey
NHS	National Health Service
NHYA	New York Heart Association
NICE	National Institute of Clinical Excellence
NYHA	New York Health Association
PI	Principle investigator
PIS	Patient information sheet
QoL	Quality of Life
REC	Research Ethics Committee
RCT	Randomised controlled trial
SCT	Social Cognitive Theory

SD	Standard deviation
SIBHFT	Survey of illness beliefs in heart failure tool
SIMD	Scottish Index of Multiple Deprivation
SIGN	Scottish Intercollegiate Guidelines Network
SPCRN	Scottish Primary Care Research Network
SPPB	Short Physical Performance Battery
SPPIR	Scottish Practices and Professionals Involved in Research
SPSS	Statistical package for social sciences
S-TOFHLA	Short-Form Test of Functional Health Literacy
TICR	Tayside Institute Cardiovascular Research
TPB	Theory of Planned Behaviour
TRA	Theory of Reasoned Action
WHO	World Health Organisation

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Declaration

I hereby declare that I am the author of this thesis, that all references cited have been consulted by me and that I have carried out the work described in this thesis. The work described within this thesis has not been previously accepted for a higher degree and I have defined the nature of my contribution to the work within the project described in thesis.

The work contained within this thesis was carried out carried out during my appointment as a Research Fellow in the Section of Ageing and Health, University of Dundee between January 2014 and December 2017.

Signed Dated 23-01-2020.

Summary

Heart Failure (HF), a condition prevalent in older adults goes hand in hand with multiple concurrent diagnoses, polypharmacy and complex drug regimens. Consequently patients with HF need to develop effective strategies to care for themselves whilst managing the burden of multi-morbidities. Currently little is known about which factors influence adherence to medication in this population.

To understand which factors consistently predict medication adherence in older people with HF a multi-methods study was undertaken. A systematic review of 21 studies reporting on interventions previously evaluated identified 8 which reported significant improvement in medication adherence. Interventions utilised a variety of approaches however heterogeneity in both intervention techniques and measurement methodology resulted in an inability to establish a clear effective approach.

A rapid review of literature reporting on the perceptions and experiences of people with HF in relation to medicines proved equally inconclusive. Ten qualitative studies were reviewed highlighting non-adherent behaviour as multi-factorial and complex in nature. Individual beliefs, level of knowledge; environmental factors and the role played by significant others emerged as having the potential to influence medication adherence in both a positive and negative way.

Utilising the information gleaned from the literature reviews a qualitative study was undertaken to explore beliefs around HF and its treatment. Using a purposive sampling strategy eight older HF patients and four nominated carers were recruited from a number of sites to participate in one to one structured interviews. Gender and recent admission to hospital were selected as key variables with carers directly nominated by the patients. Knowledge around both the condition and medication and the association between treatment and symptom control was found to be poor. While patients expressed a belief in the beneficial effects of medications, a wish to remain independent and trust in healthcare professionals were the main reasons given for adherence.

Finally, a prospective observational study of 60 community dwelling HF patients aged ≥ 70years was undertaken. The primary outcome of adherence to medication was assessed using both direct and indirect methods. The secondary outcome of determinants of adherence were selected following analysis of the qualitative data and literature reviews. Adherence ranged from 74% to 100% depending on the method used however agreement between methods was found to be poor. No single determinant was found to consistently predict adherence across the different measures.

Publication and Presentations

Publications

Fulton RL, Kroll T, McMurdo MET, Molloy GJ, Witham MD. Interventions to improve medication adherence in heart failure – A systematic review. J Preventive Cardiology 2017; 6(3):1048-1056.

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Poster Presentations

RL Fulton, T Kroll, MET McMurdo, GJ Molloy, MD Witham. Interventions to enhance medication adherence in older heart failure patients – a systematic review.

Poster presentation at both European Society Cardiology Heart Failure 2017 Congress, Paris, May 2017 & British Geriatrics Society scientific conference, Liverpool, May 2016.

Oral Presentation

RL Fulton. Improving Adherence to Medication in older Heart Failure patients – a mixed methods study.

Oral Presentation at University of Dundee CMDN Students Symposium May 2016.

Chapter 1: Introduction and overview

1.1. Overview of chapter

Heart failure (HF) has been defined as a *"clinical syndrome of symptoms which may be as a result of structural or functional cardiac or non-cardiac disorder which impairs the ability of the heart to respond to physiological demands for increased cardiac output"* [(1)] . The condition currently affects approximately 500,000 people in the UK [(2)]; both incidence and prevalence increase steeply with age [(3)]. HF is a major cause of disability, hospitalisation and death, particularly amongst older people. It is the most common hospital discharge diagnosis for patients over 65 years of age and is associated with symptoms (particularly fatigue and breathlessness), impaired physical function and poor quality of life [(4)]. Given that patients with HF are typically older adults with multiple concurrent diagnoses, polypharmacy and complex drug regimens are common. Patients with HF consequently need to develop effective strategies to care for themselves whilst managing the burden of multi-morbidities that frequently result in polypharmacy. Non-adherence in patients with HF may lead to worsening symptoms and eventually to hospitalization [(5)].

Self-care for patients with HF is complex and often burdensome. For patients with HF it involves having to develop a range of skills across several domains including adherence to complex drug regimes, changing daily activities, ongoing monitoring of symptoms as well as modifications to dietary and fluid intake [(6)]. According to European Society of Cardiology (ESC) guidelines multiple medications have been identified as being beneficial in HF and should be routinely prescribed [(7)]. Improving medication adherence ("the extent to which patients take medications as prescribed by their health care providers") [(8)] has been identified as having the potential to impact on the health of the heart failure population in a greater way than improvement in any specific medical treatment [(9)].

Enabling patients to adhere effectively to medications has been the subject of many studies in different long-term conditions such as hypertension and diabetes [(10, 11)]. A systematic review carried out by Cramer [(12)] identified 20 published studies looking at

adherence in diabetic patients between 1966 and 2003 while a Cochrane review by Fahey et al [13] identified 38 studies conducted between 1975 and 2000 looking at interventions to increase adherence to blood pressure lowering medication in adults with essential hypertension. Little research however has been conducted in the context of HF [14].

This chapter will describe the significance of the topic while defining the key terms of 'heart failure' and 'medication adherence' used in this thesis. The background to the study as well as my previous experience as a nurse and researcher will be reflected on. The setting for the research will be discussed as will an overview of the research design including the research aims. Finally, the chapter will conclude with an outline of the content of subsequent chapters.

1.2. Significance of the topic and context of the research

1.2.1. Heart Failure

The term "chronic heart failure" is defined in this thesis as:

"A complex clinical syndrome that can result from any structural or functional cardiac or non-cardiac disorder that impairs the ability of the heart to respond to physiological demands for increased cardiac output" [1]

1.2.1.1. The burden of heart failure

Chronic heart failure (CHF) has been described as an epidemic, particularly among the older population [15]. Data from the Framingham heart study, a large cohort study from Massachusetts in the United States suggests that the incidence of heart failure doubles with every decade [16]pp17. HF is diagnosed in 1 to 2% of the population in developed countries [17]. Currently around 60,000 people develop heart failure in the UK every year with prevalence expected to rise [18]. In the UK the prevalence of HF is one in 35 people aged 65-74 years and increases to one in 15 of those aged 75-85 years. For those aged 85 years and over prevalence is reported to be one in 7 [3]. In women the prevalence of HF is lower than in men at all ages. However, given the increase in incidence of HF with age, coupled with the proportionally larger number of elderly women in developed countries, the total number of men and women living with HF is similar [19]. Overall,

survival rates among patients with HF do not appear to be improving [20] and it is predicted that the number of people with HF will continue to rise [21]. While ongoing research in the development of cardiac devices, stem cell therapy and genetic treatment has and will assist patients with HF to live longer, the emergence of new medications has played a large part in the prolonging of life in those diagnosed with the condition [22]. It is also important to highlight that most previous epidemiological studies reporting on the incidence of HF have included only patients displaying signs or symptoms and did not consist of the screening of an entire population where asymptomatic patients would be included.

Despite recent improvements, prognosis for HF remains poor. The Hillingdon Heart Study found that of patients diagnosed with HF at the point of hospitalisation 40% had died within a year of that diagnosis while the Framingham Study and National Health and Nutrition Examination Survey (NHANES) survey reported high mortality and a prognosis of < 10 years [23]. Although HF is considered a chronic or long-term condition, patients suffering from the condition can experience frequent decompensation which may lead to frequent hospital admissions. A three-year study of 570,000 hospitalisations found that patients hospitalised for HF were at high risk for all-cause re-hospitalisation, with the one month readmission rate estimated at 25% [24].

Heart failure is an expensive condition currently accounting for 1-2% of all healthcare spending [25] and around 5% of all emergency hospital admissions in adults across Europe [26]. This significant burden on the National Health Service (NHS) budget is set to increase over the next few decades with hospital admissions projected to rise by over 50%. The British Society for Heart Failure audit, carried out for the year 2014-2015, reported on nearly 57,000 hospital admissions for acute HF within England and Wales [27]. Consequently this high number of hospital admissions has resulted in an estimated one million inpatient bed days (2% of the total) across the entire NHS [28]. As well as heath care costs HF also places an additional burden on other agencies such as social services and the benefits system [25] and of course on people with HF, their families and caregivers.

Despite the prevalence of the condition, public awareness of HF is poor, with the condition commonly seen as a natural consequence of ageing. Perception of the illness was investigated by the Study group on HF Awareness and Perception in Europe (SHAPE) [29]. Researchers reported a high proportion of respondents believed that HF was a natural cause of ageing with one third wrongly believing that modern medication could not prevent its development [17, 30-32].

Non-adherence to prescribed medication has been identified as a significant health challenge [33] and public health problem [34] with the World Health Organisation (WHO) identifying medication non-adherence as one of the major causes of preventable morbidity mortality and health care costs [35]. Failure to take medication as it has been prescribed may result not only the attainment of suboptimal benefits for the patient themselves but may result in increased health costs for the population as a whole.

Clinical guidelines have emphasised the need for HF patients to have a firm understanding of their condition and suggest that in order to avoid decompensation and maintain quality of life (QoL) patients should receive and make proper use of appropriate treatments, adopt lifestyle changes and receive ongoing advice from clinicians regarding medication adherence [36]. In more general terms the management of long-term conditions such as HF poses a substantial challenge for health care services, particularly acute services. In order to reduce this burden those with long-term conditions require ongoing support in order to develop skills in self-management and be fully involved in all aspects of decision making regarding their health.

1.2.2. Medication Adherence

Non-adherence to medications has been documented to occur in >60% of cardiovascular patients [37]. Improving adherence to drug therapy therefore may offer an effective way to decrease costs. Importantly improvement in adherence has been shown to be possible. A recent randomised controlled trial (RCT) of sixty-two stroke survivors with an age range of 51-85 years concluded that implementation of a simple brief intervention, especially one which identified and addressed each individuals' underlying beliefs, had the ability to

improve medication adherence not just among stroke survivors but within groups diagnosed with other long-term conditions [38].

On a theoretical level, the nature and causes of non-adherent behaviour are complex and poorly understood. The common-sense model (CSM) of illness cognitions and behavior by Leventhal et al [39] describes the factors involved in the processing of information by an individual regarding their disease or illness. The model identifies how this information is combined to provide a lay view of the illness and how this view guides coping behaviours and outcomes. Given that patients not only hold personal thoughts around their illness but also about the treatment offered Horne has subsequently proposed that the CSM may also provide a framework for understanding intentional adherence [40]. Self-efficacy, the belief that one has the power to produce an effect by completing a given task or activity related to that competency, is the most important prerequisite for behaviour change thus any intervention aimed at improving medication adherence must consider factors that directly influence self-efficacy mainly behaviours, environment, and personal cognitive factors [41].

1.3. Origins of the study and personal perspective

My clinical nursing career has spanned nearly 30 years all spent working within medicine for the elderly services. Throughout that time, it became apparent to me that medication adherence in this age group was a significant problem, was difficult to address and that non-adherence frequently led to unwanted complications including hospital admission. My early journey into research brought me into contact with older HF patients many of whom, despite all having had a clinical diagnosis, had no idea they had HF and what that meant for them as individuals. While being able to describe the symptoms they experienced most were unable to relate these back to the underlying cause and in many cases explained these often unpleasant symptoms as simply a sign of advancing age. I realised that medical and nursing staff often assume that patients have had a previous explanation regarding any diagnosis and must therefore have developed an understanding of their medical condition. This was clearly not the case with these patients

with HF and it is therefore unsurprising that patients often don't identify adherence to their medication with optimal management of their symptoms.

In recent years members of the team of researchers within Ageing and Health at the University of Dundee with whom I worked completed a systematic review of the interventions available to enhance adherence to medications in patients with HF [42]. The authors concluded that there was limited, high quality evidence evaluating the effectiveness of specific adherence enhancing interventions and recommended further research in order to identify the optimum strategies for implementation into clinical practice [42]. Oosterom-Calo et al reached similar conclusions with their systematic review in this area [43].

Analysis of data from a randomised controlled trial of exercise training in older HF patients was also conducted by the Dundee Ageing and Health team. Fifty-eight older outpatients with CHF had serum ACE levels measured and participants interviewed to assess beliefs about their illness. Whilst overall adherence to ACEI was 72%, participants who believed their illness to be a more chronic condition were more likely to be non-adherent to their medication and that a direct association could be made between medication adherence and beliefs about HF [44].

It is clear therefore that gaps in existing research knowledge exist. There is an absence of data regarding which modifiable factors are associated with poor adherence in HF and a need to develop and test a theory-based intervention within this population. It was a desire to address these issues, coupled with my experience of working with older people (a group regularly under-represented in research studies) that led to the development of this PhD.

1.4. Aims and objectives of the study

The original aims of the research that underpins this PhD thesis were:

1) To understand current beliefs around heart failure and medication in patients and spouses / informal caregivers.

2) To identify which factors around heart failure and medication consistently predict medication adherence, and which can be modified.
3) To develop a brief deliverable psychological / psychosocial intervention to enhance medication adherence in heart failure patients for evaluation in a future randomised trial.

1.5. Research setting and overview of research design

The work for this PhD was conducted within NHS Tayside, an area with a combined population of over 400,000. Older patients with HF were recruited from across Dundee, Angus and Perthshire. Community based patients with HF were chosen rather than those in acute services as they were living with HF on a day to day basis and importantly were responsible for managing their own daily medication routine. Ethically it was also deemed less appropriate to ask patients about their understanding of their condition and medication when they were acutely unwell and in a potentially vulnerable position.

As part of the work, a systematic review following Cochrane Review guidelines was conducted. Literature of key topics mainly: the nature and management of HF; factors believed to influence medication adherence particularly in HF and lay beliefs of illness, treatment and self-care in HF were reviewed.

When considering the philosophical underpinning for any research study Creswell writes about the need to focus one's attention on the research question while utilising heterogeneous approaches in order to develop knowledge about the problem [45]. When learning about the social world the traditional view is that the paradigms of qualitative and quantitative research are underpinned by fundamentally different assumptions about ontology and epistemology and are thus incompatible. However, given the complexity of human phenomena multi-methods or mixed-methods research designs have increasingly been viewed as offering a third paradigm for research [46, 47].

Despite having specific differences the terms mixed-methods and multi-methods research are often found to be used interchangeably [48]. Mixed-methods research has been defined as "research in which the investigator collects and analyses data, integrates

the findings and draws inferences using both qualitative and quantitative approaches or methods in a single study" [49]. In mixed-methods research therefore it is suggested that by combining both quantitative and qualitative research methods researchers are provided with not only a richness from the qualitative enquiry but a scientific base for clinical practice.

Alternatively, while a multi-method research design involves the undertaking of two or more research methods both qualitative and quantitative research approaches need not be involved [48]. While driven by one overall research aim each study is planned and conducted independently using its own specific research question. Unlike mixed-methods were the results from each empirical study are integrated into the other assimilation in multi-method designs need not occur until conclusions are being made [47]. Given that the work detailed within this thesis involved the undertaking of several different research methodologies with results triangulated to answer the overall research question a multi-method research approach has been adopted.

It is suggested that researchers seek to locate their research in a particular theoretical lens thus defining their epistemological, ontological and methodological stance [50]. In multi-methods research two philosophical positions direct the discussion. Qualitative researchers typically locate themselves within an interpretivist tradition while quantitative research is linked with positivism. While traditionally these paradigms have been deemed incompatible because of their differing ontological and epistemological stances it has been proposed that researchers may utilise an approach which seeks to bridge the gap between these opposing positions [51].

The multi-methods paradigm is based on the belief that both scientific knowledge and common sense are relevant and neither are considered privileged [52]. Rather than simply utilising one approach this paradigm is based around the belief that a better understanding of research problems can be achieved by the integration of both quantitative and qualitative data [53]. In a similar manner, the philosophy of pragmatism points the researcher's attention to operational rather than metaphysical concerns

advocating differing views and assumptions as well as use of multiple research methods [54].

It is clear therefore that both HF, with its complicating presentation of symptoms and comorbid conditions and the topic of non-adherence to medications lend themselves to this method of research in order to explain both the qualitative and quantitative components. Additionally, when considering an intervention to improve adherence within the HF population, a multi-method methodology is a good precursor for the development and evaluation of a complex intervention as advocated by the Medical Research Council (MRC) framework [55].

Using a research approach which encompasses of more than one method is not however without its weakness. A critical review of mixed-methods research in nursing carried out by Bressan et al reported inconsistencies in application and reporting across studies. Researchers attempts to articulate how the two distinct research methods related to one another often resulted in one or both phases having limitations with methods being applied in a less rigorous way [56]. Another criticism or weakness of a multi-methods approach is that in order to achieve a positive study outcome the researcher requires to have a basic knowledge of both quantitative and qualitative methods and importantly have an understanding of how to combine these methods appropriately. While conducting this study I was fortunate to have a supervisory team which consisted of individuals with experience of both research paradigms and how they can successfully interrelate.

1.5.1. Overall study research questions

Given that the aims of this study required research data to be generated from different perspectives a multi-methods approach was adopted in order to answer the following research questions:

1) What beliefs and attitudes do older heart failure patients and their informal caregivers hold about their disease and its treatment?
2) Which beliefs around heart failure and medication consistently predict adherence to medication?

3) Which modifiable factors predict non-adherence to medication in older people with heart failure?

1.5.2. Current study methodology

The study followed a sequential exploratory design as described by Creswell (see Figure 1.1) [45]. Using this approach, an initial phase of in-depth qualitative research sought to identify the beliefs held around heart failure and its treatment in a population of older people. Following directly on from this exploratory phase quantitative data collection was undertaken to facilitate an evaluation of the beliefs held around heart failure and medication which consistently predict medication adherence. Using this research approach enabled the results of the qualitative findings to be analysed during an interpretation phase which assisted in the selection of the outcome measurement tools for the quantitative observational study.

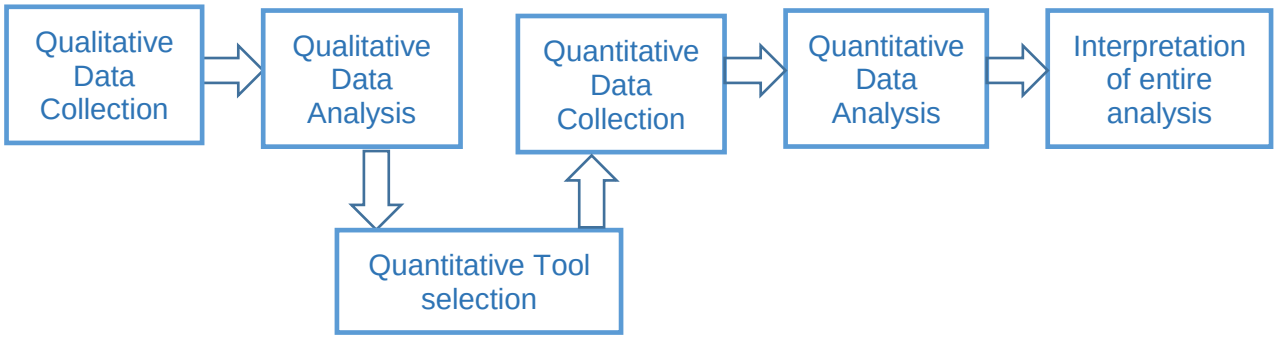

Figure 1.1 Sequential exploratory study design adapted from Creswell [45]

Undertaking a pragmatic approach to science-based healthcare involves using the method which appears best suited to the research problem while avoiding becoming caught up in philosophical debates. As a pragmatist I believe that every method has its limitations and that the different approaches can be complementary. The sequential research approach as described by Creswell [45] appeared to offer a natural methodological framework for this research. The sequential nature of the methodology, which enables a first qualitative phase to inform a second quantitative phase while

offering the flexibility to conduct both studies independently appeared well suited to both the exploratory and descriptive aspect of work contained within this PhD.

The empirical studies reported within this thesis have been conducted in two sequential phases. The first phase has explored the personal experiences relating to the condition of HF and its treatment of older HF patients and their informal carers using semi-structured interviews. Emergent themes from these interviews were examined and used to aid the selection of validated questionnaires and tools, which were then used to gather quantitative data in the second phase. The results of both studies have been combined with an updated systematic review of interventions to improve medication adherence in HF and a rapid review of qualitative studies identifying facilitators and barriers medication adherence in HF which were both completed during the period of study.

1.6. Structure of the Thesis

This thesis is structured into eight chapters according to the main arguments and processes of the research.

Chapter two reviews the literature relevant to heart failure, medication adherence and illness perception thus providing the context for the study.

Chapter three describes the updated systematic review. It defines the methods and provides the results.

Chapter four reports on the rapid review of qualitative literature. The chapter describes the methods used and reports on barriers and facilitators to medication adherence as perceived by HF patients themselves.

Chapter five describes the qualitative study; an overview of the methods is provided along with the results of the qualitative interviews and discussion of how the information from the semi-structured interviews determined the tools for the observational study.

Chapter six reports on the study design, methodology and results from the observational study.

Chapter seven integrates the findings of the literature reviews; the qualitative and quantitative phases in an overall discussion according to the aims of the study. It summarises the conclusions of this thesis, reflecting on its strengths and limitations.

Chapter eight identifies directions for future research including a description of the potential development of the (psychological / psychosocial) intervention.

Chapter nine concludes the thesis with a short personal reflection on the author's doctoral journey.

The following chapter details the key concepts of the thesis. Literature pertaining to the nature and management of HF, adherence to medication and the role played by illness perception and personal beliefs is reviewed and discussed.

Chapter 2: Background

This chapter begins by defining heart failure, its importance in epidemiological terms, and its management with a focus on the older population. The topic of adherence to medication will be discussed along with potential factors influencing adherent behaviour. This chapter aims to justify the selection of heart failure and adherence as an important topic while highlighting the importance of illness perception and treatment beliefs on adherent behaviour.

2.1. Heart Failure

2.1.1. Defining heart failure

The Scottish Intercollegiate Guidelines Network (SIGN) guides for the management of chronic heart failure describe the condition as: "*A complex clinical syndrome that can result from any structural or functional cardiac or non-cardiac disorder that impairs the ability of the heart to respond to physiological demands for increased cardiac output"* [(1)]. This definition has been adopted in this thesis as it is current, clear and broad enough to include different forms of the condition.

The main terminology used to describe HF is based on the measurement of left ventricular ejection fraction (LVEF). The grading of LVEF has been used to predict the severity of HF ranging from normal to severe left ventricular systolic dysfunction (LVSD). It is important to stress however that patients assessed as having a poor ejection fraction (EF) may be asymptomatic while patients with good EF may present with severe symptoms.

Research into HF initially concentrated on patients with LVSD thus studies assessing therapeutic interventions have focused predominantly on this group of patients. Over the last 20 years however it has become evident that almost half the patients with HF syndrome do not have LVSD. The term HF with preserved ejection fraction (HFpEF) has been widely adopted to describe patients with with the clinical syndrome of HF and no evidence of LVSD.

2.1.1.1. Patient knowledge

Heart failure is the preferred term in the UK however other terms such as "cardiac failure", "congestive cardiac failure" and "left ventricular failure" are common within the literature and are commonly used by clinicians. Patients are often uncertain about the term "heart failure" and what it means for them. Previous studies have estimated that around 20% of patients with moderate to severe HF reportedly may not know they have the diagnosis [57] while in the study conducted by Artinian et al. low levels of knowledge were reported in the areas of medications, self-care, and the ability to recognize the correct definition of HF [58]. Heart Failure is frequently incorrectly referred to as a disease, while the use of the word "failure" has a socially constructed meaning that is negative - potentially causing unnecessary anxiety for patients and carers fearing that the heart, an organ necessary for life, may suddenly cease to work [16].

2.1.2. Causes and symptoms of heart failure

For optimal management of HF identifying potential exacerbating factors or other co-morbid conditions as well establishing the underlying cause of the condition is essential [59]. HF may develop as a result of a myocardial, valvular, pericardial or endocardial disorder or indeed a combination of these. In younger patients HF is frequently a result of coronary artery disease (CAD) or a cardiomyopathy of uncertain aetiology, often presumed to be viral, with the most common cause of HF among patients under 75 years in the UK being myocardial dysfunction secondary to CAD [60].

Older HF patients differ from their younger counterparts in terms of several biological characteristics [61] including the relatively large proportion of HF patients with HFpEF. Amongst older patients systolic hypertension and consequent left ventricular hypertrophy (LVF) may be more important causes of HF and may be more likely to manifest predominantly as abnormalities of diastolic function. For these older patients the original cause of HF can often be difficult to determine as patients may have lived with symptoms as well as other co-morbid disease for several years before seeking medical attention. Given that the syndrome is characterised by features such as breathlessness on exertion,

fatigue and signs of fluid retention and many of these features can be non-specific, a diagnosis in the initial stages of the condition often proves difficult. In addition to age the aetiology of HF may also depend on ethnic origin, socioeconomic status and geographic location.

The most common type of HF is LVSD with around 50% of patients having reduced left ventricular contraction during systole [59]. It has been estimated that within the UK coronary artery disease accounts for around two thirds of HF cases with many patients having experienced a myocardial infarction (MI). A history of non-ischemic cardiomyopathy caused by either hypertension, atrial fibrillation, thyroid disease, alcohol excess or valvular disease accounts for the majority of the remainder [62].

2.1.2.1. Risk factors

Risk factors for HF include lifestyle factors such as obesity, smoking and excessive alcohol [63-65] and comorbidities such as hypertension atrial fibrillation, diabetes, renal dysfunction and dyslipidaemia [64, 66-68]. HF risk increases with age and male gender. Low physical activity levels and poorer socioeconomic status are also found to be associated with increased risk. Hypertension and CAD are by far the most common risk factors conferring a doubling of risk [69]. Figures for different ethnic groups are limited, however one population-based study carried out by Bahrami et al. in the USA reportedly found African Americans to be at significantly higher risk for incident HF compared with other ethnic groups. However the results of this study did also specify that higher rates of hypertension and diabetes mellitus associated with poverty and other environmental factors largely explained the reported ethnic differences [70].

Key to the diagnosis and on-going management of the condition is recognition of signs and symptoms that are specific for HF. When patients present with pronounced symptoms diagnosis of the condition may be straightforward. It is acknowledged however that many of the symptoms which have prompted the patient to seek medical attention are non-specific and may not therefore help distinguish between HF and other possible medical problems. Importantly there is no single symptom, sign or combination of both

that can be classed as specific for the diagnosis. While previous studies have identified the most prevalent symptoms as shortness of breath and ankle oedema [71], the clinical diagnosis of HF contains a large amount of subjectivity from both the patient's and the clinician's perspective [72]. Distinguishing the syndrome from other causes of exercise intolerance and breathlessness may therefore be more difficult in patients in the early stage of the syndrome and when symptoms are mild [73].

The often-insidious onset of HF means that patients often don't present until the condition is well advanced. Given that symptoms may have been present for several years, acceptance of a diagnosis of HF may be difficult for patients resulting in difficulty managing the condition and associated symptoms successfully.

2.1.3. Epidemiology of heart failure

2.1.3.1. Incidence and Prevalence

As previously stated, HF has been identified as an epidemic and significant public health issue particularly among those aged 65 years and over [74] with the average age at first diagnosis reported to be 77years [75]. Worldwide, around 26 million are estimated to be living with HF [76]. HF incidence and prevalence are highest amongst older people [67]. with both incidence and prevelance increasing with age, reportedly doubling with every decade [16]pp17.

In the Framingham study, data from the USA, the incidence of HF was estimated to range from 2 per 1000 per annum in individuals aged between 45 and 54, increasing to 40 per 1000 per annum in men aged between 85 and 94 years [77]. Within the UK population Cowie et al conducted a study across 31 GP practices in London over a 20-month period reporting the incidence of HF to be 1·3 cases per 1000 population per year for those aged 25 years or over with incidence rising with age to 11.6 in the population of 85 years and over, again with incidence higher in the male population [76]. More recently, in a population-based cohort study which included primary and secondary electronic health records of 4 million patients aged ≥16 years, HF incidence was reported as 332 per 100,000 person years which demonstrated a decrease of 7% between 2002 and 2014.

However, it is worth noting that while incidence was decreased, the study reported around a 23% increase in people living with HF rising from 750,127 in 2002 to 920,616 in 2014 [78].

In relation to prevalence of HF recent estimates report prevalence of HF in Scotland to be 8.72% for men and 5.97% for women over 75 years [2]. While both incidence and prevalence are lower in woman than in men at all ages the steep increase in incidence that occurs with age, along with the proportionally larger number or women in the population, results in similar numbers of men and women living with condition [19].

2.1.3.2. Comorbidity and polypharmacy

Co-morbidity is common in older patients and has grown increasingly prevalent over recent decades. Wong et al analysed data on 1,395 patients with self-reported HF from National Health and Nutrition Examination Survey (NHANES) across three different time periods. Overall while patients demonstrated overall improvements in blood pressure and cholesterol control there was a significant change in complexity in their presentation with increase in the percentage of CHF patients who had five or more chronic conditions (42% in 1988-1994 to 58% in 2003-2008). Additionally the number of medications prescribed to each individual also increased significantly from 4.1 to 6.4 prescriptions during the same period [79].

A cross sectional study carried out by Barnett et al across 314 medical practices in Scotland identified multi-morbidity (defined as the presence of two or more conditions) in 97% of all patients diagnosed with HF while 74% had 3 or more diagnosed conditions [80].

2.1.3.3. Prognosis

Despite recent advancements in the pharmacological treatments available for HF prognosis for patients with the condition is poor. Following initial diagnosis patients can anticipate an average life expectancy of around 3 years, [67] less than is expected for many other conditions and similar to some types of cancer [81]. A population study carried out in Scotland analysing data on 1.75 million patients [82] reported the 5-year survival from HF to be around 56% compared to around 68% for prostate cancer and 57% for

bladder cancer in men. In women, 5-year survival for breast cancer was reported as 78% however in HF the rate was only 50%. More recently, Mehta et al analysed data from two London based population-based studies and reported mortality to be around 14% within the first 6 months following a HF diagnosis [19].

A reduction in mortality from coronary heart disease (CHD) of around 60% has been achieved in Scotland over the last decade [83]. However, the prevalence of HF continues to rise with a 25% five-year survival rates for both sexes [82]. A Scotland-wide retrospective cohort study undertaken by MacIntyre et al using the Scottish National Health Service Linked Patient Database reported prognosis for HF patients as being worse than had been previously described in RCT's with the median survival being only 1.5 years [84]. In this cohort around 50% of all patients admitted to hospital had died within one year.

2.1.4. Healthcare burden of heart failure

Heart failure is a major and increasing public health problem causing significant costs in both economic and personal terms. Current figures estimate that around one million inpatient bed days in the UK are currently attributable to the condition. On examination these figures relate to 2% of the total NHS inpatient bed days and 5% of all emergency medical admissions to hospital [85]. Worryingly, due largely to population ageing, hospital admissions due to HF are projected to rise by around 50% over the next 25 years; [86, 87] this despite a continuing fall at around 1.5% per year of the age adjusted hospitalisation rate [88]. It is estimated therefore that around 2% of the total NHS budget is attributable to HF with the costs of hospitalisation estimated to make up 70% of this total [89].

Related co-morbidity accounts for a considerable part of prolonged hospital admissions of people with a diagnosis of HF [90]. The NHS HF survey, a survey of acute HF admissions carried out in England, Wales and Northern Ireland, found that while 99% of patients with the condition were discharged within 10 days of admission an average length of stay of around 7 or 8 days could be expected [91]. Readmissions are also common. While the Euro Heart Failure survey programme found that within 12 weeks of

hospital discharge around 24% of patients had been readmitted [28] within six months of discharge Butler estimates readmission rates to be nearer 50% [18].

In older people readmission may not always be as a result of HF itself but may be due to a disproportionate focus being placed on the exacerbation of the condition. Following hospital discharge HF patients may experience what Krumholz describes as the " 'post-hospital syndrome' - an acquired transient period of vulnerability post discharge". It may be that these patients not only have to cope with the ongoing consequences of the condition itself but must also try and manage the allostatic and physiological stress hospitalised patients typically experience [92]. Conducting an analysis of Medicare claims Jencks et al reported that only 37% of the readmissions for recently those previously admitted to hospital with HF could be directly attributed to their HF diagnosis. More frequently causes of readmission commonly included pneumonia, renal failure or nutrition related issues [93].

2.1.5. Illness trajectory in Heart Failure

Despite HF being a chronic or long-term condition, those diagnosed with the condition may experience recurrent episodes of decompensation which may result in hospital admission [94] with early hospitalisation a particular in risk for older patients [95]. Figure 2.1 presents an illness trajectory for a chronic condition such as HF. After each acute episode it is common for individuals to experience a decline in their physical, social and psychological baseline making it difficult to determine which acute phase will potentially end in death.

Importantly, behavioural factors including non-adherence to medications or self-care may contribute to these acute episodes. In a study of 578 hospitalised older adults 14% of all medical emergency admissions were reported to be as a consequence of issues with medication. Additionally, 7% of these admissions were attributable to non-adherence and worryingly 192 (33%) of all patients in the study already had a history of non-adherence [97]. It is clear therefore that people with HF need to develop and maintain strategies and behaviours to care for themselves in order to manage their condition effectively [75].

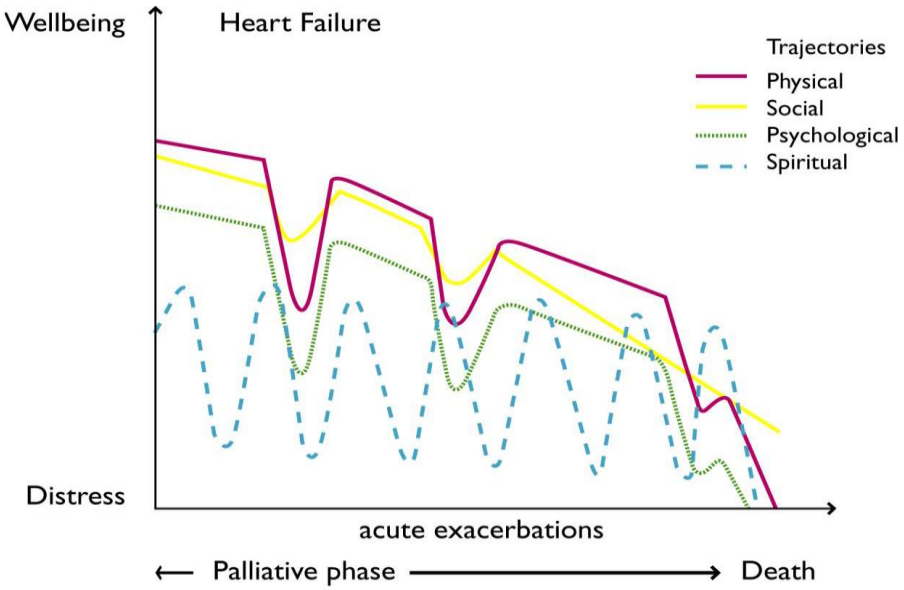

Figure2.1 Trajectories of social, psychological and existential decline in people with heart failure (reproduced from Murray et al [96])

2.1.6. Context of heart failure care

Treatment for HF usually aims primarily to relieve symptoms, while avoiding preventable hospital admission and improving survival rates. Significant involvement from both patients and healthcare providers is therefore required in order to achieve optimum management of such a complex condition. Generally, medicines have been described as being the mainstay of treatment in HF however management of the condition should be considered in terms of a range of interventions including both device and pharmacological therapies as well as self-care strategies including diet and exercise modification and continual monitoring [16].

2.1.6.1 Pharmacological therapies

Throughout the literature an extensive evidence base exists to support pharmacological management of patients with HFrEF with explicit guidelines regarding prescribing across Scotland detailed within Sign Guideline 147: Management of chronic heart failure [1]. In

parallel with the prescribing of medications such as ACEi [31], ARB's [98], aldosterone antagonists [99] and beta blockers [100] survival rates from HF have improved. Additionally, in patients with LVSD these groups of medications have been shown to improve hospitalisation rates while the prescribing of ACEi has been associated with improvements in quality of life [101,102].

The current first line treatment in HF is considered to be ACEi and beta-blockers while diuretics are prescribed to aid in the removal of excess peripheral and pulmonary fluid. In those found to be intolerant of ACEi the prescribing of ARBs is currently recommended. More recently medications which combine a neprilysin inhibitor with an angiotensin receptor blocker have been found to be superior to ACEi and ARBs for outcomes such as hospitalisation and all-cause mortality in patients with HF [103] increasing the likelihood that medications such as Sacubitril will replace these medications in the coming years.

2.1.6.2 Invasive therapies

In addition to pharmacological therapy invasive treatments such as cardiac surgery or pacemaker insertion can be considered for the management of HF. While cardiac surgery can be identified as a curative procedure the lack of available donors makes this an unrealistic treatment option for most patients, particularly for the older, co-morbid HF patient who would not make a suitable candidate for major cardiac surgery. Given the advances in pharmacological and pacemaker therapies few HF patients now require cardiac transplantation [1] however those patients with severe HF who are awaiting transplantation may have the option to undergo insertion of a mechanical circulatory support (MCS) system as an interim measure [104]. In patients whose HF has been caused by valve disease, surgery to unplace the damaged valve is possible.

In patients with HF sudden cardiac death occurs at a rate 6-9 times that of the general population [105]. The insertion of implantable cardiac electronic devices (ICEDs) have become increasingly commonplace in the management of patients with HFrEF who are already prescribed optimal medical therapy [106]. Implantable cardioverter defibrillators (ICDs) have proven to be an effective treatment for those who are experiencing life-threatening ventricular arrythmias [107] while cardiac resynchronisation therapy (CRT),

has been demonstrated to significantly reduce morbidity and mortality in HF patients with HF and a broad QRS complex on electrocardiography (ECG) [106].

2.1.6.3 Clinical management

With the advances in the pharmacological and device management of HF comes complexity in the delivery of care to patients [109]. According to NICE guidelines a multidisciplinary team approach (MDT) is essential in order to achieve individualised care which is responsive to the changing needs of the patient and which can be delivered seamlessly across both primary and secondary care [75]. Central to the delivery of care within the MDT are Heart Failure specialist nurses (HFSN) who are ideally placed only to promote collaborative working between healthcare professionals across both primary and secondary care settings but to deliver evidence-based interventions which aim to address the complex health issues faced those with a HF diagnosis [110].

Ongoing monitoring of patients with HF including assessment of functional ability, cognitive and nutritional status, fluid status, cardiac rhythm, review of medications including side-effects and renal function is an essential component of clinical management, the frequency of which should be dependent on the clinical stability of the patient [75]. While monitoring is seen largely as the responsibility of the healthcare professional, patient self-management is acknowledged as essential to achieving optimum outcomes. Through supportive relationships with clinical specialists such as HFSN patients should be given advice and education regarding their own role in the management of the condition and associated treatment in order to achieve clinical stability [111].

2.2. Medication Adherence

While the prescription of medicines is the most common healthcare care intervention in order for pharmacological therapies to be effective, adherence to the prescribed regime is key [9]. It is well documented that poor adherence to medication results in worsening of disease, a higher risk of death, and increased health care costs.

2.2.1. Compliance, Adherence and Concordance

Within the literature three main terms compliance, adherence and concordance are often used interchangeably to describe patient's medicine taking behaviour. Compliance is defined in the Oxford Dictionary, as "the practice of obeying rules or requests made by people in authority" and is commonly defined in healthcare as the degree to which a patients behaviour matches the prescribers recommendations [112]. Compliance, a phrase also meaning accepting punishment, is a word with negative associations were patients are believed to 'submit' and follow any given instruction. Inherent to a definition of compliance is the assumption that all medical advice is ultimately good for the patient therefore rational behaviour necessitates the exact following of the advice. Consequently any non-compliant behaviour could be viewed as either patient incompetence or worse disobedience.

Proposed as an alternative term to compliance, the term adherence has been defined as the extent to which people follow the instructions for prescribed treatments [8, 113]. In the doctor-patient relationship the term adherence attempts to support a collaborative relationship between the patient and the healthcare provider removing the balance of greater power from the doctor [114]. Adherence is seen to be influenced by not only the patient and their environment but by the practices of the prescriber and the characteristics of the care delivery systems [115]. While the term adherence suggests that patients take their medication after making an informed choice the term 'compliance' implies that the patient is submissive and simply complies with instruction [116]. The WHO has placed great emphasis on the need to differentiate between compliance and adherence stating that the patient's agreement to the recommendation is the main difference [35].

The third term, concordance, is often used incorrectly as a synonym for adherence within the literature and was developed by a committee of health care researchers who attempted to conceptualise the problem of adherence. Concordance acknowledges that clinicians have historically failed to take account of the patient's perspective and that for many non-adherence is a rational choice. Concordance elicits the patient's wishes and considers them to be of paramount importance [117]. Overall the term recognises that

within any interaction between the healthcare professional and the patient two sets of health beliefs are involved and that while these may be different they are equally valid.

Central to the concordance model is a requirement for patients to be able to make an informed regarding any proposed treatment, the potential benefits and possible risks. However this type of therapeutic relationship can only be successful if the patient feels there is potential benefit from their participation and may run into difficulties should patients be unwilling to participate or if they feel participation may be potentially harmful [118].

Finally rather than focusing on the patient's medicine-taking behaviour itself the term concordance refers directly to the interaction between the prescriber and the patient [119]. Given that the term adherence recognises the autonomy of the patient and requires that any recommendations given by the healthcare professional are mutually agreeable the term adherence has been adopted in this thesis.

2.2.2. Measuring adherence

Medication adherence is described as the percentage of prescribed doses which are actually taken over a specified period however there is no current consensus for what is considered ‘acceptable’ adherence [8]. Within the literature medication adherence can be reported as either continuous or dichotomous variable data with the latter used most frequently. While an eighty percent cutoff point is commonly used to classify patients into either adherent or nonadherent groups this varies between 75% and 90% and is not based on any empirical evidence [120].

Importantly there is no evidence to suggest that 100% adherence is needed to achieve optimal outcomes in patients with HF [120]. In an attempt to determine a cutoff point above which a positive relationship between level of medication adherence and event-free survival could be established Wu et al conducted a longitudinal study of 135 patients with HF. In this study the number of prescribed doses taken or the correct dose required to be taken ≥88% of the time to achieve significantly better event-free survival. However, it may be that cut-off points for adherence may vary depending on the indication for the drug.

The impact of missing or incorrectly administering drugs for conditions such as Parkinson's disease, or epilepsy or omission of medications such as oral contraceptives may be great while missing doses of a statin may not have a significant impact on either short term or long-term health outcomes.

The complexity of adherence has resulted in a lack of consensus on measurement of adherence with a variety of different methods reported within the area of HF research [121]. Traditionally, both direct and indirect measures of adherence have been used.

2.2.2.1. Direct methods of adherence

Direct methods may involve ether a direct observation of patient's medication-taking behaviour; measurement of the drug itself or seek to identify a biological effect of the medicine within bodily fluid. Additionally where biological effects cannot be directly measured the administration of tracer substances, along with the medication, facilitates blood or urine levels of the tracer as a direct test to confirm if the medication was ingested. However, while considered the most accurate, direct methods may not be appropriate in all situations. Measurements are not currently available for all medications, they may may require invasive procedures; they may not account for pharmacokinetic variability and finally they can be costly to perform [112].

The ability to obtain a true pattern of adherence may also problematic using direct methods. It is possible that given these methods usually require a pre-warning of either blood or urine sample collection or a researcher to be physically present to record the medication being administered the patient is alerted that adherence is being measured. This awareness may result in 'the toothbrush effect' were adherent behaviour is altered [122]. In a similar way that we remember to brush our teeth on the day we are due to see the dentist, when people know that they are going to have a blood test or urine test to measure adherence, they are more likely to take the medicines on that occasion. Consequently, when adherence is measured using direct methods only a simple yes/no result is generated without revealing the true pattern of nonadherence or giving the researcher insight into their causes.

2.2.2.2. Indirect methods of adherence

Indirect measurements are more commonly found in adherence research. They include: pill counts, patient self-report through questionnaires, interviews and diaries, prescription refill history through prescription dispensing data and the use of medication event monitoring systems (MEMS) [112, 123].

Commonly used as a measure of adherence within RCTs are pill counts, data collected by simply counting of the number of returned dosage items compared with the number of items received. However, pill counts have the potential to overestimate actual adherence behaviour [124] as just before the return appointment the patient may discard any remaining medication [125,126]. In addition, pill counting does not generate a medication-taking pattern and the removal of the correct number of medicines from the container does not necessarily mean the patient has followed the dosing regimen consistently or has actually ingested the medication.

Interviews and self-report are notoriously vulnerable to overestimates of adherence [112]. Many factors can account for difficulties with accurate reporting of adherence using self-report measures with social desirability and poor recall being the most common [127]. Retrospective self-report of medication adherence requires the patients to recall their experience of a repeated task over a period. However, the undertaking of a routine and recurring task such as the taking of daily medication may lead to the formation of a generic memory rather than a memory of each individual event. Additionally, when a task is repetitive, confusion may arise between the thought about taking the medication and the memory of actual taking it.

The ability to study adherence within large populations has become increasingly possible due to the recent growth in availability of electronic pharmacy data [127]. Measures of medication adherence based on pharmacy data are usually defined by the number of doses dispensed in relation to a dispensing period. While this method can support the assessment of multidrug adherence and assists in the identification of patients at risk for treatment failure [128] the validity of prescription refills depends on the completeness of the pharmacy database [112].

The Medication Events Monitoring System (MEMS) is an electronic device created specifically to monitor medication adherence behaviour. These devices contain a microprocessor that records the time and date a dose of medication was taken by recording when a medication container is opened. In this way an assessment of adherence patterns and timings of dosage can be made while nonadherent episodes can be detected [129]. Electronic monitoring devices are however not without their weaknesses. It has been suggested that use of the MEMS may lead to 'white coat adherence' where adherence is timed to meet the needs of the consultation with the doctor. Additionally, while the system produces evidence that the container has been opened there is no assurance that patients have actually taken the medication [130]. Apart from patients purposefully trying to mislead the system there is potential for them to accidentally activate the device out with the medication dosing times [129].

Overall, direct methods of detection have a higher sensitivity and specificity than the indirect methods [131]. A study examining the consensus between different measures of adherence in patients prescribed daily cholesterol-lowering medication reported that electronically monitored doses adherence and pill counting had the highest specificity (89.1% each) followed by the self-reported Morisky scale (80%). While all other measures assessed in the study had poor sensitivity and specificity three the measures recorded high sensitivity, the electronic monitoring interval adherence (84.2%), Haynes self-report (84.4%), and the pill count (89.1%) [126].

In HF, a study looking to predict hospitalisation in HF patients showed medication adherence as measured by medication event monitoring system was the best predictor of hospitalisation and concluded that it should be added to the previously used variables [132].

2.2.3. Types of non-adherence

The WHO stress that adherence to any regime may involve many different therapeutic behaviours including the seeking out of medical attention, the filling of prescriptions, the taking of medication appropriately and self-management [35].

Non-adherence has been the topic of many studies over the last 40 years. Despite around 200 variables such as socioeconomic factors and disease pathology being identified as being potentially associated with adherence a consistent link with adherence rates has been difficult to demonstrate.

Nonadherence to medication can be identified in three ways [133]:

1) Non fulfillment adherence: while the health professional provides a written prescription it is either not exchanged for the medicines or the medication is not commenced.
2) Non persistence: having commenced treatment, the patient chooses to stop taking a medication without seeking the opinion of a health professional.
3) Nonconforming: while the patient does administer the medication they do not adhere to the original prescription. This type of non-adherence may include: the skipping of doses, taking incorrect doses or taking dosage at incorrect times, taking more medication than prescribed or delaying advice from a healthcare professional.

Adherence may be classified as either non-intentional or intentional. In later life, non-intentional adherence can be common and may be the result of a number of factors including: a failure to remember to take the medication; an inability to swallow or apply the medication or an inability to understand the dosage directions due to cognitive impairment [134]. Intentional non-adherence occurs when, against the advice of their health care professional, a patient consciously elects not to take their medication. Central to intentional nonadherence is patients' beliefs about their condition [10].

Overall barriers to adherence vary widely and may include factors such as concerns about efficacy; a fear of potential side effects or safety; inconvenience; poor doctor-patient relationship; lack of social support; patient motivation, or incorrect education regarding proper use.

2.2.4. Scope of the problem

Very few patients of any age adhere perfectly to their medication regime [135]. In the general population it is estimated that between 25% and 50% [11, 35] of patients do not take their medication as prescribed [8, 11]. Even when medications are taken regularly it is estimated that as many as one half are taken incorrectly [114]. Adherence to medication taken for chronic conditions is worse than for those prescribed for acute conditions and deteriorates further after the first 6 months of treatment [8]. In the HF population adherence to medication is even more unclear with reported adherence rates varying between 10% and 98% [43].

In recent decades the number of medications prescribed for HF has expanded greatly. However unlike other conditions these medications, rather than replace existing medications have been prescribed in addition to the current regime [136]. Poor adherence to treatment has been identified as a problem in HF particularly when multiple medications are prescribed [25].

Estimates put rates of non-adherence in HF patients at between 40-60% [123] however literature looking specifically at non-adherence in older HF patients report rates ranging from 10% in patients newly prescribed digoxin [137] to ≥98% when adherence was self-reported using structured questionnaires relating to compliance [5]. In another study 27% of older HF patients were found to be non-adherent one month post hospital discharge despite being given written instructions, with the authors attributing much of this non-adherence due to poor recollection of instructions [138]. Overall establishing an accurate non-adherence rate is difficult due in the main to the wide range of adherence recording methods used across studies.

2.2.5. Consequences of non-adherence

The cost of non-adherence can be significant but may not always be evident to the individual patient while the impact non-adherence may have on health care costs may be similarly hidden [14, 139].

2.2.5.1. Personal consequences of non-adherence

There is evidence to suggest that patients with poor adherence experience worse clinical and economic outcomes than those who adequately adhere to treatment [140]. In the older population the consequences of non-adherence can be particularly significant [114]. A study by Col et al attributed 28% of hospital admissions in patients < 65 years to medication issues, with 11% of these admissions directly related to non-adherence [141]. A further study found that 26% of admissions in those over 75 years could be directly attributed to non-adherence with medication [142].

In HF positive clinical outcomes can be achieved when patients adhere to guideline recommended treatments. In one third of hospital admissions non-adherence to either prescribed medications or lifestyle modifications have been reported as a factor for admission [143, 144]. In particular, adherence to ACEi and ARB have been associated with a significant decrease in mortality and hospitalisations for patients with HF [31, 145, 146]. In the CHARM trial adherence to study medication was associated with lower all-cause mortality (HR 0.65, 95% CI 0.57-0.75, p<0.0001) [147]. This association was true for participants in both the active and the placebo arms suggesting that patients who adhere to prescribed treatment are more likely to adhere to other health-promoting behaviours.

In HF the aim of treatment is not only to improve prognosis but to relieve symptoms and maximise function in order to achieve the highest level of QoL for patients. Nonadherence to prescribed treatment may therefore potentially have a detrimental effect on an individual's health-related quality of life (HRQoL) [148, 149] impairment of which has indeed been shown to be prevalent within in the HF population [150]. In a study comparing HRQoL in HF patients with HRQoL in a sample of participants randomly selected from the general population those with HF reported more severe physical impairment of QoL than those with a history of either arthritis or chronic lung disease [151]. Similarly Juenger et al found a greater reduction in HRQoL, especially in the areas of physical functioning, social functioning and emotional functioning compared to a sample of a healthy population [152].

Within cardiovascular populations including HF, HRQoL measures have been shown to predict mortality and cardiac events [153]. In a study examining the association between

HRQoL and antihypertensive medication adherence in older adults low HRQoL scores were associated with lower levels of antihypertensive medication adherence [154]. In the SOLVD study, baseline indicators of QoL including activities of daily living; general health and symptoms of heart failure were reported to be predictive of both mortality and hospitalisations in both symptomatic and asymptomatic HF patients [155]. A systematic review and meta-analysis of pharmacological and lifestyle Interventions in patients with HF concluded that improved adherence was associated with positive effects on a range of outcomes, including quality of life [156].

While poor adherence to medication is associated with increased personal costs for individual patients [140, 147], the financial cost of medication itself has been identified in several studies as having negative consequences for adherence to medication in HF. In a qualitative study by Horowitz et al decompensation of patients with HF was directly attributed to financial difficulties when medical insurance had not covered cost of treatment [36].

2.2.5.2. Wider consequences of non-adherence

In Scotland the cost of medication prescribing is ever increasing. In 2015/16 total the number of dispensed medications in Scotland rose 1% on the previous year to 102 million items totalling a net cost to the country of £1.3 billion. Over a ten year period the net cost of medication had increased by 28% with the Scottish average sitting at just over £215 per person in 2014.

In 2012 the Department of Health reported that 58% of people in England aged 60 years and over had been diagnosed as having at least one long‑term condition. Multi-morbidity, the presence of two or more long-term conditions now currently affects around 27% of the population with numbers expected to continue to grow given the ageing population [157]. Given that multi-morbidity is a major factor in the prescribing of medicine, the need for prescribing will continue to grow with polypharmacy also becoming an increasing trend.

The waste of public resources and increasing cost to public health resulting from non-adherent behaviour is therefore a significant growing problem for the NHS. It is estimated

that medicines returned to pharmacies currently cost the NHS approximately £100 million per year while NICE report that the NHS carries an additional financial burden of between £36 million to £196 million per year on cost directly related to hospital admission as a result of patients not taking their medicines as prescribed.

Given the size of the problem and the huge financial burden attached to non-adherence, the reasons why patients do not take their medicines as prescribed has become a much researched area with published articles numbering tens of thousands [158]. However a lack of consistency exists within the field with no definitive measure of adherence nor a coherent picture of the key variables. Consequently, progress in the area of medication adherence has been slow [159].

2.2.6. Factors associated with non-adherence in heart failure

Non-adherence in HF is clearly a complex problem [136]. However in order to develop an intervention aiming to support patients in this area a clear understanding around the factors which can influence treatment adherence is required [160]. The WHO have identified five multidimensional factors to be considered when looking to address non-adherent behaviour: Socio-economic factors; health-care setting; condition related factors, treatment related factors and patient related factors (see figure 2.2).

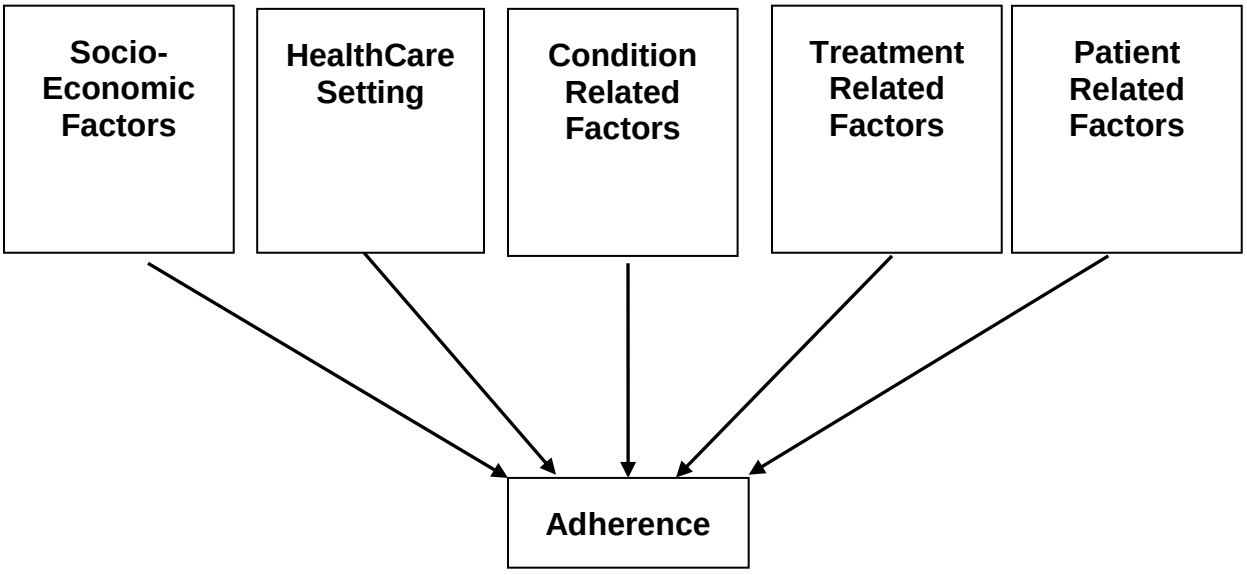

Figure2.2: WHO multidimensional adherence model

	Variables	Findings in HF literature
Socio-economic factors	Socioeconomic disadvantage	Limited evidence to support disadvantage with reduced adherence [161-165]
	Social support	Higher social support is related to higher adherence [165-169]
	Level of education	More education is related to higher adherence [160, 164, 170]
Healthcare setting factors	Healthcare services utilisation	Hospitalisation related to improved adherence [137, 171]
	Patient/provider relationship	Confidence and trust in healthcare provider a factor for medication adherence [169]
Condition related factors	Symptoms	Symptom severity related to adherence [164, 171-173]
	Co-morbidity	Inconsistent results associating comorbid disease with adherence [171, 174-177]
	Depression	Evidence of depression is associated with non-adherence to medication [5, 178-180]
Treatment related factors	Complexity of regime	Complexity of regimen including number of pills taken and dosage frequency are associated with non-adherence [181-186]
	Perceived side-effects	Perceived side-effects are associated with reduced adherence to medication [5, 145, 165, 187]
Patient related factors	Age & Gender	Inconsistent evidence for age or gender as factor for adherence in HF [144, 171, 175, 176, 186, 188, 189]
	Cognition	Evidence of cognitive impairment has a negative effect on adherence [190]
	Knowledge	Inconsistent evidence for knowledge as a factor for adherence [138, 191-193]
	Beliefs and attitudes	Inconsistent evidence for Beliefs in either condition or treatment as a factor for adherence [36, 44, 168, 177, 183, 194, 195]

Table2.1: Classes of factors potentially influencing medication adherence in heart failure

In relation to HF a narrative review undertaken as part of the background planning for this thesis found limited high-quality research in relation to the WHO adherence model (See table 2.1.).

2.2.6.1. Socio-economic factors

WHO have identified factors such as household income, marital and living status, level of education and health literacy, social support and household income as having influence on adherence [160].

Socioeconomic Disadvantage

In general terms, those who are least deprived on average live longer and in better health than those with a lower socioeconomic position. Additionally, those classed as most deprived tend to access less specialist services than those in higher socioeconomic positions but will utilise more general health care services [161]. However limited evidence currently exists on the possible effect of deprivation on medication adherence. This may be due in part from the current knowledge base being drawn largely from results of RCT's which are usually performed on a pre-selected patient population consisting of highly motivated individuals drawn from a population of individuals in the higher socio-economic groups [161].

In a cross-sectional population-based study based on data from Sweden, socioeconomic disadvantage was associated with medication non-adherence which increased with older age, particularly among women [161]. In the UK systematic analysis of medication issue data from 76 general practitioners associated higher adherence levels with those in less-deprived areas [162].

In HF, the relationship between financial status and medication adherence has not been examined in detail. In two studies Dunbar-Jacob et al [163] reported that as an individual's income increased medication adherence improved however this is contrary to findings reported by Rockwell & Riegel whose study reported no association between socioeconomic level and variance in levels of self-care [164]. However, it is worth noting

that the average household income was lower in the latter study which may have somewhat limited the results.

Impact of Social Support

Supportive relationships have demonstrated to be not only a factor for improved adherence to treatment but may also contribute to improvement in some medical outcomes [196] including mortality [197, 198]. The exact means by which this occurs however remains unclear.

The involvement of family with medical care is common. A literature review of 122 articles reported adherence to medical treatment to be 1.74 times higher when patients reported to be from a cohesive family environment than those who reported to be in dispute with next of kin. The review also reported that marital status or living with another person were also modestly associated with better adherence [199]. Family was also found to be important in a study involving a cohort of healthy medical outpatients where approximately 50% of patients reported some family involvement in their medical care including medication prompting [196]. A review conducted by DiMatteo in general populations concluded that presence of practical support had a larger impact on adherence than evidence of emotional support however it is unclear how this practical support contributed to adherence [11].

According to Leventhal et al a patient's ability to adhere to prescribed treatment is strongly influenced by the existence of a strong social network, which includes both the receiving of support as well as the participation in the social environment. For an individual any challenge to this support may result in negative outcomes on adherence [167]. The influence of social networks was investigated by Simpson et al who conducted focus groups with HF patients in order to explore barriers to medication use. Participants in this study believed it was important that family members be involved in HF education in order for them to better understand the condition; provide necessary and reinforce medication taking [165]. This positive effect was again defined by patients in a later study conducted by Simpson et al where patients who reported having a supportive network of friends and family described fewer self-reported barriers to taking medication for HF [169].

Patients' perception of the social support they received has been identified as a facilitator for adherence in other studies. Wu et al reported that HF patients who felt that they received an acceptable level of social support from family members and others were more adherent [168] while perceived social support was moderately associated with better self-reported medication adherence in a study by Sayers et al [166].

Education

In HF level of education has been associated with medication adherence [164]. Rockwell & Riegel's study reported that after controlling for other variables, education contributed 4.6% of the variance for self-care ($P = 0.009$) thus it was deemed likely that those patients who were better-educated would engage in self-care more than those who are less educated [164]. Evangelista et al investigated psychosocial variables relating to adherence. In a sample of 82 patients with HF a correlation was reported between higher education and overall adherence to treatment [170]. Similarly, Chui et al reported level of education to be a predictor of diuretic adherence in a study measuring adherence to diuretic therapy in patients with HF [200].

Health literacy has been defined as:

"*The degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions*" [201].

While currently there is no consensus on the measurement of health literacy [202] reduced levels may result in patients having difficulty processing information on how to best manage their medical conditions. Previous Studies have shown that inadequate health literacy is associated with reduced knowledge of illness [203], poorer physical and mental health [204], increased hospitalisation [205], increased mortality [206] and reduced medication adherence [207]. Overall those with low health literacy are 1.5 – 3 times more likely to experience adverse health outcomes [208]. While inadequate health literacy can affect anyone, it is more common among older people, patients with chronic conditions and those who are economically disadvantaged [209].

In HF the prevalence of low health literacy is reported to be 39% (range 17.5% to 97%). Consistent with studies in other conditions a recent systematic review found age, ethnicity, educational level, and cognition to be independent predictors of health literacy among HF patients [207].

Given that patients with inadequate health literacy are less likely to be able to understand or make informed decisions about the information they need to take their prescriptions as prescribed researchers have posited that nonadherence to medication may be associated with health literacy, particularly functional health literacy. Whilst little has been written about health literacy and its relationship to medication adherence in HF two relatively recent studies have reported results. Noureldin et al found that participants with adequate health literacy demonstrated both higher medication taking adherence and medication scheduling adherence than those with inadequate health literacy [209], while a study by Mixon et al reported that higher health literacy was associated with lower odds of misunderstanding cardiac medication [210].

2.2.6.2. Healthcare system related factors

The health care delivery system has the potential to influence the adherent behaviour of patients. Reduced access to healthcare, medication supply or medical follow-up, as well as poor provider-patient communication and relationships have all been identified as healthcare system related factors associated with reduced adherence to treatment [211].

Healthcare services utilisation

Recent hospital stay has been associated with enhanced adherence to medication in the HF population [43]. Monane et al conducted a retrospective follow up study examining over 7,000 older HF patients commencing digoxin. Using pharmacy prescription data, adherence rates were reported to be higher during the 12-month follow up period in those who had a reported hospital or nursing home stay prior to the initiation of treatment versus those with no admission [137]. Following hospitalisation, Rodgers & Ruffin reported that every all-cause admission to hospital during the previous year was associated with a 16% decrease in the risk of non-adherence in 311 patients with HF prescribed ACEi [171].

In contrast a study conducted by Bagchi et al aimed to determine rates of adherence to HF medication and examine factors associated with adherence using Medicaid data in a sample of over 45,000 HF patents. The authors reported that while patients with co-morbid conditions such as CAD or diabetes were more likely to adhere to all medications, including those prescribed for their HF, when hospitalisation had occurred for health conditions other than exacerbation of HF patients were shown to be less adherent [175]. It may be that while some co-morbidities are likely to necessitate increased healthcare contact which increases the potential for HF to be identified and treatments initiated, hospitalisation may be as a result of many different medical conditions which are then the primary focus for the healthcare team resulting in treatment for HF being overlooked.

While the above studies report some limited association between inpatient healthcare utilisation and adherence to medication there is currently no evidence to support a link between adherence and healthcare utilisation in the community setting.

Patient/Provider Relationship

As a keystone of healthcare [212] high-quality doctor–patient relationships have the potential to improve adherence to treatment plans, enhance self-management of disease, improve recall of important treatment information, as well as improve general mental and physical health status [213]. Over recent years the development of advanced nursing roles, specifically nurse prescribing, has enabled nurses to undertake some roles traditionally undertaken by medical staff [214]. Given that nurses traditionally have more opportunity to deliver holistic care, the development of roles such as HFSN have offered positive impacts on patient care in areas such as access to medicines, promotion of self-care and increased personal health-related decision making. Patient centered communication relating to adherence is an important role of advanced nurses such as HFNS who are regularly called upon to educate patients about newly prescribed medications [215].

Communication between the clinician and the patient as well as between healthcare providers have been identified as potential barriers to adherence [158]. A lack of communication regarding treatment duration, potential side-effects and costs of treatment may all have an effect on adherence to medication. Additionally, unclear information

regarding correct drug administration may cause confusion around dose and frequency of administration, especially during periods of drug titration [216].

Satisfaction with a medical consultation has been identified as a predictor not only of important health outcomes but of adherence to treatment, [217] particularly in those diagnosed with chronic conditions [218, 219]. In HF specifically, confidence and trust in the healthcare provider has been identified as a motivating factor for medication adherence in HF patients who stressed the need for healthcare providers to be knowledgeable while genuine in their concern for their patients [169].

A qualitative study aiming to identify misunderstandings associated with medication prescribing which occur between doctor and patient was reported by Britten et al. Overall those consultations where patients did not voice their expectations and preferences or express their opinion to doctors' decisions and treatment plans reportedly resulted in misunderstandings. In turn these misunderstandings were associated with potential adverse outcomes such as non-adherence to treatment [220].

A meta-analysis of literature looking at the relationship between doctor's communication and patient adherence to treatment reported that adherence to treatment was significantly related to the communication skills of the doctor. A 19% higher risk of non-adherence was reported among patients who experience poor doctor communication than among patients who have a doctor who communicates well [221]. Data from the European Social Survey (ESS) conducted across 24 countries in Europe reported that perceptions about the doctor-patient relationship were also strong predictors of non-adherence. In this study a reluctance not ask the doctor questions was associated with non-adherence as was the belief that doctors do not tell the whole truth. Equally people who believed that their doctors treated them as equals and discussed the treatment with them before a plan was established were 3% less likely to be non-adherent to the treatment than those who believed the opposite ($p=0.001$) [222].

2.2.6.3. Condition related factors

In the HF population condition related factors such as symptom severity, severity of condition, co-morbidities and mood have been hypothesised as being associated with adherence [174].

Presence of Symptoms

Effective control of symptoms is thought to improve QofL in HF thus posited as a key motivational factor for adherence [173]. Rockwell and Riegel conducted a study in which the typical participant reported moderate symptom severity and limited functional status. In this study those patients reporting more severe symptoms reported higher self-care scores [164]. In Rodgers & Ruffin's study a higher NYHA class was associated with improved reported adherence to ACEi [171]. Similarly, the severity of symptoms experienced was reportedly an important factor for patients choosing not to obtain medication when they were limited in the number of prescriptions they could acquire per month due to cost [172].

Multimorbidity

As previously discussed multimorbidity is common in HF. Almost 60% of patients with the condition have a diagnosis of five or more additional chronic conditions [76]. As a result, patients may feel overwhelmed not only by the burden of these co-existing conditions but in their management. The potential burden on HF patients has been described by Dharmarajan & Dunlay who reported that HF patients may typically spend around two hours per day partaking in health-related activities potentially requiring the assistance of another with at least one activity of daily living [223]. In addition, patients with multimorbidity may require to attend an average of fifteen outpatient appointments annually and take ten or more medications per day [224].

The relationship between multimorbidity and medication adherence is inconsistent in the HF population [174]. Cholowski et al reported an inverse relationship between adherence and the number of co-morbidities while also associating multi-morbidity with a reduced likelihood that non-adherence to medication was due to forgetfulness [177]. Conversely

Granger et al have reported an association between enhanced adherence and fewer comorbid conditions within the HF population [176].

Several studies have associated certain co-morbid diseases with the risk of non-adherence. For HF patients who also had a diagnosis of either hyperlipidaemia or chronic obstructive pulmonary disease (COPD) Rodgers & Ruffin reported a reduction in risk of nonadherence of around 11% [171]. While in the study by Bagchi et al those diagnosed with comorbid coronary artery disease (CAD) or diabetes mellitus (DM) were more likely to demonstrate higher medication adherence than people without these conditions [175].

Depression and Anxiety

While mood disorders are prevalent among patients with HF the association between mood and poor outcomes is not completely understood. Ambiguity exists over whether anxiety and depression are caused by HF or whether it is the presence of these emotions which are a risk factor for HF. Either way, it has been suggested that negative emotions may be associated with non-adherent behaviour in HF [225].

Patients with HF have been shown to experience clinical depression at a rate 2 to 3 times higher than those of the general population [226] and while approximately one in five HF patients are known to suffer from clinically significant depression the prevalence of minor depression may be greater than one in three. Additionally, the risk of depression correlates with the severity of the condition with rates increasing further when HF advances in stage [227].

Major depressive disorder in HF is associated with a poorer quality of life [228, 229] and an increase in the frequency of adverse clinical events such as hospital readmission [230] and increased risk of mortality [197]. Additionally, successful management of the condition may be impeded by the presence of depression [227].

Among the general population patients with depression were found to be three times more likely to be non-adherent with prescribed treatment than patients without depression [231]. In HF a study exploring the association between depression and medication adherence found a significant difference in self-reported medication adherence between participants

without and those diagnosed with depression (75% vs. 57%, $p = 0.008$) [179]. Similarly in a depressed population of older people with CAD Carney et al reported that patients with depression adhered to prescribed medication on an average of 45% of days as compared to 69% of days in a matched population without depression ($p < 0.02$) [180]. Finally, an improvement in recorded depression scores was found to be positively associated with an improvement in adherence in recent study of hospitalised cardiac patients diagnosed with a broad range of cardiac conditions [232].

Anxiety can be defined as “a negative emotional state resulting from an individual's perception of threat and characterized by a perceived inability to predict, control, or gain the preferred results in given situations” [225] Anxiety is known to negatively impact the cardiac output in patients with HF [233] however while much less has been written about anxiety in HF than on depression evidence suggests that it is indeed a common phenomenon [225] often co-existing with depression especially in older populations [234].

Overall in the healthy older population anxiety disorders are estimated to have a prevalence of around 4%. However, 18% of a study population of older outpatients with HF were reported to have at least one anxiety disorder [235]. A study of cardiac patients compared the anxiety scores of patients diagnosed with HF, MI of CABG a cohort of healthy older people. While the healthy older people expressed a mean anxiety score 40% lower than the normative threshold for anxiety all 3 cardiac-patient groups reported significantly higher levels of anxiety [236]. Worryingly if anxiety is persistent it may impact negatively on the health of patients with cardiac disease in the long term [225].

To date only a limited number of studies have explored the role of anxiety in HF prognosis and while results around the impact of anxiety are inconclusive a study by Clarke et al reviewing data collected as part of the SOLVD study found anxiety it to be among several psychosocial factors which could be identified as predictors of risk for severe functional limitations in patients with LVSD [237]. Finally, while no studies have reported a direct association between increased anxiety and adverse clinical outcomes in HF several studies have demonstrated an association between increased anxiety and subsequent CHD events in patients with existing coronary heart disease [238, 239].

2.2.6.4. Treatment related factors

As previously stated alongside the burden of managing multimorbidity the burden from medicines specifically prescribed for HF is ever increasing. When following National Clinical Guidelines for the treatment of advanced HF clinicians may be directed to prescribe in excess of six medications specifically for that condition alone [240]. For patients with HF therefore treatment often requires a lifelong commitment to follow an ever increasingly complex medical regime which may cause unpleasant side-effects and require frequent modification [188].

Complexity of Regime

The complexity of a patient's medication regime is influenced by several factors including the number of prescribed medications, the dosage frequency and form, as well as the instructions given for administration. Despite a number of studies reporting an association between number of prescribed medications and adherence in HF evidence in this area is inconsistent. An overly complex regime and inadequate instructions were cited as the main reasons for non-adherence in an observational study conducted by Toh et al with 47/66 (71%) of patients reporting difficulties in this area [185]. Two studies conducted by Muzzarelli et al and Gislason et al reported a positive association between an increased number of prescribed medicines and enhanced adherence [145, 186]. Conversely Roe et al described poor adherence to ACE-inhibitors as being associated a higher complexity of the medical treatment [211].

Frequency of dosing has been shown to be a contributory factor to non-adherence in populations with chronic conditions [241] including those with chronic cardiovascular disease [242]. In the HF population Riegel et al assessed adherence using MEMS and reported that those patients who required to administer medication ≥2 times per day (OR = 2.59, p=0.016) were more likely to experience a decline in adherence rather than demonstrate continued adherence [183]. Similarly, adherence to ACEi has been found to be around 90% in patients with HF prescribed daily prescriptions compared to around 68% in those where their medication was prescribed three times per day [184]. However,

in contrast, Udelson et al found that drug regimen simplification did not improve adherence to carvedilol [243].

Side-effects of treatment

Despite not taking their medication as prescribed it is possible that patients may view themselves as adherent [5]. Perceived side-effects of medication have been identified as a factor for non-adherence causing patients to either delay or miss dose administration. Van der Wal et al reported that the most important barriers to medication adherence among the HF patients interviewed in their study were nocturia and other difficulties related to diuretic therapy [5].

Several studies have described how patients choose to alter their use of diuretic therapy because of the drugs' effect on social activities [187] including a qualitative investigation by Simpson et al who reported that adverse events (actual or perceived) altered a willingness to continue therapy in patients with HF [165].

2.2.5.5. Patient related factors

The majority of literature reviewing medication adherence has focused on patient related factors [160]. In studies age, gender and cognitive function are frequently identified as a potential determinant of adherence however, a patient's knowledge of their condition and treatment as well as the beliefs they hold about the condition may also play a key role in medication adherence.

Age and Gender

While numerous studies investigating adherence have focused on patient characteristics, they have not demonstrated a consistency to predict adherence [244]. Given that older patients are often receiving treatment for multiple chronic health conditions while experiencing memory difficulties exacerbated by medications or early dementia, age has been identified by WHO as a determinant of adherence [35].

The relationship between age and medication adherence is inconsistent within the HF population. While some studies have reported a higher risk of non-adherence among a younger population [144, 171, 175, 188] others have reported no significant relationship

between age and adherence [176, 186, 189]. A systematic review analysing the evidence for age as a determinant of medication adherence in patients with HF was carried out by Krueger et al [245]. It concluded that while older age was not related to medication adherence, older patients may receive a higher level of support with medication than younger populations.

For gender, literature has identified that different patterns of adherence behaviour for men and woman who may also differ in views and beliefs regarding their amount of medication use, their adherence to medications, and their likelihood of receiving ongoing medication monitoring [246]. In HF however, as with age, association of gender and adherence are inconsistent. While several studies have not found a significant relationship between gender and adherence, [164, 168, 171, 189] nonadherence has been reported to be higher in males [144, 175, 247, 248] with Dunlay et al reporting that while men had lower ACEi/ARB adherence than women sex was not associated with adherence to other medications [188].

Cognition

Mild cognitive impairment (MCI) refers to a condition in which there are subtle cognitive deficits which do not meet the criteria for dementia. Although people with MCI may continue to perform basic activities of living reduced adherence to therapeutic advice given for chronic conditions such as diabetes has been reported in this population [249]. Additionally decreased ability to carry out essential self-care activities in HF patients with cognitive impairment has been reported [250].

There has been increasing evidence to suggest that low cardiac output is independently associated with cognitive impairment (CI) with the prevalence of MCI ranging from 53% to 58% in older people with mild to moderate HF [251]. Compared to the general population, patients with HF have been found to have up to a 4-fold higher risk of developing CI [190].

Independent of other factors, MCI has been shown to predict 30-day hospital readmission and death in patients with HF [252]. An association between medication adherence, cognition and HF was previously reported by Hawkins et al [190]. In this study medication adherence was significantly worse (78% to 70%, P=0.017) for patients with evidence of MCI compared to those without.

Inadequate knowledge in disease management

Adherence to prescribed treatments requires an understanding of both condition and treatment [160] however knowledge alone cannot guarantee adherence [182]. Lack of knowledge and misunderstanding about HF have been reported in several studies [138, 182, 182, 253, 254]. From a HF patient's perspective, the minimum information required to achieve adherence relates to the purpose, the potential benefits and the possible adverse reactions of prescribed medications as well as an understanding of all drug specific instructions [165].

To date, evidence around the influence of knowledge on HF treatment adherence is inconclusive. In patients admitted to hospital with decompensated HF Michalsen et al reported that knowledge about drug treatment was not associated with enhanced adherence [191]; conversely 25% of HF patients who presented at hospital as an emergency reported lack of knowledge as a barrier to medication adherence [193]. Overall, low levels of knowledge, especially in the area of HF medications is reported in the literature [58].

While patients can be furnished with information regarding a health condition or associated treatment, this act alone does not necessarily translate into knowledge. In a study carried out among 117 new patients visiting a HF clinic, Ni et al reported a significant correlation between adherence to self-care and knowledge (r=0.33, p<.001). However, despite 80/113 (71%) of the patients self-reporting that HF educational materials had been supplied to them, only 11/80 (14%) said they knew "a lot" about HF. Similarly Cline et al reviewed patients who had all received standardised written and verbal information regarding their medication and reported that only 12/22 (55%) of patients with HF could correctly name their prescribed medication while only 11/22 (50%) were able to describe the prescribed dosage. Worryingly, one month after hospital discharge 6 of the 22 participants previously admitted to hospital due to HF were found to be non-adherent to medication [138].

Beliefs and attitudes

Personal beliefs are known to form the foundation of any decision making [173] with beliefs held by patients regarding their illness playing an important role in decisions made regarding adherence [187, 255]. Individually held beliefs about medication have been shown to affect both intentional and unintentional adherence to medication in older people [256].

As previously stated, poor adherence to medication may result in worse outcomes in the HF population. Albert et al conducted a study of 195 HF patient attending the accident and emergency department for decompensated HF. Inaccurate HF beliefs and poor self-care adherence where reported in this group of patients reflecting a need for improved HF education [184].

Percival et al [195] explored the beliefs of 43 HF patients towards their HF medicines and self-care activities. Using the Beliefs about Medication Questionnaire (BMQ) the authors reported that those who believed their prescribed treatment to be necessary had significantly higher adherence scores than patients who reported high levels of concern around the treatment. In particular, adherent behaviour was related to the perception that HF medication was helping the heart and was related to their health.

Several studies have investigated the role of beliefs and attitudes relating to barriers to medication adherence, as perceived by patients with HF. Wu et al [168] conducted a study on 134 patients with mainly advanced HF reporting that the most consistent predictor of adherence was patient perception of barriers to medication adherence. Similarly, Cholowski & Cantwell reported that a belief in the need for medication adherence was negatively related to being careless about taking medication [177] in a population of older patients with HF. In a cross-sectional study of 58 older patients with HF Molloy et al examined whether beliefs about HF were associated with adherence to ACI. Using the illness perception questionnaire (IPQ-R) those who thought their HF to have a more chronic timeline or perceived their condition to have more consequences where found to be less likely to adherence to their medication than those who believed otherwise [44].

2.2.7. Interventions to improve adherence

Historically interventional approaches to improving medication adherence have been based mainly around a biomedical model with the provision of information regarding the medication or treatment being the main focus [116]. As previously stated however adherence is multifaceted and may include cognitive, motivational, behavioural and social factors. In order to fully address the issue of non-adherence in older HF patients a greater understanding of the perceptions and agendas of this population are thus essential [257]. Indeed before the development and evaluation of any intervention aimed at improving adherence in this population can be undertaken a better understanding of the barriers older adults face must be obtained.

Interventions looking to improve adherence have been conducted across many different health conditions. The first review of adherence interventions was conducted around thirty years ago with many systematic reviews, meta-analyses and narrative reviews having been taken place since [258]. In a recent Cochrane review of Interventions for enhancing adherence to prescribed medications several interventions were found to modestly increase adherence [259]. However, while some interventions improved patients' outcomes in the short-term, less than half of the studies showed any benefits at all with effects inconsistent across studies. The review concluded that existing methods of improving adherence for chronic health problems are mostly complex and ineffective resulting in the full benefits of treatment not being realised for patients.

On a positive note however it has been demonstrated that improvement in adherence to medication is possible. Identifying strengths and weakness of previously evaluated interventions offers potential for the development of an adherence enhancing intervention tailored to meet the needs of older HF patients. A full review of previously evaluated interventions aimed at improving medication adherence in the HF population is described later in this thesis.

2.3 Theoretical approaches

In order to improve both the likelihood of success and to aid its generalisation to different populations or health systems any intervention aiming to change health behaviours should all be based on a theoretical model which provides an explanation of that behaviour [260].

When trying to understand adherence Leventhal et al states that previous studies have been guided by five major theories of adherence: the biomedical model; operant behaviour and social learning; the rational belief theory; a communication approach and the self-regulative systems theory [261]. To varying degrees each theory concentrates on an individual's understanding of their illness; their perception of risk; their motivation to comply and the selection of coping behaviours.

Originating in the study of human anatomy and physiology the most common of these models throughout western society has been the biomedical model. Considering the patient to be the recipient of instructions provided by a healthcare provider the theory ascribes only limited consideration to the patient's actual understanding of the treatment. However previous research utilising this approach has contributed greatly to both the knowledge and understanding around the measurement of adherence as well as making valuable contributions to various scientific advances including controlled release medication, combination drugs and monitored dosage systems [131].

The biomedical model, while focusing on the transmission of information from the clinician to the patient, fails to consider the effect of underlying psychological processes on adherent behaviour. Additionally the model does not make considerations for how the healthcare professionals own behaviour may impact on the patient's adherence. It is desirable therefore to underpin the design of an intervention aiming to improve medication adherence with the use of a model of behaviour which aims to address these specific issues [134]. With this in mind Leventhal's common sense model (CSM) has been chosen as the model for the work within this thesis and the rationale for this is explained below. However, there are a number of alternative theoretical models and a brief overview of these is given first below.

2.3.1. The Health Belief Model

The Health Belief Model (HBM) was developed in the 1950's by Hochbaum, Rosenstock and Kegels, a group of social psychologists working in the United States of America who looked to explain why people failed to take up public health prevention measures before the onset of clinical symptoms. Following its development the theory has since been applied to treatment adherence regimens [262].

The HBM was first presented with main concepts: Perceived Susceptibility, Perceived Severity, Perceived Benefits, and Perceived Barriers. The concept of Cues for Action was added later to "stimulate behaviour." Finally, in 1988, the concept of Self-efficacy was added to address the challenges of habitual unhealthy behaviors such as smoking and overeating resulting in six key concepts [263] (see table 2.2).

The model is based on the understanding that a person will undertake a health-related action if they:

1. Feel that the adverse health condition can be avoided.
2. Anticipate that by taking a suggested action the adverse health condition will be avoided.
3. Believe that they can carry out the recommended health action.

In addition to personal beliefs individual factors such as age, culture, education level and past experience are now also accepted as having an indirect effect on individual perceptions and the likelihood of taking positive action and thus component parts of the model (see figure 2.3).

2.3.1.1. Studies using the HBM

The HBM has been previously utilised in the development of behaviour change interventions investigating medication adherence across a range of treatments and illnesses [264] including hypertension [265], asthma [266] and diabetes [267]. However in HF, while the HBM has been used to compare health behaviours in self-care [268][5] and to

identify predictors of non-adherence [269] there is a lack of evidence to support application of the model to interventions to improve medication adherence in HF populations [270].

Concept	Definition
Perceived Susceptibility	An individual's evaluation of how likely it is that they will get the condition. The greater the perceived risk the more likely the individual will be to undertake behaviours to reduce the risk.
Perceived Severity	An individual's evaluation of how serious a condition and its consequences may be. While individual perceptions may be based on some medical understanding it also encompass an individuals around the impact of the condition on their life in general.
Perceived Benefits	An individual's perception of how effective the proposed action may be.
Perceived Barriers	An individual's perception of both the physical and psychological costs of the proposed action
Cues to Action	What influences or plans are plans are in place to activate "readiness"
Self-Efficacy	An individual's confidence or belief in their capacity to carry out the proposed action

Table2.2: Key Concepts of the Health Belief Model

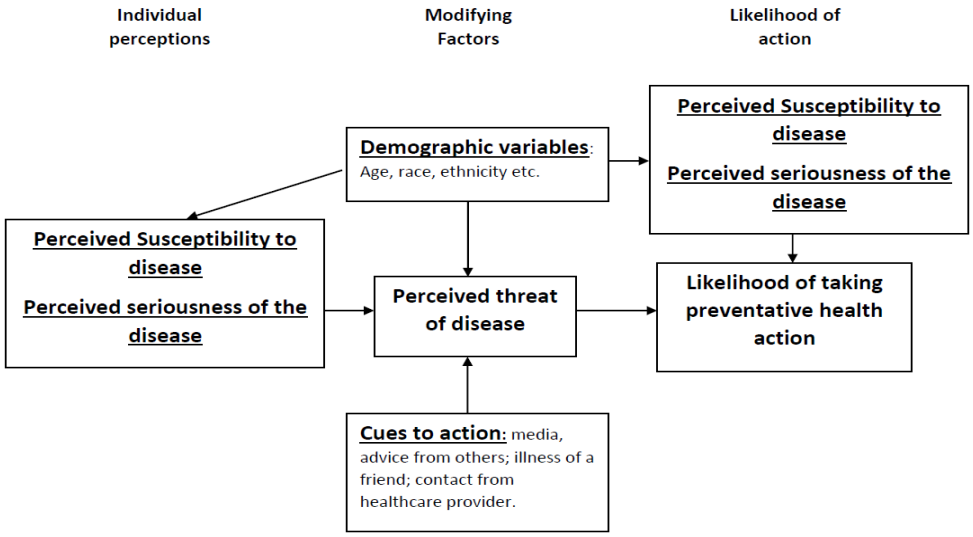

Figure 2.3 component parts of the Health belief model adapted from Janz et al 2002 [263]

2.3.1.2. Strengths and weaknesses of HBM

While the HBM has been used successfully across previous adherence enhancing intervention studies [264] it has several limitations. Firstly the model does not acknowledge the effect of personal beliefs on behaviour. It assumes that for all individuals' engagement with the behaviour is solely for health-related reasons disregarding the role played by other potential determinants [262]. Additionally the model makes the assumption that everyone has equal access to health-based information.

Criticised by Janz et al who noted that the key constructs of the model have often been utlilised inconsistently and inadequately assessed the HBM could be described more as a descriptive than explanatory model in that it does not advise on an appropriate approach for changing health-related behaviours [262].

The use of the model to successfully improve adherent behaviour is therefore unclear. A recent systematic review aimed at evaluating the effectiveness of HBM based interventions in improving adherence reported on 18 studies. While the majority of the studies reported an overall improvement in adherence 15/18 (83%) only six of the studies

had in fact used the HBM in its entirety calling in to question whether the improvements reported where indeed due to the application of model constructs [264].

2.3.2. Theory of Planned Behaviour

The Theory of Planned Behaviour (TPB) developed by Fishbein & Ajzen, is an extension of the Theory of Reasoned action (TRA) developed by due to limitations noted with the original model [271]. Comprising of six constructs (see table 2.3) the model focuses on an individual's intention to perform a specific behaviour (see figure 2.4). The key component, intention reflects the individual perception to the model that intentions capture the motivational factors that influence behaviour; they are indications of how hard people are willing to try, of how much of an effort they are planning to exert, in order to perform the behaviour. According to TPB, perceived behavioural control, together with behavioural intention, can be used directly to predict behavioural achievement. As a general rule, the stronger the intention to engage in a behaviour, the more likely should be its performance.

Concept	Definition
Intention	The motivating factors influencing the behaviour. The behaviour is more likely to be undertaken if the intention is strong.
Attitude	An individual's appraisal of the behaviour and the degree to which it is considered beneficial or detrimental.
Subjective norms	Individual beliefs held regarding the opinions of peers and whether others would approve or disapprove of the behaviour.
Social norms	The codes of behaviour considered customary within a specific group.
Perceived power	The perceived factors available to the individual which may support or obstruct the undertaking of the behaviour.
Perceived behavioral control	The Individual's perception of how problematic undertaking the behaviour may be. Received control may change depending on circumstances.

Table2.3: Key Concepts of the Theory of planned Behaviour

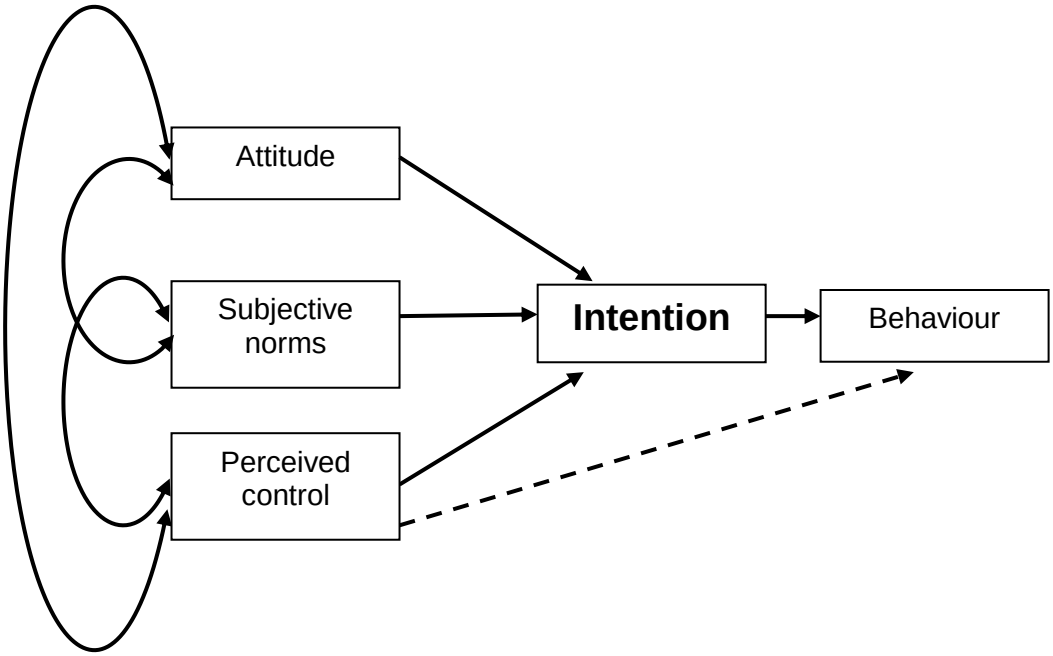

Figure2.4: Theory of Planned Behaviour reproduced from Ajzen 1991 [271]

2.3.2.1. Studies using TPB

Across a range of health conditions including diabetes [273], stroke [274] and HIV [275] the TPB has been used as a theoretical framework to both understand predictors of adherence and to guide the development of interventions [272]. In HF Wu et al recently conducted an observational study which aimed to evaluate which factors of the TPB predicted sodium intake in patients with HF. In total 244 HF patients, of which 163/244 (77%) were male, completed a sodium restriction questionnaire which comprised of subscales relating to 3 components of the TPB namely: attitude, subjective nom and perceived behavioural control towards following a low-sodium diet. The only concept found to be a predictor being subjective norm supporting the hypothesis that support from both health care providers and significant others for adhering to a low-sodium diet from can have a positive outcome [276].

Additionally, the TPB has been used as the theoretical underpinning for several interventional studies within the HF population. A TPB based educational intervention

again by Wu et al aimed to encourage positive behavioural beliefs relating to medication adherence. The intervention aimed to educate both patient and their significant others in symptom control and management via 4 educational and counselling sessions with the addition of personal feedback relating to actual levels of medication adherence for a subgroup of participants receiving the intervention. While initial results from this study are positive in that those who undertook the intervention where more adherent at follow up than those in the control group it is worth noting that the study was a sample of relatively young HF patients (mean age 60 years), had a relatively small sample size of 82 participants and a limited follow-up time of only 9 months [277].

In a similar vein, Welsh et al used the TPB to develop a 6-week educational intervention which was specifically aimed at reducing the dietary sodium intake of patients with HF. In this study daily sodium intake was assessed using food diary data for 52 HF patients. While there was no significant difference in sodium intake between groups at baseline, sodium levels in those receiving the intervention decreased at 6-month follow-up while an increase in sodium intake was reported in the control group while attitudes towards following a low sodium diet also improved in the intervention group. While initial results for use of the TPB seem positive the results of this study are limited by the small sample size and the possibility that participants completed the food diaries inaccurately simply to meet the social norm [278].

2.3.2.2. Strengths & weaknesses of TPB

The TPB has been widely used and has found to be successful in predicting a range of health intentions [272]. However it is not without criticism. A review of the TPB conducted by McEachan et al found that when studies were longitudinal in nature or when outcomes were measured objectively rather subjectively the TPB appeared to be less successful in predicting behaviour [279]. Additionally, the model assumes that individuals looking to undertake a specific health related behaviour will have both the means and the opportunity available to them. It does not account for other variables such as psychological, environmental or economic factors or an individual's past experiences [280].

2.3.3. The experience of illness

Overall the majority of people can expect to enjoy a reasonable level of health with ill health usually confined to the final few years of life [281]. As previously stated one major challenge facing healthcare systems today is the rising prevalence of long term conditions such as HF. When chronic illness is diagnosed increased involvement with healthcare professionals usually follows [281]. Despite their importance however patient's opinions are seldom sought during medical consultations where patients traditionally did not discuss their illness beliefs with their doctor [282]. Despite this lack of disclosure it is clear that in order maintain a reasonable QoL patients must have the ability to integrate their long term condition into their daily life by finding a way to make sense of the condition and its symptoms.

Self-regulation, as defined by Zeidner et al, "*is a systematic process involving conscious efforts to modulate thoughts, emotions and behaviours in order to achieve goals within a changing environment*" [283]. "Survival and coherence" according to Carver and Scheier are the two natural goals possessed by humans and form the basis on which all other goals are produced [284]. Given that an experience of illness has the potential to threaten both survival and coherence presenting significant challenges to self-regulation it is necessary to consider both of these goals when attempting to understand how behavioural patterns develop over the course of a health threat experience.

2.3.3.1. The Common Sense Model (CSM)

As previously stated the guiding theoretical framework for this study is the Common Sense Model (CSM) of illness cognitions and behaviour [261]. The model provides a theoretical framework to help understand how an individual's conceptualisation of their condition can impact both their coping behaviour and ultimately their health outcomes. It describes a process of self-regulation which involves the setting of personal goals; the development and enacting of approaches to realise these personal goals and an evaluation of progress with potential for modification of both goals and approaches [285]. In this way self-regulation can be viewed as a structure which is not only functional and

motivational but encompasses the individual's emotional response to ill health linking it directly to the cognitive processes [160].

CSM is an extension of the parallel processing model [39] which evolved from an early study investigating the influence of fear on smoking behaviour. While Leventhal and colleagues demonstrated some positive short-term effects any change in smoking behaviour did not continue over time thus demonstrating that the processing of the health threat and the processing of the fear emotion were in fact two separate pathways [286].

The CSM suggests that when an individual receives a diagnosis or is challenged with the management of ill health they will inevitably develop their own individual beliefs about the condition which may or may not be related to the clinical features of the condition [282]. Based on the individual's understanding or experience of the condition these beliefs or "illness representations" run in parallel to emotional responses shaping the individuals coping strategies and action plans this providing what Leventhal et al call a "framework for action" [287]. Given that these representations are formed in the minds of individuals the CSM identifies what the authors believe are individual, "common sense" beliefs about illness.

A three-stage structure (see figure 2.5), the CSM hypothesises that when an individual recognises that they are faced with a health threat (stimuli) they will respond to it. Dependant on personal symptoms, understanding of the condition and any pre-existing beliefs the individual will form their own representation of the illness (*stage one*) which in turn will direct the selection of coping responses *(stage two*) which are in turn evaluated in terms of how they have removed or managed the health threat *(stage three)*. The coping strategy (*stage two*) will be dependent on how the threat has been viewed by the individual (*stage one*) and may include strategies including the seeking out of medical attention, emotional expression emotion or denial of the stimuli [134].

In addition to the formulation of illness representations the challenge of a health treat also provokes an emotional response. In an attempt to control these emotions the individual needs to acquire coping responses which are in turn evaluated in a similar way to the illness representations.

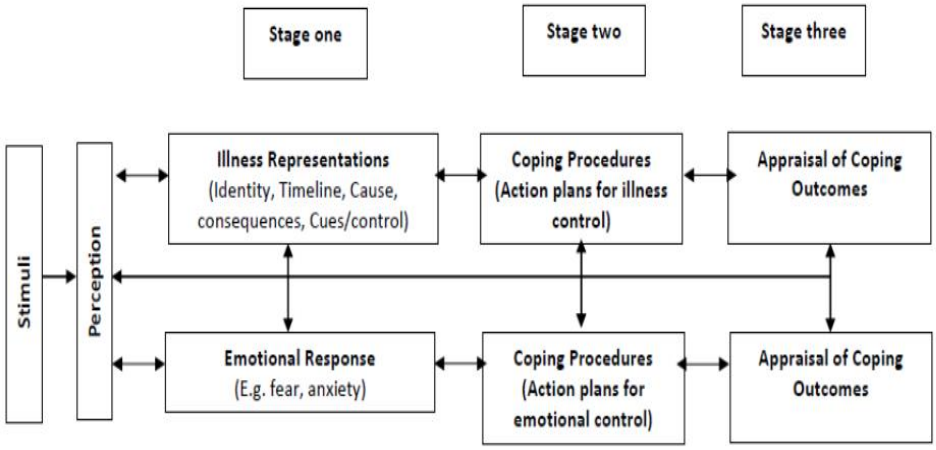

Figure2.5 Leventhal's Common-Sense Model reproduced from [39]

Once an individual has acknowledged the health threat the next step is for this threat to be conceptualised as an illness. Lau and Hartman classify Illness representations into five main domains: identity, timeline, consequences, cause and control [288]. Formed from a range of both social and cultural influences these five domains are not independent but inter-related and have been incorporated into the CSM (see table 2.4) [289].

A clear and significant strength of the CSM model is that it is a dynamic process requiring the individual to undertake ongoing appraisal not only of the effectiveness of their coping strategies and health behaviours but of the illness itself. A meta-analysis of 45 studies conducted by Hagger and Orbel has provided support for Leventhal's CSM. Across the included studies the authors found a strong negative association between the control dimension of the model and illness identity, consequences and timeline while a positive correlation could consistently be found between the three dimensions of timeline, consequences and illness identity. In terms of coping behaviours expressing emotions and avoidance or denial were positively associated with serious consequences and a strong illness identity across the included studies while the ability to seek support and problem-focused coping was associated positively with the control dimension of the CSM.

Importantly a high level of perceived control over the illness or condition consistently correlated with psychological well-being across the included studies [290].

The model does however make a number of assumptions. Firstly, it presumes that individuals are self-motivated and able to utilise both current knowledge and past experiences to manage the health threat. Secondly the process of forming an illness representation is both time and situation specific and finally because the model assumes that cognitive processes are not directly visible observers are required to undertake their own appraisal in this area.

Illness representation	**Definition**
Identity	The label a person gives to their illness. It is based on an individual's knowledge about the symptoms associated with the condition.
Timeline	Specifies the length of time an individual expects their illness to last and the timescale of their symptoms.
Consequences	Encompasses an individual's beliefs about the seriousness of their illness and its likely impact on their overall well-being.
Causes	Describes the factors an individual considers to be the cause for the illness.
Control	Specifies the extent to which an individual believes they have control over their illness. Related to beliefs around efficacy of treatment.

Table2.4: Domains of Illness Representation in Leventhal's Common-Sense Model

2.3.3.2. CSM and heart failure

A number of studies have explored illness representations in HF. In a qualitative study of

12 older HF patients, interviewed using a schedule based on CSM, MacInnes investigated illness representations and treatment beliefs and concluded that HF lacked a clear illness identity despite patients having been told they had HF [291]. The illness was commonly attributed to external factors such as family history, other illnesses, medication and stress. Patients in the study were unable to make connections between previous CAD and their current condition however they did have an accurate view of the condition in terms of timeline and the seriousness of the condition, and they held consistent beliefs about the importance of medication in controlling symptoms and the necessity of this medication [291].

Similarly illness representations were investigated by Horowitz et al who also reported a poor association between symptoms and HF with symptoms frequently attributed to other conditions. In this study however patients described HF as an acute condition and did not recognise that symptoms worsened over time resulting in poor symptom management and acute exacerbations [36].

Quantitative studies have also studied illness representation in HF. The revised Illness Perception Questionnaire (IPQ-R) was used by Voelmeck in a sample of 98 patients with HF. In this study no correlation was found between illness representations and self-care [292]. Similarly MacInnes conducted a cross-sectional survey in 169 HF patients aiming to determine relationships between illness representations, beliefs about treatment and self-care. In this study along with perceived medication knowledge and beliefs about medication necessity illness coherence was found to be moderately correlated with self-care. Additionally three factors were found to be significant predictors of self-care: knowledge of medication; a belief that the illness may have serious consequences and the impact of medication on lifestyle [293].

Cherrington studied 22 patients with HF and concluded that while participants believed their HF to be a chronic disease, serious outcomes could be controlled through treatment. Additionally, participants in this study believed that they had a good understanding of their condition and did not have a negative affective response to their HF [294]. In contrast however, Albert and Zeller used the Survey of illness beliefs in heart failure tool (SIBHFT)

concluding that patients actually held inaccurate beliefs and perceived little control over their HF [295].

In a cross-sectional study Albert et al looked at the accuracy of illness beliefs around HF and self-care in patients admitted to A&E with decompensated HF. Using the SIBHFT accuracy and certainty of patients' HF illness beliefs related to the five CSM illness representation domains were measured. Patients were found to hold inaccurate HF illness beliefs in certain areas including a belief that their HF could be cured with medication and other therapies; a belief that HF was a condition which was only present when symptoms were present and a belief that HF medicines are most effective when symptoms are present [194].

2.3.3.3. CSM and medication adherence

The use of various social cognition models has provided evidence to suggest that an individual's decision regarding treatment can be significantly influenced by their belief about the need for treatment and their thoughts on the benefits and risks associated with commencing that treatment [134]. As the CSM looks to address factors underlying health related behaviour, it has been suggested that it provides a solid framework for predicting adherence to treatments [296]. A recent review of literature on the topic of patient illness perceptions and medication adherence which included a total of 11 studies spanning different patient populations including asthma, hypertension, diabetes and HF concluded that with the exception of illness coherence each of the illness perception factors were shown to have a positive impact in medication on medication adherence however this was not consistent for all patient populations across all perception factors [134].

A strong belief that medication would improve symptoms was positively associated with medication adherence in a group of patients randomised in the carvedilol or metoprolol European trial (COMET) [297]. While studies such as this have demonstrated that beliefs about medication can influence an individual's initial treatment preferences ongoing adherence is determined not just by ones beliefs about medication but is also determined by what concerns they hold regarding the treatment.

Expanding on the CSM work Horne developed the Necessity-Concern framework.

According to Horne, while non-intentional non-adherence can be viewed in terms of an individual's inability to adhere to treatment intentional non-adherence must be understood in terms of the individuals personal motivation to commence and continue with treatment The Necessity-Concern framework describes medication adherence as a function of an individual's beliefs which may lead them to question the actual necessity of the medication. If an individual believes medicines to be harmful or unnatural this questioning may lead to intentional non-adherence [298].

In order to ensure that patients with HF capitalise on pharmacological therapeutic benefits healthcare professionals need to improve their understanding of what influences HF patients to make decisions regarding their health [299]. In an attempt to understand illness and treatment beliefs in HF a number of previous studies have measured illness representation and as such the CSM has been selected to underpin the design of both the qualitative and quantitative explorative studies aiming to identify predictors of non-adherence in older HF patients contained within this thesis.

2.3.4. Self-Efficacy

As previously stated the CSM can be utilised to help understand the illness perceptions of HF patients and the beliefs which may underpin adherent behaviour however a deeper understanding of how an individual manages complex treatment plans is also necessary.

Self-efficacy, a modifiable factor, is the belief in one's own ability to successfully complete a task has been recognised as a key component in a number of theoretical models. Rather than focusing on an individual's skills and physical ability to perform a task self-efficacy concentrates on the individuals opinion of what can be done with those skills. According to Albert Bandura's Social Cognitive Theory (SCT) individuals, rather than simply being responsive, are actually "self-organising; proactive; reflective and self-regulating" in nature [300]. From a SCT perspective an individual's functioning is shaped by the dynamic interaction between personal, behavioral, and environmental determinates, all of which are possible target areas when considering interventions aimed at improving health outcomes.

Identified as an important predictor of behaviour [301], an individual's self-efficacy beliefs are said to be shaped by four sources: personal previous achievements; experience of observing others successfully perform the task; social persuasions and the individual's emotional state (see table 2.5). The theory proposes that the level of confidence one has in their ability to undertake a health behaviour will ultimately determine the amount of effort and commitment they will afford to those behaviours [302]. Additionally, self-efficacy not only influences the goals an individual will set but will also determine an individual's expectations of the outcome and what they believe may be facilitators and barriers to undertaking the behaviour (see figure 2.6) [303]. Failure to persevere with the behaviour is less likely if a commitment to the setting and maintaining has been made and the individual has been able to face challenges with an increased and continued effort [304].

Sources of self -efficacy	Definition
Mastery of past performance	An individual's previous experience of overcoming difficulties. Once an individual believes they are able to overcome difficulties they will be more likely to persist.
Observed experience of others	Observing others undertake similar behaviours facilitates knowledge transfer and the teaching of self-care skills.
Social persuasion	Verbal encouragement reassures individuals that they have the skills to undertake and sustain the task if problems arise.
Emotional and Physiological stress	Stress levels are a way for individuals to assess their own abilities. However it is not the stress reaction itself but the individual's perception and understanding of it which is important.

Table2.5: sources of self-efficacy

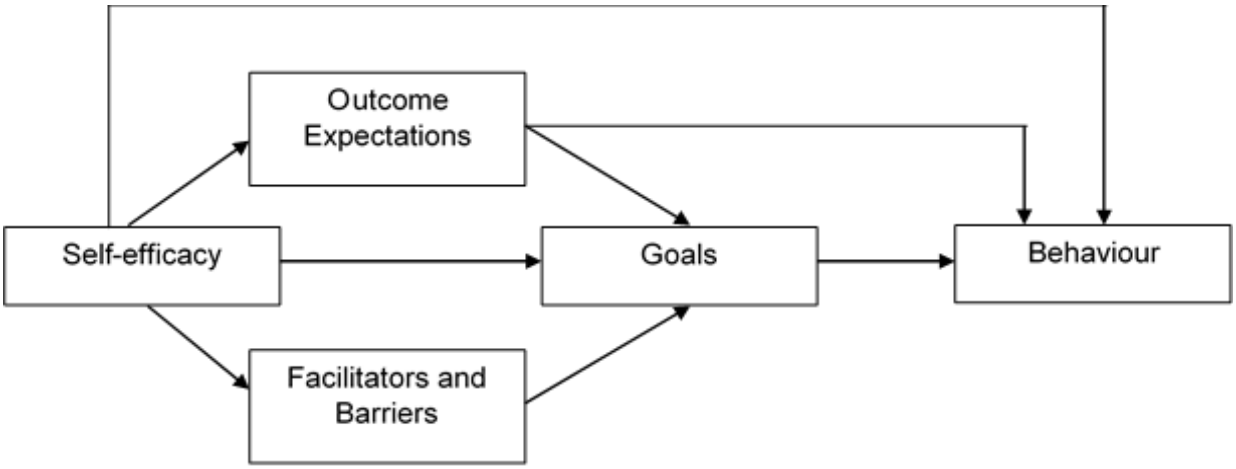

Figure2.6: impact of self-efficacy on behaviour adapted from Bandura [303]

2.3.4.1. Self-Efficacy and heart failure

Belief in self-efficacy therefore has the potential to affect an individual's QofL, particularly in a chronic often cyclical condition such as HF. For patients who require to adhere to complex treatment regimes a belief in personal ability is necessary in order for the behaviour to be completed successfully long term.

Previous literature has demonstrated a link between improved self-efficacy and self-care [304, 305]. In a study looking at the determinants of self-care in 65 patients with HF self-efficacy, as measured by level of self-confidence, was shown to significantly influence self-care behaviour [306]. Patients who believed in their ability to recognise and manage their symptoms were much more likely to engage in self-care activities such as medication adherence. Additionally, patients who had not reported a hospital admission within the previous six months reported higher self-confidence rates than those who had.

Similarly Schweitzer et al reported self-efficacy as measured by self-confidence in maintaining health to be a strong predictor for self-care in patients with HF [189]. Self-efficacy was found to predict adherent behaviour for all self-care behaviours including sodium restrictions; smoking and alcohol avoidance and exercise adherence except for adherence to medication and fluid restriction. However given the modifiable nature of self-

efficacy in that it can be tailored to either the task (adherence to medication) of the condition interventions looking to improve adherence should insure that it is targeted for improvement through improved knowledge and patient motivation [305].

2.4 Summary

In this chapter three main areas of literature have been examined: the nature and management of heart failure has been described mainly from a biomedical perspective; medication adherence and potential factors influencing adherent behaviour in HF have been discussed and finally the importance of illness perception and treatment beliefs on adherence has been highlighted.

In summary HF, a prevalent clinical syndrome, is a major cause of disability, hospitalisation and death, particularly amongst older people. For some patients defining what HF is can be problematic, not only due to the various terms used by their clinicians but due to the lack of a definitive diagnosis. The often-insidious onset of HF may result in a lengthy delay in diagnosis causing difficulty in its acceptance and association to ongoing symptoms. This, coupled with the presence of multi-morbidity, may result in suboptimal symptom management and consequentially recurrent episodes of decompensation causing significant costs in both economic and personal terms.

Medication adherence, the extent to which people follow instructions to prescribed treatment, is strongly influenced by the individual, their environment as well as the practices of associated health care professional and the care delivery system. While adherence can be measured in several different ways each method is not without limitation and currently there is no agreement on a ‘gold standard’ method of assessment. Importantly there is no evidence to suggest that 100% of adherence is needed to achieve optimal outcomes in HF.

Recent improvements which have been achieved in symptoms and mortality with the HF population can in part be attributed to the prescribing of effective medications such as ACEi, beta-blockers and spironolactone. While there is evidence to suggest that these medications can improve outcomes, there is also evidence to suggest that adherence to

medication is sub-optimal in these patients, especially amongst the older population. Results from the CHARM study where an improvement was found in all-cause mortality even in the placebo group suggests that adherent behaviour itself is associated with clinical outcome and highlights the requirement to find ways to improve medication adherence.

Beliefs around illness have influenced several theoretical models which aim to both explain and predict adherent behaviour. Leventhal et al's CSM is a widely used theoretical framework which recognises emotional influence on behaviour. The interaction between beliefs and behaviour is seen as a dynamic process which involves an appraisal of outcomes influencing beliefs. In an attempt to understand illness and treatment beliefs in HF illness representation has been measured in a limited number of qualitative and quantitative studies the later utilising both the IPQ-R and BMQ tools.

The aim of the work contained within this thesis is to establish a basis on which to develop an intervention aimed at improving adherence within the HF population. Any intervention aiming to understand and ultimately improve nonadherent behaviour must be founded on an understanding of the complexity of the problem. A narrative review undertaken based around the WHO multidimensional adherence model found limited high-quality evidence to support socio-economic; health care setting; condition related; treatment related and patient related factors as potentially influencing medication adherence in HF. Further research around the impact of these potential factors for adherence therefore requires further investigation in the older HF population.

Despite this lack of evidence previous studies have attempted to develop and evaluate interventions to improve both self-care and medication adherence within the HF population. The following chapter describes the methodology and results of a systematic review undertaken in order to evaluate such studies.

Chapter 3: Systematic Review of Interventions to Improve Medication Adherence in Heart Failure.

3.1. Background

The previous chapter highlighted that whilst achieving optimal control in chronic conditions medication adherence is vital, as many as half of all medications prescribed for long-term conditions are not taken as proposed [35]. With increasing numbers of effective self-administered treatments available, there is a clear need for better understanding and management of non-adherence within the HF population [307].

The problem of non-adherence is often multifactorial, thus programs aiming to improve medication adherence need to adopt comprehensive approaches. These interventions may include: improving patients understanding, ensuring access to adherence tools and strategies to enhance adherence and self-monitoring as well as counselling in order to be effective [306]. A literature review investigating interventions to enhance medication adherence in CHF was completed by Molloy et al in 2010 [42]. It concluded that while improvement in adherence to medication may be possible in this patient population there was a lack of clarity around the specification of effective techniques and called for further research in this area. Given that available evidence is dynamic and evolving, and that systematic reviews are most useful when they are up to date [309] this chapter continues with a description of a systematic review carried out reviewing medication adherence enhancing interventions in the HF population.

3.2. Study Design

The best research evidence available should inform decisions for health care. Systematic reviews aim to identify, evaluate and summarise the findings of all high-quality relevant studies, combining the results of several studies to obtain a more reliable and precise estimate of an intervention's effectiveness than one study alone [310].

Systematic reviews adhere to a strict scientific design based on explicit, pre-specified and reproducible methods. This systematic review was conducted using the method

described by Khan [311] to identify all relevant literature relating to interventions used to improve medication adherence in HF patients. Firstly, a clear research question was formulated before the undertaking of an extensive search using multiple resources was conducted. An assessment of for methodological quality for each included study was completed along with a summary and interpretation of the findings.

3.3. Methods

The methods described in the next section of this chapter outline the process used when searching for and evaluating the relevant literature.

3.3.1. Framing the Question

The first step in systematic reviewing is defining the research question as part of the research protocol [310]. The undertaking of an initial scoping exercise helped identify the characteristics of the question in terms of

- Who – the specific population to be studied
- What – the content of any intervention carried out as part of an RCT were a comparator was clearly identified and the
- How – what affect the intervention had in terms of outcomes

Following the initial scoping exercise the following research question was established:

"Which interventions to enhance medication adherence in patients with chronic heart failure have been tested and which, if any, have been effective?"

3.3.2. Protocol Development

Following the formulation of the research question the second step in the process is the development of the protocol. This was written to ensure the methods for literature searching, screening, data extraction, and analysis were all established within a written document to minimise bias prior to commencing the literature search. Appendix A shows the Protocol used for this systematic review.

The systematic review was registered on the PROPERO database, an international database of prospectively registered systematic reviews in health and social care and public health, registration number *CRD42015019092*.

https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015019092

3.3.3. Inclusion Criteria

3.3.3.1. Types of studies

Given the focus of the question was to identify which therapies were available randomised controlled trials (RCT's) were selected in order to include research studies yielding the highest level of evidence. RCTs where an intervention was compared to usual care or a clearly justified comparison group and where the intervention strategy clearly had a primary or secondary aim of increasing adherence to HF medication were eligible. In order to assess efficacy of the intervention included trials also required to have used a measurement of medication adherence as an outcome. Adherence reported by pill count, electronic monitoring, refill or prescription records, self-report, or biochemical measures of drug ingestion specific to heart failure medications were all eligible for inclusion.

3.3.3.2. Types of participants

The review included trials enrolling patients' ≥ 18 years of age, with a clinical diagnosis of HF, who did not have their daily medication administered by a healthcare professional. Children were excluded as not only do causes and presentation of HF in this population usually differ from adults, children are not normally responsible for adhering to their medication regime without supervision.

3.3.3.3. Types of interventions

All interventions aimed at enhancing adherence to heart failure medication compared to usual care were included. Any interventions to enhance medication adherence in other chronic diseases or those not directed at patients (e.g. trials aimed at improving the education of healthcare professionals about the importance of adherence) were excluded. For the purpose of the review studies were grouped by intervention type and categorised into one of four groups previously used elsewhere [42, 313].

1) *Patient Education and Information:* Interventions designed primarily to educate patients using methods such as face to face oral, written material, visual aids or mailed instructional materials. This method is based on the premise that patients who possess greater knowledge of their illness and treatment will be more informed and therefore more likely to adhere to prescribed therapies. Interventions are usually designed primarily to educate patients using methods such as face-to-face oral, written material, visual aids or mailed instructional materials.

2) *Intensified Patient Care:* Interventions designed to increase the contact between participant and health care professional either by direct patient contact or by telephone / tele-monitoring programs.

3) *Complex Behavioural Approaches:* These interventions usually include several components and aim to bring about changes in an individual's behaviour through changes in cognitions. They may involve processes for planning and implementing a comprehensive, strategic set of interventions and activities to change behaviours at many levels and are usually theory based.

4) *Simplification of the Drug regimen:* These interventions enhance adherence by amending dosage schedules in order to simplify the regime. This can be by either reducing the number of pills taken and/or the number of doses taken daily. This approach aims to reduce the burden associated with pill taking.

3.3.4. Exclusion criteria

The following set of exclusion criteria were applied to the reviewed studies:

1. Interventions were not aimed at enhancing adherence to heart failure medication.
2. Interventions aimed to enhance medication adherence in other chronic diseases.
3. Interventions not directed at the heart failure patients themselves. While the role health care professionals play may be an important facilitator in adherence the focus of the work in this thesis is aimed at developing an intervention that could be applied to individual HF patients. Interventions focused on the education of healthcare professionals about the importance of adherence were thus excluded.

4. Studies that did not report the results in full (e.g. conference abstracts) or studies where further information (sufficient to make a fair appraisal of the methodological quality and results of the study) were not available from the authors.
5. Non-randomised studies.

3.3.5. Electronic Search Methods

To identify and retrieve all relevant RCTs of medication adherence in HF the electronic databases of Medline, CINAHL, Embase, PsycINFO and Cochrane Central Register of Controlled Trials were searched from date of inception to end of March 2015.

For completeness, a search was made of Controlled Clinical Trials.com and National Health Service Scotland e-library (The Knowledge Network) while grey literature was identified from Google. A supplementary hand search of bibliographies of extracted articles and reviews to acquire records not identified electronically was also conducted. No limits on either language or publication status were imposed.

3.3.6. Search Terms

Before conducting the search the key words and search strings used by the author of the previous review and of authors of related articles were reviewed. The terms ‘randomized controlled trial’ or ‘controlled clinical trial’ were combined with keywords relating to non-adherence: ‘patient compliance’, ‘treatment refusal’, ‘patient dropouts ’, ‘attitude to health, ‘patient satisfaction’ ‘adherence OR non-adherence’, ‘compliance OR noncompliance or non-compliance’, ‘’ refuse’, ‘dropout’ as well as ‘heart failure’ or ‘cardiac failure’. To make the search strategy more comprehensive key terms were mapped to database specific subject headings (MeSH) then ‘exploded’ to include all relevant sub-categories. Truncations and Boolean operators (e.g. ‘AND’, ‘OR’) were used where necessary to broaden the search window.

3.3.7. Selection of studies

All identified records were imported into RefWorks 2.0 reference manager (ProQuest, Michigan, USA), and all duplicated items were removed. The files containing all the

selected titles were then exported to the second reviewer who independently pre-screened all search results (titles) for possible inclusion at the same time as I reviewed each title. Each reviewer indicated whether:

- A citation was relevant (i.e. appeared to meet the inclusion criteria)
- A citation was clearly not relevant
- A citation gave insufficient information to make a judgement.

All discrepancies were resolved by discussion and consensus, overseen by a third review author, with abstracts for all potentially relevant titles subsequently obtained and the process repeated.

Full text articles were obtained either where abstracts appeared relevant or when insufficient information was provided from which an adequate assessment of relevance could be made from the abstract alone.

3.3.8. Data extraction

The standardised data extraction form (see Appendix B) was developed using guidelines in the Cochrane Collaboration Handbook [314] and then piloted on a random sample of two studies. The following data were collected:

a) Study characteristics: including the study design, inclusion/exclusion criteria; recruitment procedures used (e.g. details of randomisation, blinding).

b) Patient characteristics: including age, gender, ethnicity, severity of illness, co-morbidities; current medication, as well as number of participants in each characteristic category for intervention and control group.

c) Intervention and setting: including the setting in which the intervention is delivered; method of delivery; description of the intervention and control; duration of treatment period; sample size and description of co-interventions if relevant.

d) Outcome data/results: including outcome names; measurement tool or method used for outcome measures; length of follow-up number and/or times of follow-up

measurements; number of withdrawals, exclusions, deaths or recorded hospitalisation and results of study analysis.

3.3.9. Assessment of Risk of Bias

An overall risk of bias assessment was conducted on all included studies based on checklists recommended by the Cochrane collaboration [315]. For each study a summary assessment was made for the primary outcome (high, low or unclear risk of bias). Each study was assessed for adequate sequence generation and allocation concealment (selection bias), the presence of blinding in outcome assessment (performance and detection bias), and whether reporting of losses to follow-up and intention-to-treat analysis were specified (attrition bias) using a standardised quality checklist developed from the Cochrane Collaboration quality assessment tool (See table 3.1 for classification scheme).

Type of Bias	Description	Relevant domain in Cochrane's Risk of Bias tool
Selection bias	Systematic differences between baseline characteristics of the groups that are compared.	Sequence generation Allocation generation
Performance bias	Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.	Blinding of participants and personnel
Detection bias	Systematic differences between groups in how outcomes are determined.	Blinding of outcome assessment Other potential threats to validity
Attrition bias	Systematic differences between groups in withdrawals from a study.	Incomplete outcome data
Reporting bias	Systematic differences between reported and unreported findings.	Selective outcome reporting

Table3.1: Classification scheme for Bias adapted from Cochrane Handbook [315]

3.3.10. Data Synthesis

Clinical and methodological heterogeneity across the included studies was evaluated by comparing the characteristics of participants, interventions and study designs. Where data were missing or insufficient or missing additional information was sought from the study authors. Meta-analysis, the process of pooling collected data quantitatively and re-analysed using established statistical methods [316] was considered, but included studies were found to be insufficiently homogeneous in terms of design and measurement of adherence to allow meta-analysis of results.

3.4. Results

The five main databases searched yielded a total of 3279 records as shown in Table 3.2

Database	Number of records
Medline	1937
Embase	502
PsycINFO	1
Cinahl	740
Cochrane Central Register of Controlled Trials	99
Total	**3279**

Table3.2: Records identified by database searches

The Knowledge Network library identified 178 studies while clinical trials.gov identified 24 giving a total of 3,481 records. A review of literature in Google did not produce any previously unidentified records. After combining the search results into one library using RefWorks 2.0 and removing 1,680 duplicated records 1,801 records remained. Figure 3.1 shows the PRISMA diagram depicting the flow of information through the different phases of the systematic review.

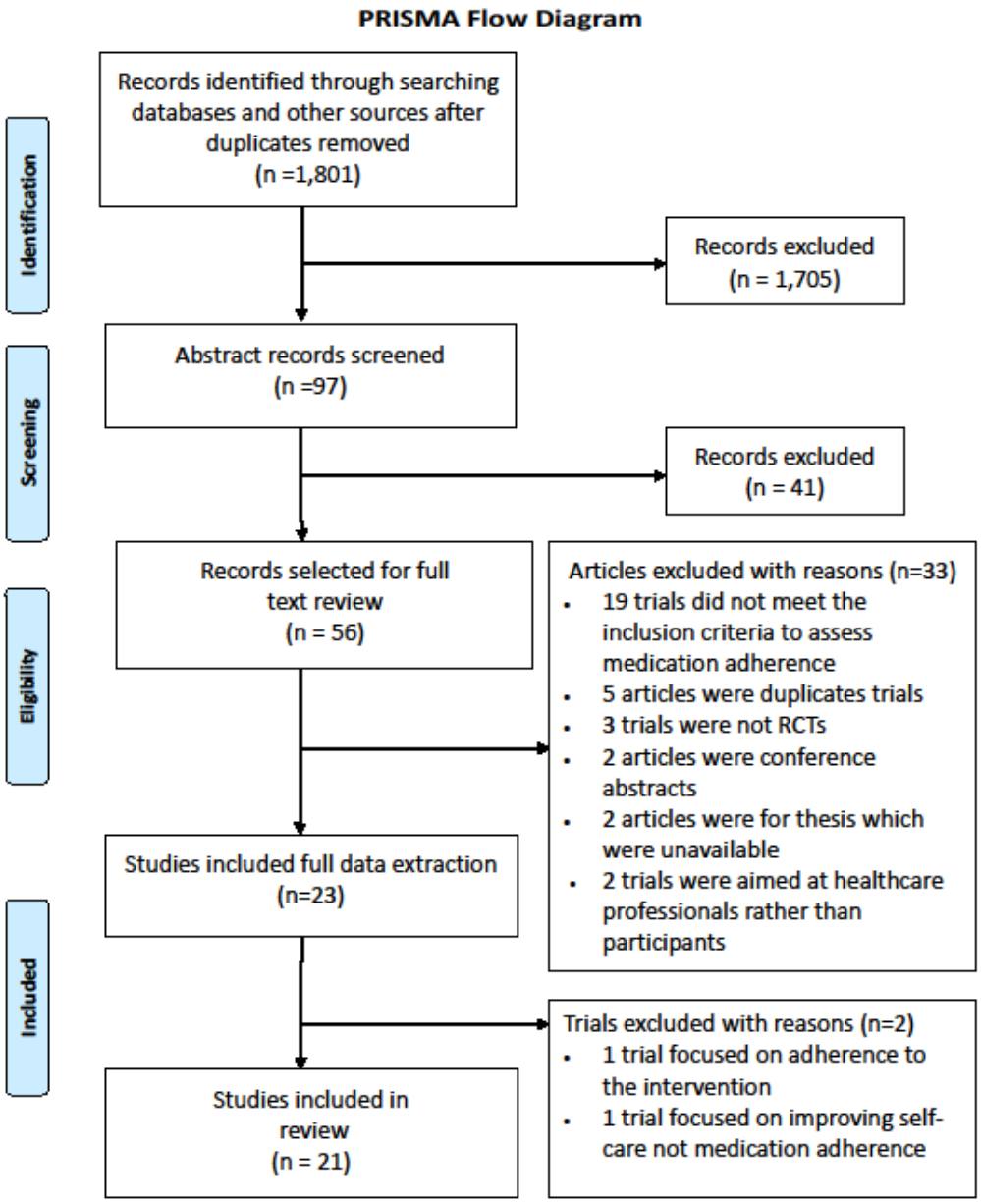

Figure3.1 PRISMA flow diagram for systematic review (reproduced from Fulton, 2017 [317]

After reviewing the titles and abstracts of all 1,801 records 56 articles were considered suitable for full text appraisal. Almost half of the records were excluded following a review of the full text for the following reasons:

1) The majority of the records (19/35) excluded from the narrative review were excluded because the aims of the interventions did not include improving medication adherence [316-334]

2) Two records were identified as conference abstracts. Several attempts were made to contact the authors of the first [337] however non-response meant this article was excluded as the abstract contained insufficient data from which an inadequate assessment of risk of bias could be made. The second conference abstract record was not included as this was found to be related to another title which contained all the data required to make a judgement on possible inclusion [338]

3) Five records on closer inspection were found to be in fact duplicates of four independent trials which had been selected for inclusion in the narrative review [339-343].

4) Two records [344, 345] were abstracts for theses. Attempts were made to locate and contact authors; one was unobtainable, while an email was sent to the other. No response was received thus both were excluded.

5) Two studies [346, 347] were excluded as the intervention being trialled was directed at the healthcare professional rather than the heart failure patient.

6) Three records were found to be non-randomised controlled trials and thus did not meet the inclusion criteria [348-350].

7) On closer inspection another two articles were subsequently excluded for inclusion in the narrative synthesis. The trial by Goldstein et al [351], although looking to improve medication adherence, focused the use of the adherence aids themselves while the trial conducted by Bocchi et al focused on improving self-care not medication adherence [352].

Therefore the evaluation of the 56 full texts yielded 21 studies that met the inclusion criteria for the systematic review. No further studies were identified following hand searching of the reference lists of the 21 studies. Characteristics of the included studies are presented in table 3.3.

Lead Author	Sample size Follow up (%)	Mean Age, Years (SD)	Male %	Adherence Measurement	Follow up in months	Key Study Findings Relating to Adherence Intervention group	Key Study Findings Relating to Adherence Control group
Goodyer (1995) United Kingdom[355]	100 (80%)	C: 85 (5.4) I: 84 (4.5)	C: 24% I: 30%	Pill counts	3	61% at baseline 93% at follow-up	49% at baseline 51% at follow-up
Rich (1996) United States [3564]	156 (not supplied)	C: 78 (6.1) I: 81 (5.7)	C: 41% I: 26%	Pill counts	1	88% Adherence ≥ 80% achieved by 85%	81% Adherence ≥ 80% achieved by 70%
Fulmer (1999) United States[357]	50 (84%)	C: 74 (5.3) I1: 76 (8.8) I2: 73 (6.5)	C: ? I1: ? I2: ?	Medication event monitoring system to measure up to 4 heart failure-related medications	2 weeks	Telephone intervention remained stable: 76-74% Video-telephone intervention remained stable: 82-84%	Adherence dropped from 81-57%
Varma (1999) Northern Ireland[358]	83 (28-59%)	C: 76 (7) I: 76 (6)	C: 37% I: 45%	Self-reported binary and drug use profiles using patient records.	12	10/13 (77%) according to patient medication records: n=23 for this analysis	3/10 (30%) according to patient medication records: n=23 for this analysis
Bouvy (2003) The Netherlands[359]	152 (60%)	C: 70 (11.2) I: 69 (10.2)	C: 60% I: 72%	Medication event monitoring system to measure loop diuretic adherence	6	140/7656 (2%) days Reported without the use of loop diuretic	337/6196 (5%) days Reported without the use of loop diuretic

Lead Author	Sample size Follow up (%)	Mean Age, Years (SD)	Male %	Adherence Measurement	Follow up in months	Key Study Findings Relating to Adherence Intervention group	Key Study Findings Relating to Adherence Control group
Laramee (2003) United States[360]	287 (82%)	C: 71(12.2) I: 71 (11.4)	C: 50% I: 58%	Self-reported measure of medication taking on a 5- point scale: 1 – never; 5 always.	3	No Significant difference between groups. Each group self-reported excellent adherence	
Ross (2004) United States[3]	107 (76%)	C: 55 I: 57	C: 74% I: 80%	Self-report: General Adherence Scale from Medical outcomes Study	12	3.6 / 4 at 12 mo follow-up	3.4 / 4 at 12 mo follow-up
Tsuyuki (2004) Canada[362]	276 (100%)	C: 72 (12) I: 71 (12)	C: 58% I: 58%	Pharmacy records: medication procession ratio calculated based on number of days ACE inhibitor dispensed divided by no. days of follow- up	6	84%	86%
Gwadry-Sridhar (2005) Canada [354]	136 (99%)	C: 65 (12) I: 67 (14)	C: 69% I: 76%	Heart failure medication refill records.	12	ACE inhibitor 87% B Blockers 87% Digoxin 85% Diuretics 77%	ACE inhibitor 83% B Blockers:8% Digoxin 81% Diuretics 77%

Lead Author	Sample size Follow up (%)	Mean Age, Years (SD)	Male %	Adherence Measurement	Follow up in months	Key Study Findings Relating to Adherence Intervention group	Key Study Findings Relating to Adherence Control group
Sadik (2005) United Arab Emirates [363]	314 (86%)	C: 63 (8.8) I: 61 (7.7)	C: 34% I: 32%	Medication event monitoring system to measure taking and scheduling adherence to cardiovascular medications	12	Adherence was self-reported as 82% at 12 mo follow-up	Adherence was self-reported as 34% at 12 mo follow-up
Lopez- Cabezas (2006) Spain [364]	134 (not supplied)	C: 76 (9.4) I: 75 (8.4)	C: 47% I: 41%	Pill counts	12	88% at 2 mo 91% at 6 mo 85% at 12 mo	61% at 2 m 69% at 6 m 74% at 12 m
Murray (2007) United States[365]	314 (86%)	C: 63 (8.8) I: 61 (7.7)	C: 34% I: 32%	Medication event monitoring system to measure taking and scheduling adherence to cardiovascular	12	Adherence was 79% Reducing to 71% at 3mo follow-up Medications taken on schedule 53% 49% at 3mo follow-up	Adherence was 68% Reducing to 67% at 3 mo follow-up Medications taken on schedule 47% 49% at 3mo follow-up
Udelson (2009) United States[243]	269 (91%)	C: 66 (12.8) I: 65 (11.9)	C: 71% I: 77%	Medication event monitoring system to measure carvedilol adherence	5	88%	89%

Lead Author	Sample size Follow up (%)	Mean Age, Years (SD)	Male %	Adherence Measurement	Follow up in months	Key Study Findings Relating to Adherence Intervention group	Key Study Findings Relating to Adherence Control group
Wakefield (2009) United States[366]	148 (74%)	C: 63 (8.5) Tele I: 72 (10.2) Video I: 69 (9.6)	C: 98% Tele I: 80% Video I: 98%	Self-report: The proportion of medications for which the participants' responses agreed with the directions for use	6	86%	91%
Antonicelli (2010) Italy[367]	57 (not provided)	C: 79 (6) I: 77 (8)	C: 66% I: 57%	Self-report by telephone: No other detail provided	12	90%	36%
Powell (2010) United States[352]	902 (70%)	C: 63 (13.3) I: 64 (13.7)	C: 52% I: 54%	Medication event monitoring system to measure to ACE inhibitors adherence or βBlocker when ACE was not prescribed	12		
Wu (2012) United States[276]	82 (not provided)	C: 59 (13.5) I1: 64 (11.9) I2: 57 (13.3)	C: 46% I1: 63% I2: 63%	Medication event monitoring system to measure hear failure medication Adherence was assessed as ≥ 88%	9	I1 group 70% at baseline 74% at 9 mo follow-up I2 group 59% at baseline 65% at 9 mo follow-up	64% at baseline 36% at 9 mo follow-up

Lead Author	Sample size Follow up (%)	Mean Age, Years (SD)	Male %	Adherence Measurement	Follow up in months	Key Study Findings Relating to Adherence Intervention group	Key Study Findings Relating to Adherence Control group
Dunbar (2013) United States[368]	117(69%)	C: 56 (10.3) I1: 57 (11.1) I2: 55 (10.2)	C: 68% I1: 55& I2: 68%	Medication event monitoring system (MEMS) for 2 wk. period & Morisky Medication Adherence Scale(MMAS) Adherence was assessed as ≥ 80%	8	MEMS - I1 -91% at baseline – 90% at 8 mo follow-up I2 -87% at baseline – 83% at 8 mo follow-up MMAS for I1 – 85% at baseline 77% at 3 mo follow-up MMAS for I2 – 89% at baseline – 81% at 3 mo follow-up	MEMS – 8 0 % at baseline – 88% at 8 mo follow-up MMAS – 82% at baseline - 86% at 3 mo follow- up
Mussi (2013) Brazil [369]	287 (82%)	C: 63 (12.1) I: 63 (13.7)	C: 64% I: 63%	Self-reported measure of medication taking on a 5-point scale: 1 – never; 5 always	3		
Boyne (2014) The Netherlands[341]	382	C: 72(10.5) I: 71 (11.9)	C: 60% I: 58%	Self-reported 5 point Likert scale: 0 – never; 4 always	12	100% at follow-up	99% at follow-up
Granger (2015) United States[370]	86 (87%)	C: 60 (11.5) I: 60 (11.6)	C: 52% I: 76%	Pill counts & Morisky Medication Adherence Scale(MMAS)	12	≥ 80% pills taken in 55% at 3 m follow-up 70% at 12 m follow-up MMAS - 5.03 at baseline 7.04 at 12 mo.	≥ 80% pills taken in 28% at 3 m follow-up 30% at 12 m follow-up MMAS - 4.80 at baseline 6.12 at 12 m

Table3.3: Characteristics of included studies (Adapted from Fulton, 2017 [315].

C, Control group; I, Intervention group; 11, Intervention group 1; 12, Intervention group 2; MMES, Medication event monitoring system; MMAS, Morisky Medication Adherence Scale

3.4.1. Assessment of Risk of Bias

The reporting quality of the 21 included studies was sufficient to adequately assess the potential risk of bias. Judgements regarding the risk of bias for each study were categorised as: “Low risk of bias”, High risk of bias” or “Unclear risk of bias”. Table 3.4 shows the risk of bias assessment for each of the included studies.

Sixteen trials provided information about adequate sequence generation, however allocation concealment was unclear in 10 of the 21 studies. Although masking participants to intervention allocation is difficult in most behavioural studies, two of the included studies did make an attempt to do this by offering an educational intervention to both groups [342, 343]. Information regarding the blinding of adherence assessors that was sufficient to make a judgement was available in only 13 of the 21 studies, with clear blinding of outcome data evident in only eleven of the of the included studies. Seventeen studies reported details for participants lost to follow up but only twelve studies specified intention to treat analysis. None of the trials met all the criteria.

3.4.2. Characteristics of Included Studies

Twenty-one randomised controlled trials were identified containing a total sample of 4,346 patients. The median sample size was 148 patients with a range from 50-902.

More than half the studies (11/21) were carried out in United States with 6/21 carried out within Europe. The average age of the participants ranged from 56 to 85 years with male participation ranging from 27% to 92%. The median follow-up time was 9 months, ranging from 2 weeks to 12 months, with 10 of 21 (48%) of studies having follow-up times of ≤6 months. The mean percentage of patients included at follow-up was 80.7% in the 17/21studies that provided these data with a range of 28–100%. Adherence to medication was measured in several different ways across the included studies. Participant self-report was used as an outcome measure in 8 studies, the medication event monitoring system in 7 studies; tablet counts in 4 studies,

	Random Sequence Generation (selection bias)	Allocation Concealment (Selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome data (detection bias)	Incomplete outcome data (attrition bias)	Selective outcome reporting (reporting bias)
Goodyer (1995)	L	U	H	L	L	L
Rich (1996)	L	L	H	L	L	L
Fulmer (1999)	L	L	H	H	H	L
Varma (1999)	L	U	H	U	L	L
Bouvy (2003)	L	L	H	U	L	L
Laramee (2003)	U	U	H	H	L	L
Ross (2004)	L	L	H	U	L	L
Tsuyuki (2004)	L	L	H	U	L	L
Gwadry-Sridhar (2005)	L	L	L	L	L	L
Sadik (2005)	L	U	H	L	L	L
Lopez-Cabezas (2006)	L	L	H	L	H	L
Murray (2007)	L	L	H	L	H	L
Udelson (2009)	L	U	H	U	L	L
Wakefield (2009)	L	L	H	U	L	L
Antonicelli (2010)	U	U	U	L	H	H
Powell (2010)	L	L	L	L	L	L
Wu (2012)	U	U	H	U	L	L
Dunbar (2013)	U	U	H	L	H	L
Mussi (2013)	L	L	H	L	L	L
Boyne (2014)	L	U	H	U	L	L
Granger (2015)	U	U	H	H	L	U

L= Low risk of bias H= High risk of bias U= Unclear risk of bias

Table3.4: Risk of bias assessment for each of the included studies reproduced from Fulton, 2017 [317]

and medication refill records in 2 studies. Two studies using other methods also measured Morisky Medication Adherence Score (MMAS).

Adherence rates across the studies ranged from 28% to 93% however across the 21 studies the 21 studies the heterogeneity of measurement of adherence and limitations in reporting make it difficult to carry out a meta-analysis of rates of adherence or results for the reviewed studies.

3.4.3. Reported Intervention Techniques

Intervention techniques varied widely across the studies. While the reviewed trials were classified into four categories it is important to highlight that several of the trials contained multicomponent interventions that could have been included in more than one of these categories. A clear alternative categorization of strategies did not emerge.

3.4.3.1. Patient Education and Information

Three trial interventions were classified as patient education [354, 364, 368] offered as individual sessions except for Dunbar and colleagues [368] who offered group education. Written and verbal Information was delivered in all of the studies while family education was included in 2/3 studies [364,368]. The study described by Lopez-Cabezas [364] found that initial improvements to adherence noted between groups had disappeared by 12-month follow-up while neither of the other two trials found evidence that this class of intervention led to enhanced adherence. All studies did however report adherence rates of ≥ 74% at follow-up. Two of the three studies were carried out on patients post hospital discharge with only Dunbar et al targeting outpatients while two of the three trials were delivered by a pharmacist [368,354]. It is important to note that this intervention also incorporated intensified patient care and simplification or optimisation of medication regimens.

3.4.3.2. Intensified Patient Care

The majority of trials (14/21) were categorized as intensified patient care and could be further subdivided into (a) nine direct patient contact interventions [355, 356, 358-360, 362, 363, 365, 369] and (b) five telephone or tele monitoring programs [341, 357, 361, 366, 367]. Five of the nine direct patient contact interventions led to

enhanced medication adherence [355, 356, 358, 359, 363], whereas only 1 of the telephone or tele monitoring programs led to enhanced adherence [367]. Of the 5 telemonitoring studies 3/5 involved contact with a healthcare professional via a telephone or video phone [357, 366,367] with the others increasing contact with patients online [369] or by other electronic devices [341]. Only 1/5 trials categorized as telephone/tele monitoring carried out by Antonicelli and colleagues reported enhanced medication adherence. The intervention involved contact with the patient or next of kin by telephone call at least weekly, to obtain information on adherence and clinical symptoms in order to evaluate and modify therapeutic regimes. However, the sample size was small, follow up was not reported and no detail was given regarding the outcome method other than self-report. Unfortunately several of the other telemonitoring studies reported consistently high adherence levels throughout reducing the potential for significant findings relating to the intervention itself. Five of the eight direct patient contact interventions were pharmacist-led.

3.4.3.3. Complex Behavioural Approaches

Three studies examining complex multicomponent interventions to enhance medication adherence in HF were identified in this review [276, 352, 370]. The study carried out by Powell and colleagues in over 900 HF patients found no evidence that a complex multicomponent intervention that included a range of behavior change techniques led to enhanced medication adherence. A smaller study by Granger et al which also used a complex intervention (in-depth interviewing to determine beliefs, concerns and perceived necessity for medication in order to develop a symptom response plan) did however report a significant between-group difference in adherence (70% vs. 30%) in favour of intervention group at 12 month follow-up [370].

Wu et al also recorded a significant between-group difference in their study which evaluated an intervention based on the TPB [276]. Eighty-two participants were randomised to one of three groups: a) education and behaviour change counselling, b) education, behaviour change counselling and feedback from medication taking using MEMS or c) usual care. Enhanced medication adherence was reported in both the intervention groups at 9-month follow-up.

3.4.3.4. Simplification of the Drug Regimen

Only one study solely targeted simplification [243]. This study attempted to evaluate medication simplification to a simpler controlled release regime but did not find evidence of enhanced adherence. Attempts to simplify medication regimens did occur in some of the other studies included in this review [356, 363] although not necessarily directly by the research team. A full description of the interventions used in each study is detailed in Table 3.5.

3.4.4. Studies showing positive results

Of the 21 studies included in the review only 8 showed significant improvements in medication adherence compared to the control group. More than half of these (6/8) used intensified patient care and the other two complex behavioural approaches.

3.4.4.1. Intensified patient contact trials:

I. Bouvy et al [359] evaluated a pharmacist led intervention aiming to enhance compliance to diuretic therapy in heart failure patients. Structured interviews using medication history facilitated discussion of drug use, reasons for non-adherence, possible side effects and the integration of medicines into daily life. Those participants allocated to the intervention group received monthly interviews for the six-month follow up period. Medication event monitoring system (MEMS) data were collected on loop diuretic medication only. Total adherence was recorded as total possible days without diuretic: intervention group 140/7656 possible days versus control group 337/6196 (relative risk 0.32 [95%CI 0.19-0.55]).

II. Goodyer et al [355] carried out a counselling-based intervention delivered to outpatients with heart failure aged 70 years and over. Each participant received three episodes of counselling over a 3-month period by a pharmacist who incorporated individual verbal counselling, medication calendars and written information leaflets into the trial. The primary

	Knowledge and skills assessment	Patient education in groups	Patient education individual	Telephone strengthening	Direct follow-up	Web-based information system	Verbal information	Written information	Audio-visual information	Active learning activities	Identification of medication beliefs	Identification of barriers	Family education/participation	Eliciting support from health care providers	Enhancing communication between health care providers	Tele-health remote Symptom control	Self-monitoring	Individual feedback of self-monitoring	Discharge planning with participant	Goal setting	Establishment of symptom response plan	tele prompts to take medication	Use of adherence aids	Simplification of the medication regimen
Goodyer [1995]			✓				✓	✓															✓	
Rich [1996]			✓				✓	✓																✓
Fulmer [1999]							✓															✓		
Varma [1999]			✓				✓	✓						✓	✓		✓							
Bouvy [2003]			✓				✓					✓			✓									
Laramee [2003]			✓	✓			✓	✓					✓	✓	✓		✓		✓				✓	
Ross [2004]			✓			✓			✓														✓	
Tsuyuki [2004]			✓	✓				✓									✓						✓	
Gwadry-Sridhar [2005]			✓				✓	✓	✓															
Sadik [2005]			✓				✓	✓							✓		✓							✓
Lopez-Cabezas [2006]			✓	✓			✓	✓					✓											
Murray [2007]	✓						✓	✓						✓	✓								✓	
Udelson [2009]																								✓
Wakefield [2009]															✓	✓	✓		✓	✓				
Antonicelli [2010]																✓								
Powell [2010]			✓					✓				✓					✓							
Wu [2012]			✓	✓			✓				✓	✓	✓		✓									
Dunbar 2013		✓		✓			✓	✓	✓	✓			✓				✓	✓						
Mussi [2013]			✓	✓			✓						✓				✓							
Boyne [2014]							✓	✓								✓								
Granger [2015]			✓	✓	✓			✓		✓	✓						✓				✓		✓	

Table3.5: Description of Study interventions (shaded areas represent studies reporting significant improvement in medication adherence)

outcome measurement was the mean adherence scores, expressed as a percentage of the maximum medication that should have been taken. While there was no significant between-group difference at baseline: control group 49% (SD 33%) versus intervention group 61% (SD 31%), by three months adherence was reported as 51% (SD 32%) in the control group versus 93% (SD 11.7%) in the intervention group ($p<0.001$).

III. Rich et al [356] targeted inpatients with heart failure aged 70 years and over. Using a prepared teaching guide those participants receiving the intervention received daily visits until hospital discharge from the study nurse who repeatedly emphasised the need for medication adherence. Members of the wider multidisciplinary team including a dietitian, social services representative and a geriatrician who carried out a medication review also visited as part of the intervention. Following discharge, participants in the intervention group received regular contact from the study nurse until the 30 day follow up appointment as well as a visit from the homecare team. Outcome measurement was by pill count at 30-day follow-up. Overall adherence was measured in two ways: firstly, the percentage of pills taken correctly for each medication was calculated then values averaged, and secondly the total number of pills taken was divided by the total number which should have been taken. For method 1, adherence was 88% ± 12% in the treatment group verses 81% ± 17% in the control group ($p=0.003$) while adherence rates using the second method were 88 ± 13% versus 81 ± 17% ($p=0.004$).

IV. Another pharmacy led trial reported by Sadik et al [363] involved a pharmacist who identified possible areas for drug simplification with the physician of participants in the intervention group; each participant then received an information booklet and advice on self-monitoring. Self-monitoring diaries were issued to participants in the intervention group and used to facilitate discussion about their condition at any subsequent appointments with their physicians. In addition completed diary cards

where returned to the research pharmacist each time medication was re-issued with the pharmacist reviewing and offering guidance as required. Outcome measurement was adherence by self-report which was measured at 3 monthly intervals until the trial was complete at 12 months. The number of intervention group patients versus control who exhibited self-reported medication as demonstrated by completed entries in the self-monitoring diary was reported as 85 versus 35 at 12 months ($p < 0.05$).

V. Varma et al [358] conducted a trial in 83 older HF patients. Participants in the intervention group received a pharmacist led education programme focusing on the condition, its treatment and symptom control along with simplification of their medication regime. Outcome measurement relating to medication adherence was collected by self-report and knowledge of HF medication with additional analysis of pharmacy drug use profiles (DUP) available in 26/83 (31%) of participants. At 12-month follow-up the intervention group demonstrated an increased knowledge of medication compared to the control group ($p=<0.05$) and while DUP reported a statistically significant difference in adherence between groups ($p=0.039$) no significant difference was noted using the self-report data.

VI. Antonicelli et al [367] conducted the only successful intensified contact trial that investigated the impact of telemonitoring systems on medication adherence in heart failure. During the 12 month follow up period a member of the telemonitoring team contacted each participant in the intervention group at least weekly by telephone to obtain information on heart rate, blood pressure and other clinical signs, which were evaluated by the team, and the therapeutic regime modified as necessary. All participants, regardless of group allocation, were seen by their hospital clinician every 4 months. The outcome measure was self-report however no other information on this outcome was provided. Adherence was reported as 90% in the intervention group versus 36% in the control group ($P<0.03$). Several unsuccessful attempts were made to contact the authors for further information thus it is difficult to determine the true effect of this intervention given those in the intervention group had

significant changes made to their medication regime by the study team in direct response to the ongoing clinical information being gathered which may have had more of an impact on their adherence behaviour than the intervention itself.

3.4.4.2. Complex Behavioural Approach Trials

VII. Granger et al [370] conducted a trial exploring the theoretical linkage between symptom experiences and medicines with the aim of improving adherence to medication. A symptom response plan was developed following an in-depth interview where participants and carers were encouraged to establish meaningful associations between adherence and symptom onset. Skill-based learning was used to facilitate learning of the medication regime. Adherence was measure by both nurse assisted pill counts and by using the Morisky Medication Adherence Scale (MMAS). Using an adherence cut off of 80%, results pooled over all time points reported that participants in the intervention group were 4 times more likely to be adherent to medications than those in the control group (odds ratio 3.92, p=0.0007). Participant reporting using the MMAS mean score also indicated higher adherence: intervention group 7.04 (SD 1.55) versus control 6.12 (SD 1.33; p=0.005).

VIII. Wu et al [276] trialled an intervention based on the theory of planned behaviour, which included personalised feedback of medication-taking behaviour by a nurse to enhance medication adherence in a younger population with heart failure (mean age 60 years). Two intervention groups were established, one which received four sessions of counselling and teaching (Lite) and another (Plus) which received feedback in addition to the teaching and counselling to encourage positive behaviours. The intervention groups both participated in two face to face teaching/counselling sessions delivered during months one and two with telephone follow up sessions conducted two weeks after each face to face session. All participants, including those in the control group, received a monthly telephone call to collect outcome data between months 3 and 9. MEMs was again used to assess adherence at 1, 2 and

9-month time points with 88% of medications taken chosen by the study team as the cut-off point for adherence. The trial reported that both intervention groups were more adherent to medications at 9-month follow-up: Plus group 74%; Lite group 65% versus control group 36% (p=0.015).

3.4.5. Components of interventions

3.4.5.1. Personnel

Across the 21 included studies interventions were carried out by a variety of qualified people including specialist cardiac nurses and medics and other professional disciplines with a cardiac background. A multidisciplinary team approach was employed in one study [356] however a number of interventions were delivered by staff who did not have obvious clinical experience of heart failure [352, 357, 360, 362, 366, 368]. In the main pharmacist input appeared to be utilised more often than others in successful direct patient contact interventions [358, 359, 363].

3.4.5.2. Education

Education on condition or treatment was identified as the most commonly utilised component and reported as an element in the majority of studies 15/21(71%) [276,353-356,358-364,368-370]. Within these studies participants received educational information on a one to one basis, except for those undertaking the study by Dunbar et al where group educational sessions were delivered [366]. All included studies provided participants with increased information in varying forms with the exception of the study by Udelson which focused on simplification of medication regime [243] and two studies focusing on telehealth [364,365]. For those eight studies reporting positive results [276,355,356,358,359,363,367, 370] all except one [367] provided participants with either written or verbal information as part of the intervention.

3.4.5.3. Self-monitoring

A self-monitoring component was identified in 9/21(43%) studies with participants engaging in activities such as the monitoring of shortness of breath and tiredness as well as the recording of daily weights and oedema.

However less than half of these included structured guidance if symptoms deteriorated [358, 360, 363, 370]. Overall self-monitoring was included in 3 of the 8 studies reporting positive results [358, 363, 370].

3.4.5.4. Prompts/restructuring

Several of the studies identified a need for review or restructuring of the treatment regime. Several studies addressed burden of treatment by looking to simplify prescribed treatments [243, 356, 363] while prompts and adherence aids were utilised in several others [355, 357, 360, 362, 365, 370]. Overall 4/8(50%) interventions which reported positive results included this component in their design.

3.4.5.5. Beliefs around medication

Finally while only two studies focused on the role of individual beliefs around medication both reported positive outcomes [276,3708]. Granger et al utilised a framework which encouraged HF patients to identify personal beliefs and concerns around prescribed treatment in order to develop meaningful association between symptoms and treatment [370]. The intervention by Wu et al looked to encourage positive beliefs about medication again by establishing an association between the condition, symptoms and treatment [276].

3.5. Discussion

In common with previous reviews of the literature, the proportion of patients adhering to their medication varied greatly between studies [11, 112]. However the overall estimate of approximately one third of patients not taking medications as prescribed underlines the importance of being able to identify and offer appropriate interventions to this large group of patients.

Successful management of HF is complex, requiring significant input from patients, carers and healthcare providers to achieve optimal control. Treatment for the condition usually encompasses pharmacological therapies, behaviour modification and ongoing monitoring [371] and the multifactorial nature of non-adherence requires programs aiming to improve medication adherence to adopt comprehensive approaches. In this systematic review of interventions to enhance medication adherence in patients with CHF

medication adherence was reported to be significantly higher in the intervention group compared to control group by the end of follow-up in 8 studies. Evidence of effective interventions using various different techniques was found however a set of clearly efficacious intervention strategies did not emerge. The most commonly used intervention was the provision of education to enhance knowledge of heart failure and drug therapy, however the evidence suggests that simply supplying information without enhanced contact from professionals within the healthcare team does not appear to be a successful way to help patients optimise the use of their medication. Five of the eight direct patient contact interventions were pharmacist-led which may go some way to explain why the use of aids to adherence such as medication calendars, pillboxes or simplification of drug regimens interventions [355, 356, 360, 362, 363, 365].

As with the previous systematic review in this area, there was evidence to support pharmacist-led interventions, especially when such initiatives were underpinned by engagement with other healthcare professionals [358, 359, 363]. Two of the three trials adopting a complex behavioural approach reported enhanced adherence. Both were much smaller than the third trial which did not show a benefit. Interestingly though, both of these smaller trials adopted an educational component and telephone follow-up as part of their intervention [276, 370]. Given that adherence has multidimensional contributory factors it may be that a complex behavioural intervention, underpinned by a clear theoretical framework and combining components of knowledge, self-monitoring and enhanced communication between health care providers may achieve better results.

Although the average age for first diagnosis of heart failure is 76 years [83] the majority of trials included in the review enrolled participants with a lower mean age and are thus not representative of the typical heart failure patient seen in clinical practice. This limits the generalisability of the findings and calls into question how transferrable some of the interventions may be to older, frailer heart failure patients. It is also well documented that the average rates of adherence in clinical trials can be remarkably high, owing to the attention study patients receive and to selection biases operating in recruitment. With no general consensus around what is an acceptable level of adherence it is

difficult to compare results even in trials that claim to report positive results but where no definition of what is meant by ‘adherent’ is given.

Given that lack of adherence is an issue common across populations with chronic disease and not specific to patients with heart failure, interventions may be better targeted towards high risk groups that cut across disease silos, for example those with a low level of health literacy, sensory impairment or linguistic and cultural differences, rather than targeting the intervention at one particular disease.

3.6. Limitations

As with any systematic review it is possible that some trials may have been missed despite a detailed search of databases, grey literature and thorough hand searching of reference lists. The quality of the review results is limited by the methodological choices and the quality of reporting of the primary study researchers, which resulted in research methodology and intervention techniques varying widely.

Heterogeneity in intervention techniques, limitations in intervention reporting and measurement methodology left an inability to conduct a meta-analysis or provide a coherent method of categorising the identified studies, while lack of response from authors of original papers and abstracts resulted in the exclusion of several trials due to inadequate reporting of intervention methods and outcome data. Tallying positive studies has well-recognised limitations and therefore the results should be interpreted with caution.

The categorisation method chosen also deserves comment; the grouping was chosen on pragmatic grounds based on the emergent features of the included studies, however the four categories were not necessarily mutually exclusive nor systematically developed.

The difficulty in measuring adherence accurately is a significant limitation for any systematic review seeking to assess the effectiveness of different adherence enhancing strategies. Currently there is no ‘gold standard’ for measuring adherence to medication with no agreed method of measurement [(8)]. It is also worth noting that the high levels of adherence at baseline found in

many of the trials included in this review might reduce the efficacy of interventions (the ‘ceiling effect’) and may thus lead to under-estimation of the intervention effect in less adherent populations.

3.7. Conclusions

This review sought to broaden understanding of interventions on adherence in patients with chronic heart failure. A review of the literature concluded that the reasons for non-adherence to medication in patients with HF are complex and multi-factorial with health behaviours and outcomes influenced at several levels, starting with the individual and continuing with the family and the community, the health care system, and ending at the environmental level. RCTs in this area however are still limited in both number and quality.

Heterogeneity in both intervention techniques and measurement methodology resulted in an inability to establish a reliable and effective intervention approach. Importantly the lack of a mutual agreement on valid methods for measuring adherence as well a lack of representative inclusion of older patients with chronic heart failure failed to give a realistic picture on which interventions are successful in patients routinely seen within clinical practice. Few studies included in this review failed to include long term follow-up, of 12 months and more, which may have provided a more realistic picture of adherence to life-long treatment and allowed for the evaluation of morbidity and costs.

While this review provided evidence to suggest adherence to medication can be improved in patients with chronic heart failure a clear picture of specific effective interventions did not emerge. The results highlight the need for future research focusing on multi-component interventions, acknowledging patients’ beliefs and preferences and incorporating them into adherence-enhancing interventions which combine a number of strategies including information provision, reminding and reinforcement.

In order therefore to develop an effective complex intervention aimed at improving adherence in HF patient’s perceptions and experiences of this group of patients in relation to medicines and self-care activities requires further

exploration. The following chapter describes the methods and results of a rapid review of qualitative literature undertaken in order to examine this area further.

Chapter 4: Rapid Review of Qualitative Literature

As noted in previous chapters, an understanding of barriers and drivers to adherence is essential in when considering the design of an intervention to enhance medication adherence. As discussed in chapter two, intentional non-adherence occurs when the patient consciously chooses not to take their medication against the advice of their health care professional with patients' beliefs about their disease being central to adherence [10]. Examining the personal experiences of people with HF in relation to medicines and self-care activities may help inform the development of interventions which aim to change perceptions which in turn could improve adherence. This chapter commences with a summary of the methods used to conduct a review of such literature and continues with results and discussion identifying current gaps in knowledge which will shape the design and conduct of the qualitative work presented in this thesis.

4.1. Design

While systematic reviews are considered to be the gold standard in knowledge synthesis they are not without their limitations. Systematic reviews usually require between 6 months and 2 years to complete and often focus on a narrow clinical question. Rapid review is an emerging methodology which can be viewed as part of a "continuum of methodologies in assessing evidence" [372].

In the rapid review elements such as proficient searching and the use of extended search techniques are utilised within shorter timeframes than for other evidence-based summaries however, while rapid reviewing offers the opportunity to provide a timely and valid view of evidence rigor may be compromised [373]. Given that the rationale behind the qualitative review was not to seek decisive answers but to obtain an overview of existing work in order to guide the work detailed in subsequent chapters, rapid review methodology chosen purely on pragmatic grounds for this piece of work.

The purpose of this of a rapid review was to systematically assess qualitative evidence answer the following research question:

"What are the barriers and facilitators to medication adherence in heart failure patients based on patient's perceptions and experiences?"

4.2. Methods

The review protocol was registered on the PROSPERO database of systematic reviews:

https://www.crd.york.ac.uk/PROSPERO/printPDF.php?RecordID=38948&UserID=10693

4.2.1. Search strategy

A comprehensive search was conducted using Medline; CINAHL and Embase to retrieve all relevant articles for studies published up to end April 2016. No restrictions were placed on language or publication status. Guided by the study inclusion/exclusion criteria (see figure 4.1) all titles and abstracts were screened to determine eligibility followed by a review of the reference lists of all retrieved articles to identify any additional publications.

4.2.2. Data extraction

Details including aims, participant demographics, methodology, and methods of data collection and analysis were collected. Participant quotes and observations (first-order constructs) and authors' themes, concepts and interpretations (second-order constructs) were also extracted. All included papers were entered in and managed with QSR's NVivo 10 software. All text under the sections of "results" and "findings" were considered as data.

4.2.3. Data synthesis

To aggregate the findings a thematic synthesis approach as described by Thomas et al [374] was adapted and used to synthesise the data from the selected articles. Firstly, the data were coded line by line before being organised into related areas to create descriptive themes. Descriptive summaries of data extracted from each study were created enabling a table of

barriers and facilitators associated with medication adherence to be presented.

Inclusion criteria

Types of studies: Qualitative studies using interviews or focus groups, mixed methods studies reporting qualitative findings were also included.

Participants/population: Adult participants (>18 years of age) with a clinical diagnosis of heart failure

Intervention/exposure: Phenomenon of interest: in order to be included studies required to directly explore

- Factors and barriers that correspond to adherence to medications
- Any aspect of the patients experience or perceptions regarding medication taking

Exclusion criteria

- Studies using structured questionnaires as the sole method for data collection
- Quantitative studies reporting quantitative assessments of quality of life or reporting only quantitative data not elicited from the patients themselves.
- Observational epidemiological studies, editorials, reviews, non-research articles and studies that do not elicit data directly from heart failure patients.

Figure4.1: Rapid Review inclusion & exclusion criteria

4.2.4. Quality assessment of studies

For qualitative studies, the Centre for Reviews and Dissemination (CRD) emphasises the importance of using a structured approach to quality assessment when assessing inclusion in reviews. The CRD does however acknowledge the lack of consensus around the definition of poor quality [310]. While a selection of appraisal tools are available there is currently no consensus on how to assess qualitative evidence. Given that quality assessment can be a useful way to gain an understanding of the relative strengths and weaknesses of studies the methodological quality of the studies which were included was in this review were assessed using a tool from the Critical Appraisal Skills Programme (CASP) [375] criteria for qualitative studies.

No studies were however excluded on the basis of quality. Three domains were assessed: adequate reporting of the research, appropriateness of research design, and research conduct.

4.3. Results

When duplicates were removed the database search yielded 309 citations. Based on information in the title seventy-three articles were assessed as relevant and abstracts were obtained. A further a further 50 articles were excluded following screening of the abstract resulting in a total of 23 empirical papers being selected for full text review. Of these only 10 studies were included in the final analysis with others excluded because they focused purely on self-care. The majority of studies were conducted in either the United Kingdom (4) or the United States of America (4), with single studies conducted in Malaysia and the Netherlands. More than half of the studies did not specify a particular qualitative methodology. The 10 included studies incorporated data from 228 patients. Table 4.1 lists a summary of included studies. The results of the quality assessment indicated that the majority of studies were of medium to high quality.

4.3.1 Demographic Characteristics

Across the included studies information such as demographics, comorbid disease, prescribed medication and level of HF were described however reporting was consistent across the studies. The sample in the included studies comprised participants ranging in age from 27-94 years. Of the 9 studies reporting gender 124/191 (65%) of the participants were male, while 7 studies provided demographic characteristics such as ethnicity, education level and home living circumstances. Five studies reported length of time with a chronic HF diagnosis which ranged from 1 – 16 years.

Across studies convenience, purposive and maximum variation sampling strategies were employed from various recruitment sources including outpatient clinics, inpatient wards and utilisation of computer records. Eight of the included studies reported approval by an institutional review board with the other studies obtaining participant consent prior to interview.

Author/ year/country	Study design/ tools	Sampling Strategy / population	Aim	Quality Rank L/M/H	Main Strengths (+) and Weaknesses (-)
Riegel & Carlson [182] 2002 USA	Structured interviews	convenience sample (n=26)	To explore how HF patients adapt to life with HF and what facilitated or impedes self-care	M	+Basic descriptive design and approach to analysis reported in an easy to read manner. Interview guidelines supplied -Lack of clarity around rigour of qualitative design; Participants enrolled had previously been involved with studies. While Themes were reported the results lacked adequate representation from the participants.
Rogers et al [376] 2002 UK	In-depth interviews	theoretical sampling (n=27)	To explore patients understanding of their symptoms and treatment	M	+Clear description of methods used in both collection and analysis of data. - Theoretical background unclear. Limited reference back to participants despite relatively large sample size. Emergent themes unclear
Scotto [367] 2005 USA	semi-structured interviews	convenience sample (n=14)	To identify the lived experiences of H/F patients in relation to adherence	H	+Theoretical approach clearly identified. Methodological approach clearly reported. Participants' views clearly represented throughout. - None identified

Table4.1: Summary of Studies included in Rapid Review (n=10)

Quality Appraisal Quality Rank Key: H = High; M = Moderate; L = Low

Field et al [378] 2006 UK	Modified grounded theory / open-ended narrative interviews/	maximum variation sampling - guided by an expert advisory panel (n=37)	To investigate how awareness of medicines equips patients to participate in informed discussion	M	+Clear description of research methodology. Good use of supporting quotes from participants - Emergent themes not identified
Reid et al [379] 2006 UK	In-depth interviews	not identified (n=50)	To explore patients views of the management of medication of CHF	H	+Rigorous methodology described. Interview guide supplied. Large sample size with patients well represented in the data. -Patients recruited from outpatient HF clinics with access to a cardiologist thus may have received increased support for medication management
Wu et al [167] 2007 USA	In-depth interviews	purposive sampling (n=16)	To explore factors influencing adherence to prescribed medication	M	+. Participants are clearly represented throughout supporting themes. -No linkage between methods chosen and research question. Sampling criteria not fully described. Themes appear a little basic while interview guide appears directive.
Van der Wal et al [308] 2010 Netherlands	semi-structured interviews	convenience sample (n=16)	To explore patients' reasons and motivations for compliance	M	+Theoretical approach clearly used as basis for interview questions. Clear description of methods. Recommendations for daily practice useful. -Selected to use the term 'compliance' which is outdated and may have influenced methods used. Themes appear broad and overlap. Participants had recently completed a trial, content of which was not discussed. Lack of data from participants

Table4.1 cont.: Summary of Studies included in Rapid Review (n=10)

Quality Appraisal Quality Rank Key: H = High; M = Moderate; L = Low

Ming et al [381] 2011 Malaysia	Semi-structured interviews	purposive sampling (n=20)	To identify factors influencing adherence to medications in readmitted HF patients	M	+Good description of data analysis and list of identified themes supplied; Patients well represented via use of supporting quotes. -Exclusion of discussion on theoretical basis. The interview guide was not provided
Granger et al [372] 2013 USA	Mixed methods (triangulation) - structured interviews	convenience sample (n=10)	To explore the theoretical linkages between symptom experiences and meaning associated with medication adherence	M	+Clear use of theoretical framework to structure the interview guide and conduct analysis; Mixed methods approach with qualitative the dominant paradigm. -There is a lack of patient data to support results
MacInnes [291] 2013 UK	Semi-structured interviews	purposive sampling (n=12)	To explore the beliefs patients with heart failure hold about their illness and its treatment	H	+Use of theoretical framework to structure the interview guide. Good use of supporting quotes from participants linking back to theory throughout. -Interview guide not supplied; population currently managed by H/F nurses (these patients may already be receiving support for medication management)

Table4.1 cont.: Summary of Studies included in Rapid Review (n=10)

Quality Appraisal Quality Rank Key: H = High; M = Moderate; L = Low

4.3.2. Aims of Included Studies

Although the aims of the included studies differed, some commonalities were evident. Six of the ten studies focused fully on medication [167, 376, 378, 379, 381, 382] while four studies discussed medication adherence as part of self-care in HF [182, 219, 377, 380]. The main aims of included studies ranged from gaining a deeper understanding of personal beliefs and knowledge held around HF, symptoms and medications to identifying which factors influence both medication adherence and the management of the condition. While not addressing medication adherence directly one study sought to explore the beliefs that patients with HF held about the condition and its treatment [219] while another looked at participants' level of awareness regarding their heart failure and treatment in order to determine how equipped individuals were to make informed decisions regarding their treatment [378].

4.3.3. Emergent Themes

In Table 4.2 articles are organized chronologically. The table summarises the main findings relating to the facilitators and barriers to medication adherence in patients with HF which emerged from the 10 studies. Within the table barriers to adherence are highlighted in red text while facilitators are highlighted in green text. These can be grouped into three categories: factors related to the condition of HF; factors related to beliefs and experiences of medicines; and factors related to the role of significant others.

Several of the studies (6/10) reported main motivating factors for adherent behavior. These factors are recorded within the last column of the table. Across the ten studies, a lack of knowledge around HF itself as well as a poor understanding of the role of medications, medication side-effects or the need for long term medication were identified as barriers to optimal medication adherence. Studies identified individual patient beliefs as both barriers and facilitators. Holding the belief that a medicine could be stopped in the absence of symptoms or the belief that an absence of symptoms could be a contributing factor to forgetting to take medicine were identified as potential barriers to adherence.

	Knowledge and beliefs around condition and medications		Difficulties regarding medications		Communication with significant others		Main motivating factor for adherence
	Barrier	Facilitator	Barrier	Facilitator	Barrier	Facilitator	
Riegel & Carlson (2002) USA [182]		Improving knowledge – books to educate self &; learning from others	Coping with treatment regime	Memory aids to assist Adapting regime if going out	Lack of emotional support – too much help	Medic primary information Receiving help from others	To stay out of hospital
Rogers et al. (2002) UK [376]	Poor understanding of role of medication	Good understanding of condition	Polypharmacy & Side-effects. Information caused concern	Adapting regime if going out	Difficulty raising concerns with medical staff		Not reported
Scotto (2005) (USA) [377]	Personal beliefs about medication	Acceptance of diagnosis leading to changes in self-care	Unusual circumstances	Adherent behaviour becomes part of normal life	Felling of being misunderstood and unsupported	Advice from healthcare professionals	Wish to remain at home
Field et al (2006) UK [378]	Lack of understanding of side-effects or need for long term medication			Pill boxes Giving up responsibility to others			Not reported

Table 4.2: Facilitators and barriers to medication adherence in HF taken from included studies.

Red text =barriers to adherence. Green text = facilitators for adherence

Reid et al (2006) UK [379]	Knowledge poor		Side-effects; poor memory, Regime Complexity & Medications running out at different times	Development of a routine Visual and verbal cues Medications being part of everyday life		Receiving support and help from family Trust in prescriber	Not reported
Wu (2007) USA [167]		Making connections: understanding symptoms & relating them to condition Effectiveness of medications	Frequency of meds & Polypharmacy, Side-effects, Cost & Forgetfulness	Developing a habit Use of personal cues	Limited communication with healthcare providers	Positive relationship with healthcare provider Help from family	Be as well as possible To stay out of hospital Preserve a good quality of life
Van der Wal et al. (2010) Netherlands [370]	Lack of understanding around condition or medications		Side-effects	Use of medication aids Establishment of a daily routine			Fear of rehospitalisation and fluid retention Feeling better when complying to regime
Ming et al. (2011) Malaysia [381]	Belief medicine could be stopped in absence of symptoms Belief that forgetfulness was cause in absence of symptoms \	Belief medicines would cure condition Correlating the need for medicines with negative consequences of not taking	Lack of information Regime complexity Dislike of taking medicines	Pill boxes Development of a routine Using personal diaries Visual cues	Limited communication with health care providers	Good support from family	Desire to stay alive and be healthy

Table 4.2 cont.: Facilitators and barriers to medication adherence in HF taken from included studies.

Red text =barriers to adherence, Green text = facilitators for adherence

Granger et al. (2012) (USA) [382]		Good knowledge of medications Expectation that medicines would improve condition	Polypharmacy	Medicines become part of life	Feeling that carers have insufficient time		Avoid death
MacInnes (2013) [291] UK		Belief that medication is necessary & Symptoms improve with treatment	Drug interactions, side-effects & drug information sheets caused concern		Use of various labels used for the condition by healthcare professionals		Not reported

Table 4.2 cont: Facilitators and barriers to medication adherence in HF taken from included studies.

Red text =barriers to adherence Green text = facilitators for adherence

Having a belief in the potential for medicines to cure the condition or believing that prescribed medicines were indeed necessary were reported as potential facilitators.

Practical difficulties including coping with complex drug regimes, polypharmacy and the availability of medications were cited throughout the ten studies as barriers to adherence. Aids to assist memory, adapting drug regimens if going out, the development of a routine, use of visual and verbal cues, and making medication taking part of everyday life were all identified as facilitators.

The roles of significant others including healthcare providers, family as well as social care providers were also identified as being important to adherence. Having trust and a positive relationship with healthcare providers as well as the availability of emotional and physical support of others was identified across several of the studies.

4.3.3.1. Factors related to the condition of heart failure

Across the studies knowledge of HF was generally poor. Field et al reported that HF patients regularly identified themselves as having a 'heart problem' with participants having difficulty differentiating HF from other kinds of heart disease [378]. This issue with illness identity was also reported by MacInnes [219] who found that differentiating HF from other conditions as well as the various different terminology used by different healthcare professionals led to difficulties for patients. In both these studies [291, 378] patients displayed a lack of understanding despite input from the Heart Failure Nursing Service.

Although a lack of understanding around HF was reported, participants in both the studies by Riegel and Carlson [182] and Field [378] felt they had been well informed about their condition. Field also reported that along with poor knowledge a gradual deterioration in their condition had left some patients downhearted, feeling nothing more could be done for them. In this instance patients wished to limit the amount of information they were given, preferring to leave decisions regarding treatment to healthcare professionals. Reid et al [379] identified a lack of communication as an issue, commencing at diagnosis

with patients reporting that none of their healthcare professionals had actually given them an exact diagnosis.

Patients in the MacInnes study identified HF as a chronic condition, and attributed the condition in to external factors such as family history and other conditions. HF in these patients was reported to have major consequences on their lives [291]. In only one study, conducted by Rogers et al, did patients appear to have a good understanding of their condition; however participants in this study still lacked knowledge around medications prescribed for the condition [376].

Co-morbidities appeared to complicate participants understanding of HF [279, 376] with ageing noted as an influencing factor [291]. Nonspecific symptoms could also complicate matters for patients who reportedly had difficultly determining whether symptoms were related to the HF itself or occurred as a negative consequence of prescribed medication [281,366]. Where misunderstanding about the condition occurs there is potential that patients will be unable to monitor their symptoms of the side-effects of medication effectively [378].

4.3.3.2. Factors related to beliefs and experiences of medicines

Association between medication taking and positive symptom outcomes was identified in two studies [167, 382]. Granger et al reported a link between medication adherence and meaningful associations with medications. In this study participants who could identify a direct association between symptom control and medication taking were more likely to be adherent [382]. Granger also highlighted that adherence may not always be associated with positive sentiments. The study identified participants who reported negative associations related to intention with one viewing medication adherence as the way to avoid death and other who felt that medicines were simply part of life. Wu et al [167] also reported a link between knowledge of condition, individual symptoms and the effectiveness of medications to decrease these symptoms. Reported facilitators for adherence included an individual's ability to make these connections, as well as their ability to assimilate medicine taking into their daily routine, and the use of environmental cues.

Field et al [378] found that participants who were described as being the least aware of their medication regime had difficulty accepting that medicine was the only available treatment for them. These participants did not understand the long-term nature of the treatment and were unable to directly link side-effects of the medicines with symptoms. The necessity for medication was identified as a factor for adherence identified by MacInnes [291]. In this study participants reportedly held the belief that control of symptoms had been gained as a result of medication regimes. Drug information sheets and potential side-effects however caused concern among these participants [291].

Medication adherence is not necessarily dependent on a person's understanding of the condition or the role prescribed medicines play in reducing symptoms. Reid et al [379] identified a lack of knowledge around most medications except for diuretics which were frequently mentioned as their side-effects were easily demonstrable and understood. Poor understanding of medications was also reported in two further studies. Rogers et al [376] found participants were concerned about the dosage of medications they were prescribed as well as the combination of drugs they were taking. Van der Wal [380] also reported misconceptions about medication linking it directly to adherence in one participant.

4.3.3.3. Factors related to the role of significant others

Supportive environments created by family, healthcare providers or carers facilitated adherence [167, 182, 377, 379, 381]. The role of healthcare professionals was cited in several studies as being a positive experience. The study by Scotto [377] however identified a lack of understanding and perceived lack of support from health care professionals as being a deterrent to maintaining positive self-care practices which included medication adherence. Two of the studies, those carried out by Ming et al [381] and Wu et al [167], described respect for health care providers and a trust in them to provide the best treatment. While participants in the studies by both Reid et al [379] and Riegel and Carlson [182] described generally positive relationships between healthcare providers and patients this was not always the case for all patients.

Family support was identified as a key facilitator for adherence in studies by Ming et al [371] and Riegel and Carlson [171]. In the study by Ming et al 85% of participants lived with family members who appeared to have active roles in maintaining adherence while Riegel and Carlson describe emotional support as being offered from a variety of sources.

4.3.4. Limitations of included studies

While the focus of the studies included in this review was the HF population the results have a number of limitations. Firstly, despite a number of studies being identified within this review the overwhelming literature has attempted to identify facilitators and barriers to self-care in HF with limited focus on medication adherence specifically. The evidence therefore remains inconsistent due to the relatively small number of studies looking at barriers and facilitators to medication adherence. Additionally, while the included studies reported an age range from 27-94 years very little work has conducted specifically in older HF patients who also have the added burden of co-morbid disease. It is unclear therefore from the literature how much of an impact the presence of other conditions has on the management of HF medication.

When considering how the results of this review can be applied to the development of an intervention to be delivered within the local area it is important to consider what potential the impact of culture and national health policy may have on adherent behaviour. None of the reported studies have been conducted in Scotland where the health and social care system is different not only from the rest of the UK but significantly different form the health care systems present in Europe and North America where the majority of the reported studies were conducted.

4.4. Conclusion

This review has once again highlighted the multi-factorial and complex nature of non-adherent behaviour in patients with HF. Individual beliefs and level of knowledge have the potential to influence medication adherence in both a positive and negative way. Environmental factors such as memory aids have potential to facilitate adherence while experience of polypharmacy and

complex drug regimens can potentially pose serious barriers for patients who may be struggling to understand and manage multi-morbidity. Importantly the key role played by significant others as both barrier and facilitator to adherence should be acknowledged.

It clear then that any future interventions aimed at improving adherence to medication in patients with HF must consider potential factors relating to the beliefs held about the condition itself, the medication prescribed as well as the role played by significant others. However, while this review has identified potential barriers and facilitators to adherence in HF it is still unclear what illness beliefs older HF patients and their informal caregivers hold about both the condition and its treatment. The following chapter describes the explorative qualitative study undertaken to identify illness and treatment beliefs held by older HF patients and their informal carers with the local population.

Chapter 5: Qualitative Study Phase

As reported in chapter four the majority of the literature identified in the qualitative rapid review focuses on the theme of adherence to self-care in HF. In order to ensure that any future intervention aiming to improve adherence to medication in older HF patients is underpinned by a suitable behaviour change intervention gaps in current knowledge relating to the experiences and perceptions of this population require to be addressed. While potential barriers and facilitators to medication adherence have been reported in previous studies the beliefs older HF patients and their informal caregivers hold about both the condition and its treatment remain unclear. The aim of this phase was to undertake an exploratory qualitative study in order to answer the following research questions:

I. What are experiences of older patients with heart failure and their informal caregivers around their disease and its treatment?

II. What are the barriers and drivers to medication adherence for older patients with heart failure?

Following completion of this phase results were to be used to guide the selection of outcome measures indicative of local patient experiences and assist in the adaption and modification of validated measurement instruments to assess medication adherence in a similar population to be undertaken in phase two, a prospective observational study

5. 1. Qualitative Study Methods

As discussed in chapter one, the work contained within this thesis was undertaken using a sequential exploratory multi-method research design as described by Creswell [45]. While quantitative research can test theories, look at cause and effect or make predictions qualitative research, which shares its philosophical foundation with the interpretive paradigm, supports the view that reality is multiple and subjective [383]. With this is mind, and given the aims of this phase of the research, the author considered an exploratory qualitative research design to be the best approach when undertaking a study exploring the phenomenon of beliefs and behaviour. The methods

undertaken to complete this exploratory qualitative study, were data was collected via semi-structured one to one interviews and analysed using Framework Analysis based on initial themes taken from the CSM are described below and can be found in the study protocol (see Appendix C). (Figure 5.1 details a summary of qualitative procedures)

5.1.1. Study Approval

The study was conducted at a single site (NHS Tayside) and was approved by Tayside committee on Medical Research Ethics (ref number 14/ES/0066) on 22nd May 2014. The study was conducted in accordance with the principles of the good clinical practice. Based on the principles of the Declaration of Helsinki, written informed consent was obtained from each participant prior to the interview (see appendix D).

Fieldwork for this study was undertaken over 8 months in 2014 - 2015. Data were collected using semi-structured interviews which were audiotaped. All audio-taped interviews were transcribed verbatim by RF. All transcribed interviews, field notes, reports, and other records were identified in a manner designed to maintain participant confidentiality will all records kept in the allocated secure storage area within Department of Ageing & Health, Ninewells Hospital, Dundee.

5.1.2. Study Population

Participants were all community dwelling people ages 70 and over with a diagnosis of CHF according to the European Society of Cardiology (ESC) guidelines see figure 5.2 for inclusion/exclusion criteria.

Given that the aim of the study was to explore barriers and drivers to adherence from the patient's perspective, those currently residing in a nursing or residential home and those currently receiving daily visits from district nursing service to administer medications were also excluded on the grounds that responsibility for medication in this group lies in the main with a healthcare professional and not the individual themselves.

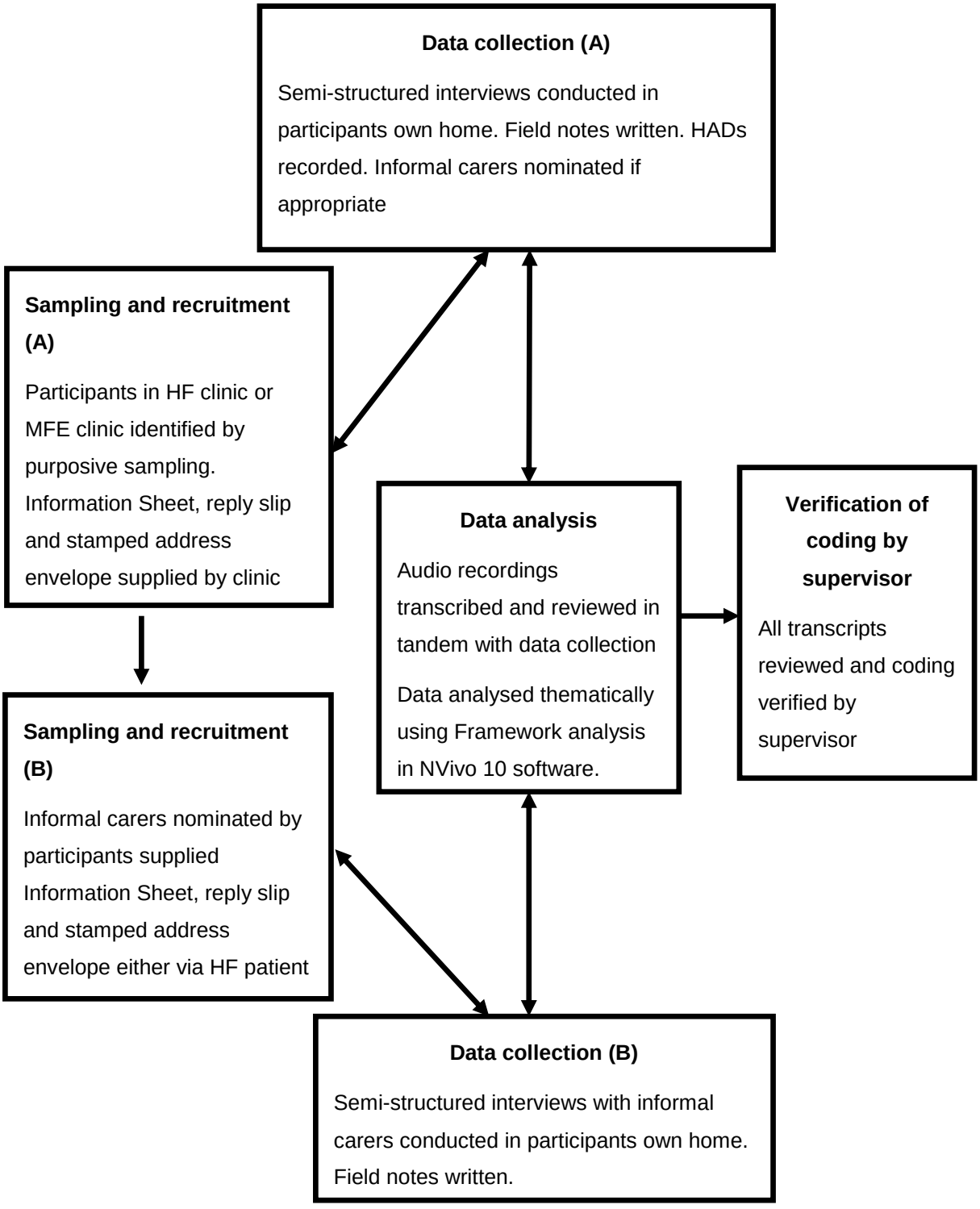

Figure 5.1 summary of qualitative procedures

All participants were recruited from secondary care via HF and Medicine for the Elderly outpatient clinics, or from medical wards in Ninewells Hospital, Dundee. The range of recruitment sites aimed to ensure that the study population included recently hospitalised patients whose HF may not be optimally controlled, as well as those patients who were being managed successfully within the community. Given the use of a purposive sampling strategy recruitment from primary care was deemed to be more problematic than approach in a clinic setting where the patient's recent history was easily obtainable.

INCLUSION CRITERIA

- Community dwelling people aged 70 years and over with a diagnosis of chronic heart failure according to the European Society of Cardiology (ESC) guidelines
- Patients with New York Heart Association (NYHA) class II to IV symptoms
- Nominated informal carers of the participants described above

EXCLUSION CRITERIA

- Unable to give written informed consent
- Residing in Nursing home or Residential Home Environment
- Currently receiving daily visits from district nursing service to administer medications
- Currently enrolled in another trial, or within 30 days of completing another trial

Figure5.2: qualitative study inclusion and exclusion criteria

5.1.3. Sampling Strategy

Eligible participants were recruited to participate in the study using a purposive sampling strategy as described by Patton [(384)]. A non-probability method of sampling, purposive sampling (also known as subjective, judgement or selective sampling) is where the researcher relies on his or her own judgement

when choosing members of a population to participate in a study. In short, the researcher actively selects who they consider will be the most productive sample in order to answer the research question. According to Marshall, while utilising a random sampling method may facilitate the generalisation of results to an entire population it is not the most effective way to gain an understanding of complex issues relating to human behaviour [385]. Given that the purpose of the study was to provide a detailed picture of living with HF, a purposive sample of eligible participants was chosen using a framework of variables which might affect an individual's contribution.

Based on personal practical knowledge of the research area along with information gleaned from the reading of current literature, the following two key variables were chosen as selection criteria and entered into a sampling matrix:

a) Gender

b) Recent hospital admission (admission ≤ 12 months) following an episode of decompensated heart failure.

While ensuring that the two key a priori variables were used as essential selection criteria the sample was monitored to ensure variability in other factors – e.g. age, presence of a spouse and comorbid disease.

5.1.4. Sample Size

Recommendations for sample size vary widely with many researchers reluctant to suggest what constitutes a sufficient sample size [386]. Given that qualitative research is concerned with exploring different representations of a topic sampling depends on the methods used, time constraints, the quality of data obtained and the nature of the phenomena being studied [387].

When determining sample size, the concept of data saturation - the point in data collection when no new or relevant information emerges has been identified an important factor [388]. Prior to data collection however saturation, while helpful at the conceptual level, provides the researcher with little practical guidance for estimating sample sizes. Guest et al carried out a review of a previous study involving 56 interviews concluding that data saturation had actually occurred after the first twelve interviews with the basic elements for

meta-themes present even earlier [389]. In a similar field to this current study Scotto [377] explored the experiences of patients living with HF and their adherence to prescribed regimens interviewing a total of 14 participants while Ming et al [381] conducted 20 interviews when exploring the factors influencing adherence in HF patients.

While sampling in qualitative research is concerned with the richness of the data collected O'Reilly et al propose "appropriateness and adequacy" as the two key elements necessary to guide sampling and suggest that qualitative research should be undertaken using an approach which is both pragmatic and flexible [387]. Based on the nature of the topic a sample size of approximately 12 HF patients and 12 informal carers was initially estimated, however the final number would be determined when it was deemed that the research question had been sufficiently answered.

5.1.5. Participant Enrolment

Potential participants were identified within the relevant clinic or inpatient areas by members of the medical and nursing team who supplied a copy of the Participant information Sheet (PIS) (see appendix E), a reply slip and a stamped addressed envelope. After reading the PIS only those individuals who wished to know more about the study were asked to respond by returning the reply slip. All respondents expressing interest were then contacted by telephone. During these initial contacts potential participants were given a brief outline of the purpose of the study and were encouraged to ask questions at any point during the phone call. Referring to the sampling matrix, personal details were obtained to establish if the individual met the sampling selection criteria. All participants meeting the inclusion criteria were asked to nominate an informal carer to participate in the carer's interview. Those patients unable to nominate a carer were still eligible to participate in the individual interview if they met the selection criteria as directed by the sampling matrix (see table 5.1).

Participants who were selected were invited to participate in the individual interview. All interviews were conducted primarily in the participants own home in order to reduce any inconvenience, however all were given the opportunity

to nominate an alternative setting should they wish. Nominated carers were contacted separately and asked if they would agree to participate in a separate, individual interview at the location of their choice (see appendix F for the Carers Participant Information Sheet & appendix G for the Carers Informed consent sheet).

	Target sample number	
	Male	Female
Record of Hospital admission due to decompensated HF within last 6 months	3	3
No record of Hospital admission due to decompensated HF within last 6 months	3	3

Table 5.1 Qualitative sampling matrix

5.1.6. Ethical Considerations

According to Beauchamp and Childress four principles underpin medical ethics: autonomy, justice, non-maleficence and beneficence [(390)]. Autonomy considers study participants to be independent individuals who can make their own choices and who should be able to make an informed choice to engage in studies without coercion. According to Polit and Beck, 'informed consent means that participants have adequate information about the study, comprehend the information, and have the power of free choice, enabling them to consent to or decline participation in the research voluntarily" [(383)].

Within this study all participant information was supplied to the patient in written form, at least one full week prior to them agreeing to participate in the study visit. This period was deemed to be sufficient to allow patients to consider the information, discuss the content with significant others if they wished and make an informed choice regarding participation. For this study no formal cognitive assessment was conducted in order to assess the individual's ability to comprehend the information supplied. All participants had been supplied the PIS by either medical or nursing staff within an outpatient clinic setting and

thus it was assumed that the information had only been supplied to those individuals who were suitable to receive it. Despite being reassured that refusal to take part would not in any way effect the healthcare they received it could be argued that by adopting an approach were initial contact was via a healthcare professional with whom the participant had a patient-clinician relationship some individuals may have agreed to consent to please their clinician.

Within the PIS, content relating to: the nature and purpose of the research; how the individual came to be selected; the procedure involved along with how their personal information would be stored, utilised and disseminated was included. In addition, contact details for the researchers were included to facilitate any queries. At the being of the study visit the research was introduced with a copy of the PIS used as a prompt for discussions, confidentiality was explained before the consent document was read through with the participant ensuring the content was understood before written informed consent was taken. A signed copy of the completed consent form was given to the participant for personal reference with another copy placed in the trial master file. All participants were reassured that they could withdraw at any point during the study and that no monetary award was offered.

According to the ethical principle of justice all individuals, regardless of age, gender, ethnic origin, disability or other criteria should have equal opportunity to take part in research studies [390]. Within this the target population was aged ≥ 70 years, a population frequently underrepresented in research studies while study visits were carried out within the participants own home to avoid potentially difficult travel.

Two of the most fundamental ethical principles applicable to research are non-maleficence and beneficence. Researchers have a responsibility to balance potential benefits of the research against potential risks, protecting and safeguarding participants from harm [391]. For this study all clinical staff were asked to exclude any patient deemed too unwell to take participate thus minimising the potential for both physical and psychological discomfort. Given that there was potential for some participants to become upset during the

interview all participants were informed that they could invite a significant other to attend the interview and should they become fatigued or upset the interview could be concluded early. Regarding the principle of beneficence, given that taking part in this study was unlikely to directly benefit the participant this was explained in the PIS. It was suggested however that some participants may value the opportunity to walk about their health.

Relating directly to the four underpinning principles are the concepts of confidentiality and privacy. To ensure the anonymity of participants all identifying data relating to the individuals, their families and the organisations they discussed such as local hospitals and healthcare professionals were changed. Additionally, within the PIS participants were informed that anonymity would be maintained during any future write up or publication of this research. Given that the interviews were conducted out with the healthcare setting and to protect the safety of the researcher information regarding the scheduled interviews such as date and time of appointment and the address of each visit was given to the study CI prior to each appointment and destroyed by the researcher on return to the department.

Given that confidentiality prohibits the sharing of any personal data without an individual's consent all tapes, transcripts and any other documents which could potentially identify an individual were stored securely within a locked cabinet within the department of Ageing and Health, University of Dundee. All data which required to be stored electronically, including transcripts, were stored on an encrypted file on the University of Dundee's secure drive. At the conclusion of the study all audio-tape recordings were destroyed.

Finally, when conducting qualitative research, the relationship between the researcher and the participant is an important consideration. When the aim of the study is to encourage participants to speak openly it is unrealistic to expect the researcher to remain an objective outsider. The researcher in this study was aware that the existence of prior knowledge of HF coupled with pervious nursing experience with older people meant that interviews had the potential to be approached with preconceived ideas and expectations. According to Holloway & Wheeler a health professional's own assumptions may result in a

loss of focus on the patient's own concerns during interviews offering potential for the discussion to be driven along a different path [392]. Conscious that should participants be made aware of the researcher's clinical background they may view the interview more as a clinical consultation the researcher introduced themselves as a research student and avoided divulging any more personal information than was necessary.

5.1.7. Data Trustworthiness

While methodological rigour can be described in terms of internal validity, reliability, objectivity and external validity within quantitative research, in qualitative research these criteria can be replaced credibility, dependability, confirmability and transferability [393]. Within qualitative research credibility, the confidence which can be placed in the plausibility of the research findings, can be demonstrated through the use of strategies such as triangulation of data and member checking. Within this study the decision was taken not to use member checks, the practice of returning transcripts of interviews back to participants for feedback [394], on a purely pragmatic basis.

Given the use of a purposive sampling strategy within this study transferability of the findings of this study was not a major consideration however the researcher collected background data, detailed within this thesis, which aimed to assist with the transferability judgement of others. Additionally the concepts of dependability and confirmability were considered. To ensure inter-subjectivity throughout the coding process the researcher met regularly with her supervisory team to discuss the coding data with verification of coding was undertaken by one supervisor.

5.1.8. Data Collection

While various qualitative data collection methods such as observations, focus groups or individual interviews exist, the emphasis of this phase of the study was on the experiences of individuals rather than a collective response. With this is mind in-depth interviews were deemed to be most appropriate. While interviews can potentially be carried out either face-to-face, on the telephone or online, the age group under study advocated the adoption of a face-to-face

approach. This method was adopted to avoid potential difficulties with communication deficits and to ensure that non-verbal cues could be detected in order to assist with both running the interviews and interpreting the discussion. A semi-structured format enabled the phenomenon to be studied in detail but remain focused.

An interview topic guide (appendix H) was developed and theoretically informed but not confined to, elements of the CSM as well as adherence and self-efficacy literature. In order to explore each participants adherent behaviour the topic guide aimed to outline key themes and areas of questioning thus enabling the interviewer to probe individual beliefs about HF before seeking out individual coping practices and motivating factors for adherent behaviour. Additionally, while it ensured a degree of constancy in the data collection process the topic guide offered the interviewer a degree of flexibility in order that details relevant to each individual could be explored.

Field notes, a mechanism to remember and record the behaviours, activities, events, and other features of an interview were collected immediately following each interview. Each record contained both descriptive and reflective information and was used primarily as a reflective tool. Field notes, along with the transcripts of previous interviews were reviewed by the researcher between each interview in an attempt to identify missed questions or emerging themes not covered in the interview guide. Using an iterative approach to data generation the researcher repeatedly reviewed the data between each interview using this evolving understanding to guide the next data collection. This process continued until the data collection was complete.

5.1.8.1. Interviews

According to Richie et al [(395)] in-depth interviewing consists of six component parts: stage one: the arrival and introduction; stage two: introducing the research; stage three: beginning the interview; stage four: during the interview; stage five: ending the interview and stage six: after the interview.

The researcher allocated either a full morning or afternoon to undertake the study visit. Each participant was advised that the study visit would last around 90 minutes to 2 hours which would which would give enough to conduct an

interview of around one hour's duration without making the participant feel rushed. At the beginning of each interview and following the brief personal introduction and informed consent permission to tape record the interview for transcribing at a later date was obtained. In order to collect important contextual information all interviews commenced with some introductory questions such as 'can you tell me how old you are?' These easy to answer factual questions aimed to place the participant at ease and establish a rapport. Information on other demographics including home circumstances and formal help at home were also collected at this time, along with a list of the patient's current medication.

Key themes of illness representation, self–efficacy and beliefs about medication where explored using open questions such as *"Can you tell me a little bit about any medical conditions you have?*" and "*Are you able to describe to me any symptoms you may have which you feel are related to your heart condition".* In general, the topic guide was used to guide the order in which topics were discussed. If however a topic was discussed by the participant at an earlier stage of the interview they were encouraged to continue to ensure the interview flowed like a conversation.

The review of the literature had highlighted depression as a common variable in medication adherence thus mood was formally assessed in all participants with their permission using a commonly used assessment tool - the Hospital Anxiety and Depressions Scale (HADS) [(396)]. While ideally this scale would have been conducted before the start of the in-depth interview the researcher was keen to avoid the asking of formal, potentially upsetting questions at the beginning of the interview. Before ending the interview, permission was sought for the HADS to be completed once the interview had been concluded.

After the conclusion of the interview time was allocated to explain what was to happen next with the information that had been collected. Occasionally this elicited some new information. Permission was sought to use this 'doorstep data' however, rather than restarting the recorder, this extra data was added to the field notes immediately following the interview. Conducting in-depth research interviews requires skill and experience to develop good techniques.

However due to time constraints pilot interviews were not undertaken instead refining of the interview technique developed over the duration of the study.

Interviews with participants continued alongside data analysis with the recruitment of participants continuing until it was considered that the research questions had been answered.

5.1.8.2. Carers Interviews.

While all participants were asked to nominate an informal carer only 6/8 (75%) of those enrolled in the study felt they could do so. Approach was therefore made to these six carers with subsequent interviews conducted with four. All interviews with nominated informal carers were carried out at their home address. Two of the carers requested that their interviews be carried out on the same day as their spouse. One carer requested that the participant and carer interview be conducted at the same time while the other was conducted immediately following the interview with the HF patient. Carer's interviews all followed the same format at those carried out with the participants themselves except that a formal assessment of mood was not carried out.

5.1.9. Data Analysis

All data was anonymised and allocated a unique identifier for the study. Following transcription all data was uploaded and stored in an encrypted file on the University of Dundee's secure drive. Analysis of all the data was conducted using a computer-assisted qualitative data software package (NVivo 10, QSR International Pty Ltd). This was chosen on practical grounds as it was a software package currently licensed for use by the University and therefore easily accessible. Formal training in the use of NVivo was undertaken prior to any data being collected. In order to enhance familiarisation of the data the researcher transcribed all taped interviews following the interview as soon as was practicably possible. Transcripts along with all accompanying field notes were uploaded into NVivo 10 in preparation for data analysis.

Identifying and refining important concepts is a key part of the iterative process of qualitative research. Unlike quantitative analysis however there are currently no clear guidelines for analysing qualitative data [397]. While many different

approaches to qualitative analysis exist, most are tied to a particular theoretical or epistemological position. One analytic approach, thematic analysis, is a method independent of theory and epistemology which can be applied across a range of theoretical or epistemological approaches [397]. In thematic analysis the process of identifying, analysing and reporting patterns within the data enables the researcher to identify which themes are important in the description of the phenomenon under study.

5.1.9.1. Framework Analysis

Data analysis followed the framework approach based on work developed at the National Centre for Social Research by Ritchie and Lewis [395]. In order to assist the researcher attain a deeper understanding of the patient experience this approach draws on features of the scientific model adapting them to suit the nature of qualitative data [398]. Described by Ritchie et al [395] as both a deductive and inductive form of thematic analysis the approach directly contrasts other entirely inductive approaches such as grounded theory and is underpinned by the principle of balancing interpretivism and reflexivity with pragmatism and transparency [399].

Widely used in healthcare research, the framework approach acknowledges that neutrality and objectivity can never be totally achieved in qualitative research. In order to reduce the degree of authority the researcher has on each participant and to enhance the rigour of the analytical processes the framework approach charges the researcher to remain as objective and unbiased as possible during the collection, interpretation and presentation of the data [398]. In this study the use of the framework approach provided a structure to undertake the process of qualitative data analysis systematically thus enabling the exploration of the data in depth, while simultaneously maintaining an effective and transparent audit trail. Using this approach initial themes are pre-set based on the research questions while further themes develop from the interviews with participants. The five key stages of framework analysis as described by Pope are as follows [400]:

- *Familiarisation with the interview*: The researcher reads and re-reads the transcripts and contextual or reflective notes and listens to the audio

recordings of the interviews formulating a list of key ideas and recurrent themes.

- *Identifying a thematic framework*: Deductively and inductively a-priori themes and recurring themes emerging from the data are identified an index of key themes is formulated.
- *Indexing*: The thematic framework is systematically applied to all the data.
- *Charting:* A chart of each theme is created including summaries of the views and experiences of participants under each theme heading.
- *Mapping and interpretation:* The range and nature of the phenomena are mapped. This stage is influenced by both the research questions and the themes which emerged from the interviews.

The thematic framework used in this study was initially based on illness and treatment representations and health behaviour. During the various stages of the analysis however other issues emerged which were incorporated into the thematic framework, which was refined as more data were collected. During indexing the thematic framework was manually applied to the data. The text relevant to each theme was highlighted in each transcript before charting the data by theme. The final stage of the analysis, the mapping and interpretation stage was guided by Rabiee's criteria for interpreting coded data [401]. The following criteria were used to assist not only in the interpretation of individual quotes but in the linking of the data as a whole:

1. Consideration of the actual words used and their meaning
2. The context of the comments made by participants
3. The frequency and extensiveness of the comments
4. The intensity of the comments
5. The checking of internal consistency of comments between participants
6. The specificity of responses.

5.2. Qualitative Study Results

5.2.1. Recruitment

Fieldwork for this study was undertaken over 8 months in 2014 - 2015. An initial approach was made to 31 HF patients of which 22 agreed to read the patient information sheet. In total eight older patients with HF participated in a semi- structured interview, as did four nominated carers. Six of the eight participants were recruited from the Heart Failure clinic at Ninewells Hospital and two from Medicine for the Elderly Clinic at Royal Victoria Hospital Dundee. All interviews were conducted in the participants' own homes except for one which was conducted in a palliative care day hospital setting during the participant's routine weekly visit. The average interview produced just under one hour of audio recording with the shortest interview taking 38 minutes and the longest around 1 hour 15 minutes. Table 5.2 details recruitment according to the key variables of gender and recent hospital stay.

Given that 75% of recruitment came from the heart failure clinic it is perhaps unsurprising that the recruitment of female participants who had no recent record of hospital admission proved difficult. Given that women with HF tend to be older than men and their HF aetiology is more likely to be attributable to hypertension (in contrast with ischaemic heart disease in men), it may be that the majority of female patients with HF are being managed in the community by their GP.

	Male	Female
Record of Hospital admission due to decompensated heart failure within last 6 months	D F	A G
No record of Hospital admission due to decompensated heart failure within last 6 months	B C E	H

Table 5.2 Record of Recruitment to the Qualitative Study

The recruitment of informal carers also proved difficult. In total six of the eight participants identified an informal carer. One participant stated that they did not require ‘care’ from their family and thus did not feel it appropriate to nominate someone while another stated that a recent marital separation left them with no-one suitable to nominate. Additionally, two people who had been nominated as an informal carer did not feel it was their place to discuss the health or treatment of their loved one. In one case a nominated carer declined as they felt inadequately knowledgeable about their relative’s health.

5.2.2. Characteristics of sample

Participants had a mean age of 77 years (range 71-85 years). All three female participants lived alone at home while three of the five male participants lived at home with their wife / partner. The median number of multi-morbidities recorded was 8.5 (range 4-11) while the median number of medications prescribed was 9 (range 4-18). Seven of the eight participants were of White, British ethnic origin with one drawn from a South Asian ethic group. Of the eight participants only two did not use a medication aid to assist with medication adherence. None of the participants had received a formal diagnosis of cognitive impairment.

Assessment at interview indicated that seven of the participants were in NYHA class II with one in NYHA class III. Six of the eight participants agreed to complete a HADS at the end of the interview. Of these, two of the male participants reported high scores in both the anxiety and depression domains neither of which were in receipt of antidepressant medication. However, during subsequent discussion with these two participants the first described a strong relationship with their GP who was fully aware of their long-standing issues with mood while the second and their spouse agreed that while there was a reluctance to add to an already extensive list of prescribed medications they would discuss the matter with the GP at a future appointment. HADS scores for all others fell within normal range. All participants described symptoms relating to their HF diagnosis.

Of the four carers who agreed to take part in the study all were female; two carers were the daughters of participants with the other two being partners of

participants. Of these one partner did not live at home with the participant. The age range of the carers was 52-64 years. Of the participants who nominated their partners both were older in age by around 22 years than their respective partners. This age gap was as a result of being in second relationships following the deaths of a previous spouse.

5.2.3. Themes

Table 5.3 shows the a priori themes which were sought in the data based on the research questions, and other themes which emerged during the analysis process.

5.2.3.1 Identity

The identity domain is composed of the label or name given to the condition and associated symptoms [402]. The following describes the theme of identity in terms of knowledge transfer and retention; confusion with other cardiac conditions; emotional representations and the recognition of related symptoms.

Knowledge Transfer and Retention

Nearly all participants had a poor understanding of HF and struggled to describe the condition. The label 'heart failure' was not a term routinely used by the participants in this study who seemed to prefer the use of the label "the heart" when describing heart failure. Although some participants denied any previous consultation regarding a diagnosis most could recall being given some kind of explanation as to the nature of the condition:

> "*Someone told me about a chamber that is not working is that it? I forget, I do forget a lot but that's it vaguely, is that it?"* [P01].

> "*Well I know like that half of the heart is not working"* [P04]

	Theme	Summary of theme
A Priori Themes	Identity	The label a person gives to their heart failure identity and reflects their knowledge about symptoms associated with the condition
	Cause	Reflects factors or conditions believed to be cause for their heart failure
	Timeline	Indicates how long the person expects their heart failure will last and the timescale of symptoms
	Consequences	Comprises of a person's beliefs about the severity of their heart failure and likely impact of illness on physical, psychological and social well-being
	Control	The extent to which an individual believes that he/she has personal control over their heart failure and beliefs related to efficacy of treatment to cure the condition or control the symptoms
Emergent Themes	Doctor - Patient Relationship	Patients account of the interaction with healthcare professionals particularly their doctor

Table5.3: a priori themes

While several participants could relate their HF to difficulties occurring within the chambers of the heart and could recall being given a diagnosis by their doctor, participants had difficulty retaining this information:

> *"The right side of, I can't remember if it's the right or the left side, one side of my heart is no working"* [P07]

"I only know the word heart failure I don't know what it is" [P02]

"I think I have probably been told that in the past but it never sunk in" [P08]

One participant had actually attended a specialised heart failure clinic the week before interview but was unable to recall a single discussion regarding their diagnosis or related symptoms.

Participants were not alone in having difficulty retaining information. One carer tried to recall whether a healthcare professional had offered either her mother or the family a full explanation regarding the condition:

"I can't think that anyone sat down and actually explained it, they may have done and I am maybe just not remembering it properly" [C01daughter]

Acute or chronic? Confusion with other cardiac conditions:

By using the term "my heart" rather than HF most of the participants in this study were unable to separate previous or potential future acute cardiac events with having a chronic condition like HF:

"I died for a couple of minutes on the table he said you left us and that lady and gentleman brought you back" [P06]

"If it comes it happens, it gets sorted out by all these kind professionals, experts and I'm saved for another while" [P01]

In these examples participants are describing HF as an acute event which has the potential to reoccur in the future. Participants would frequently refer back to these acute episodes when asked to talk about their experience of heart failure. Only one participant, who was receiving palliative care, appeared to be able to make a direct distinction between heart failure and an acute cardiac episode:

"Well heart failure is usually there for keeps and the heart attack you can take it and come out of it in minutes" [P04]

For most other participants however there did not appear to be any difference:

> *"Much the same… it's still a heart problem isn't it?"* [P05]

For carers the nature of HF was also difficult to understand. Two of the carers interviewed also confused their relative's HF diagnosis with an acute cardiac episode:

> *"So straight away the mind goes heart failure oh, heart attack, what will happen now?"* [P02]

However both of the carers who were children to the participants appeared to understand that the condition was a chronic and progressive condition:

> "*I am not waiting for her to have another big heart attack or anything I just see that progressive decline, that's what I see I just see that progressive decline getting worse"* [C01daughter]

Confusion around cardiac conditions was not limited to heart attacks. One participant appeared to be describing their diagnosis of arrhythmia when talking about their HF diagnosis:

> *"They say this pulse beat (and) the heartbeat, the two are different, they should be the same. That is heart failure*" [P02]

Emotional representations

Emotional representations' such as anxiety or depression are the feelings that may arise following diagnosis of a condition. When recollecting their HF diagnosis some participants recalled feeling afraid and uncertain as to what heart failure meant, particularly if they could not identify anyone they knew as having the condition:

> *"And I took the book home and read it and then I knew I had heart failure… its worrying, disconcerting"* [P04]

> *"The doctors told me there and I got a bit frightened cause I thought oh I have no got long then…but at that time I didna know anyone with heart failure"* [P07]

The label 'heart failure' itself also caused concern for one participant who recalled the doctor having to give the diagnosis:

> *"She said it's a terrible heading heart failure, I wish I could think of something different"* [P04]

Anxiety regarding their relative's diagnosis was described by all of the carers. One daughter described feeling stressed about her mother at the thought her mother may collapse at any time while another carer was clearly upset about the lack of explanation or support they had been given post diagnosis:

> *"Oh it scared the, it scared the bejesus out of me I tell you, I don't know how he felt but it scared me… It's the fact that they tell you that you have got heart failure and then you are just left to your own devices, I mean, you don't know how bad that heart failure is. Well it could come up at any time"* [C03]

This carer described how, while symptoms of the condition had been present for some time, her partner had been recently given the diagnosis by a heart failure consultant and advised that a HFSN would contact in due course to offer further advice regarding medication. Unfortunately the HFSN allocated was on annual leave resulting in a delay in the post diagnostic visit. The carer had attempted to speed up the visit by telephoning another member of the HF liaison team but was left with feelings of anger and frustration that other nurses within the team had not appeared to understand the urgency for the support requested.

Recognising associated symptoms

While the majority of participants were able to identify typical HF symptoms such as breathlessness, tiredness and ankle swelling these were infrequently related directly to having heart failure. More often symptoms were labelled as a consequence of ageing or explained away as consequences of other medical conditions:

> *"Well it's hard to say how much of that is getting older and how much is to do with actual symptoms of your heart not working as well"* [P08]

> *"My whole leg was swollen up, I think that was because of the diabetes"* [P05]

> *"Is that (leg swelling) vascular or is that your heart as well?" [P01]*

However one carer in particular made accurate associations between symptoms and the condition. When discussing the symptoms associated with their mother's HF diagnosis one daughter was able to draw on past experiences as her father had been diagnosed with the condition before his death:

> "*The reason why I can see that is because my dad went through the same thing"* [C01]

In summary identifying the nature of HF was difficult for most participants. This could be attributed to several factors. Transfer and retention of knowledge around the condition appeared poor. Few participants used the term 'heart failure' throughout the interviews. The explanations of HF given by participants in this sample contained language such as "ventricle" and "enlarged heart". This language had been clearly used at some point previously by healthcare professionals to describe the condition however it is clear that the full explanations had not retained by the participants.

A lack of purposeful information from healthcare professionals and an inability to identify significant others as having heart failure may have caused difficulty for individuals trying to establish a clear picture of the condition. Finally the lack of a clear condition identity alongside the existence of multi-morbidities may have attributed to participants failure to associate related symptoms to their HF diagnosis.

5.2.3.2. Cause

Causative factors can usually be grouped into external and internal factors and behaviours. However, beliefs about causation around heart failure were difficult to assess in this sample due in large part to the difficulty with identity.

Internal and external factors

Given that the majority of participants in the study failed to identify HF as a condition the only causal internal factor identified was advancing years. Age was used to explain away the reason for symptoms, not the condition itself:

> *"I think maybe its just old age you know"* [P08]

Several participants talked about stress as an external factor. Again however again, this stress was mainly viewed as a cause of general ill health or a contributing factor to a previous acute cardiac episode rather than a direct causal factor for heart failure. One participant described running his own business involving frequent travel. The stress caused by this situation was cited as being a contributory factor in the negative life style choices he made. Another participant recalled a conversion he had had many years back when starting a new job in social work:

> *"The guy told us, in this job you are heading for haemorrhoids, heart failure and diabetes and different things. He says it runs throughout the profession and he was dead right cause of the stress"* [P04]

The carers in this sample also described poor understanding on causation. One carer attributed a recent exacerbation of the condition to an extreme drop in weather temperature while abroad:

> *"And slowly and gradually his legs swoll up and we don't know what is happening to him and we thought it was because the weather is very cold"* [C02]

Instead of identifying external factors participants referred directly back to other cardiac conditions causation for their HF:

> *"I had a bypass and probably the valve or whatever they have put in is no working well as it should work and that's that"* [P07]

In one instance causation was described by a carer as the permanent damage caused to her mother's heart following a previous heart attack:

> *"When you have a heart attack there is although you may recover from the heart attack … there is em irreparable damage made and the whole functioning of the heart is impaired"* [C01]

However, while two of the carers did appear to have a basic understanding of causation they described a lack of explanation from healthcare professionals, similar to what had been identified by the participants:

> *"Heart failure to me would be that the hearts not functioning at the proper level but the actual heart bit wasn't actually explained"* [C04]

Behaviours

Several participants in the study cited lifestyle factors as causation:

> *"Heart eh failure primarily is putting too much strain on the heart for a variety of reasons one of which may be running too fast, I don't mean in a physical way but mentally you know running too fast and I always did that, I was always on the go always a hard worker"* [P03]

> *"Just bad living I think, eating the wrong things and smoking. Smoking didn't help, I blame the smoking for it actually, cause we all like things which are supposed to be no good for you"* [P05]

In both of these examples participants appear to be identifying lifestyle choices as factors for ill health relating their heart in general. Identifying HF as a condition was difficult for these two participants who both had a history of myocardial infarction and angina.

In summary the cause of HF was attributed to external factors and behaviours such as lifestyle choices and stress. As previously stated, participants had difficulty in differentiating the condition from other cardiac and non-cardiac disorders with several participants referring to previous acute events or cardiac surgery such as coronary artery bypass grafting (CABG) identifying them as contributary factors for the condition and their current HF symptoms. Several participants referred to a family history of heart problems but did not expand as to whether they considered this to be a factor in their own diagnosis. One participant cited advancing age as a cause.

5.2.3.3 Timeline

The timeline domain refers to the predictive belief about how long the condition might last. It describes the expected illness trajectory including symptoms and timeline to recovery. Timeline beliefs may be acute or chronic.

Uncertainty around Acuteness or Chronicity of condition

Participants had difficulty identifying HF as a chronic condition and while they appeared unable to predict future progression they did expect the condition to get worse:

> *"I don't think it (my heart) will change for the better but It will change for the worse and it's just a case of what sort of rate it will change"* [P03]

> *"I think it will get worse I don't think it's gonna get any better, well no its no gonna get any better"* [P08]

Participants frequently related their HF back to having an acute event, which in the future could potentially prove fatal:

> *"I think someday I am going to go out the door and just drop down dead"* [P05]

This sudden end to life was seen by some to be more preferable than progressively becoming sicker and more dependent on others:

> *"I know we have all got to die and I would rather just go like that, boom (laughs), I signed it, I don't want resuscitated cause look what I am suffering now. What would I be doing then?*" [P04]

> *"I wouldn't like to be a burden on someone, better out of way"* [P05]

Unfortunately healthcare practitioners did not appear to have clarified the question of prognosis for participants:

> *"I asked him the prognosis and he laughed and he just telt me well I can say you have ten years but it's no like cancer where you can say you have only got so long you, can go any time really he has no got a crystal ball….the doctor did explain that heart failure was nothing to worry about, you can go on for ten years or you can just get knocked down by a bus. That is the way he explained it"* [P07]

Carers' beliefs around illness trajectory:

On a similar theme the illness trajectory of their relatives' HF was unclear for the nominated carers within this sample. While the condition was described as progressive by both of the daughters interviewed, the partners considered heart failure to be an acute condition and that their relative may meet a sudden end:

"Yeah I don't know how much damage there is to the heart so that is obviously irrecoverable and how quickly that could go downhill I don't know" [C04daughter]

"When I see my mums ankles getting bad and her breathlessness and I think oh god so it does make me a bit more kind off pessimistic… Oh yeah its gonna get worse, I mean I don't see that improving at all" [C01daughter]

"You don't know how bad that heart failure is, well it could come up at any time. He could be on his own in here" [C03partner]

Despite acknowledging that treatment had been initiated, one carer remained unclear as to the treatment plan or the prognosis:

"I don't really know what will happen what with the medication, again that wasn't explained to me… but now-one has actually said this is what to look out for"

Finally the ability to draw on past experiences had enabled one carer to recognise similarities and the possible long-term outcome. This they acknowledged had enabled them to support and inform other family members who were also caring for their mum:

"I can see my dad and we got to the stage where my dad was doing all these different things, he was going for that treatment and he was going for that treatment and really in the long term it wasn't having any impact and I kinda see that with my mum" [C01daughter]

In summary HF was seen by some participants and their carers in terms of a previous acute event or other cardiac condition which had the potential to reoccur at any point, potentially bringing their life to an abrupt end. For participants who identified their HF as chronic, it was viewed as a condition which would not improve and likely to worsen over time. While carers were also uncertain of prognosis, having previous experience of the condition enabled one carer to recognise the condition as one where a gradual deterioration in health and functional ability may ensue.

5.2.3.4. Consequences

The consequences domain describes the beliefs an individual holds about the effects of the condition and how this will impact on them physically, psychologically, financially and socially. These representations may or may not develop into more realistic beliefs over time.

Overall participants felt their health had deteriorated as a result of their condition:

> *"My health is not so good now"* [P02]
>
> *"Well it's put the brakes on me in many ways"* [P03]
>
> *"Heart failure stops you from doing a lot of things"* [P07]

Only one participant who described an extensive cardiac history including MI and CABG was able to discuss how the diagnosis of HF they had received 2 years earlier had affected them physiologically:

> *"Well, I know that if the fluid starts there or the build up there I will end up with fluid on the lungs and I will be short of breath but … Four or five times I have been in and out of hospital, six monthly, three monthly all with shortage of breath*" [P04]

Identifying the consequences of having the condition was difficult for the majority of these participants due in large part to not having a clear picture of what HF is and being unable to relate directly to it.

Physical Consequences

Physical consequences of HF were most frequently described in terms of symptoms including shortness of breath, swollen ankles, and tiredness. One participant described loss of appetite. Four participants described depression, which could be categorised as either a symptom or a consequence of the condition.

Seven of the eight participants described breathlessness:

> *"Definitely short of breath yeah, as you can hear my voice keeps going" [P05]*
>
> *"I get breathlessness and I'm much slower"* [P01]

Increasing breathlessness led to consequences such as limiting how active participants could be:

> *"I've seen me walking out the step there and up the road there.. Now it's only a small hill and when I get to the top I can hardly breathe"* [P01]

Six of the eight participants described leg or ankle swelling:

> *"Well my ankles swell up"* [P05]

> *"My legs were swollen and my ankles really swell up"* [P07]

While fatigue or tiredness was described by half the participants:

> *"Oh yeah I get tired easy… more than fifty yards and I'm beat"* [P05]

And this resulted in periods of inactivity:

> *"In the morning I will not do anything, I just sit"* [P06]

A concern for most participants was a reduction in mobility limiting their ability to participate in everyday activities:

> *"My movement, my walking is slow, slower than before"* [P02]

> *"No I used to take the dog out quite regular, I used to go away up the hills and now I don't take him out at all"* [P05]

This reduction in physical ability resulted in a home move for one participant:

> *"I moved here because it's all on the flat, I had stairs, I had to wash the stair and the close so I moved here four years ago"* [P07]

Psychologically participants could not describe any direct consequences of their heart failure with several participants not viewing themselves as being "ill"

> *"There are some people that love being ill and I don't and I dinna feel ill, I know I don't look ill you know"* [P01]

Instead they talked with concern about having a future heart attack with some admitting to altering their daily activities to try and prevent having another acute cardiac episode"

> *"I am frightened I strain my heart*" [P01]

When thinking of how their HF may impact them in the future one participant thought:

> *"I think I will be housebound I won't be able to get out anywhere"* [P05]

Psychological Consequences

While undue anxiety was not identified as a feature for the participants within this study five of the eight participants described psychological symptoms of depression, which could be categorised as either a symptom or a consequence of HF.

For two participants, depression had been diagnosed in the past with one participant still in receipt of ongoing prescriptions of anti-depressant medication:

> *"Aww yeah, you get affy depressed, I was suffering from depression. I had to take tablets"* [P06]

HADS scores collected on six of the eight participants reported scores below the recognised cut off point for anxiety (8/21) for all those who completed the questionnaire (further discussion of HADS measurement tool can be found in chapter 6). Regarding depression however two participants who were currently prescribed treatment for a mood disorder, reported scores above the cut-off point of 8/21.

Social consequences

The social consequences of living with HF were again difficult to assess. While examples of how life had changed where given, participants often did not attribute these changes to their condition but rather to advancing age or other medical conditions. Participants indicated that while they had had to make changes they tried to maintain their activities as much as possible:

> *"Normally we would leave about three and we would have a wander around... but he knows I canna go and walk about, I would be tired and not be able to enjoy the show, the music so eh that's the way it is now, I try not do things to make myself worse"* [P01]

> *"There is a pub I used to go into, I don't go now because it is too far for me to go"* [P03]

While help from family members assisted some to manage at home successfully:

> *"I can't do housework which gets me but my family do it"* [P01]

> "*She sees to me as well and she looks after me and sometimes I say to her I'm ok, I'm fine, you dinna want to put pressure on them, they have enough to do when they are working"* [P07]

Consequences described by carers

For carers the consequences of HF were described in terms of the effect on their relative and on themselves. When discussing the effect the condtion had on the patient themselves carers described symptoms of the condition and how they felt they had affected them on a day-to-day basis both physically and mentally:

> *"Well certainly her levels of energy, em breathlessness em I look at her ankles and seems to have got, her ankles are getting worse over the past months"* [C01daughter]

> " *I don't think she had realised it that she was so out of breath that she wasn't seeing it like we were seeing it from outside, I don't think that she realised that she was so out of breath and puggled [(a)]…She really was down and not eating you* know" [C04daughter]

Carers focused on what the condition had stopped their relative doing. All felt that their relative had deteriorated physically and that independence had suffered because of heart failure. As a result of this carers felt their relative had suffered social consequences:

> " *But now the key thing that is missing from mums life now is the ability to go out independently, go into the town. When she gets into town she doesn't have the energy and that's the thing that has limited that element of her life and for her that is a big thing, it's a big big thing"* [C01daughter]

[a] "puggled" - a word often used by older people residing in Dundee meaning exhausted

> *"It got her out and got her socializing but she has given that up now and she used to occasionally go into town on her own you know but now that has stopped. She used to come with me every week for the shopping and em every time we went round she was puggled, struggling for breath and eh hanging on to the shelves"* [C04daughter]

Three of the four carers described having their own ongoing medical conditions. One carer diagnosed with COPD described how she worried that her relative's HF would result in an acute event that she would be unable to manage. Another carer described her own feelings of increased stress caused by witnessing her mum's symptoms:

> *"It (heart failure) doesn't seem to worry him but to me I couldn't lift him or anything, I mean I carry my phone and I would just have to phone the hospital. I panic and then end up taking a COPD attack or a panic attack and then I wouldna be any use to him"* [C03partner]

> *"she was breathless and she was dizzy I was quite worried….*
> *I thought you know she was going to collapse right away… I used to get all stressed because I thought she was gonna collapse one day"* [C04daughter]

All carers felt a responsibility for the mental welfare of their relative that impacted on them in a practical way. Both of the daughters described times when they had to either stay with their relative or bring their relative to live with them during a period of ill health:

> *"I saw that she wasn't coping mentally and I went up and said mum why don't you pack a bag and come down stay with us for the weekend and I felt she needed a little bit of company, social support. She didn't take any persuasion she just did it and she stayed here two weeks until she was ready to go"* [C01daughter]

> *"I said to my husband you know if she just had someone there who was running back and forward making cups of tea…so I just go and mollycoddle her a bit, so I stayed for must have been about five days. I stayed with her but she really did pick up"* [C04daughter]

In summary the majority of participants did not appear to have a clear understanding of the condition and thus had difficulty in identifying how heart failure was impacting on their life. Most people did not feel their physical health would improve but indeed worsen over time. It is unclear if the participants contributed this outcome directly to heart failure or to ageing and other co-morbid conditions.

All eight participants described physical symptoms that in some instances were contributed to their “heart”. Reducing physical activity and the worry of a potential acute cardiac event in the future caused concern for the majority of participants. In order to maintain independence and participate in social activities several participants discussed changes they had made to their life. However, they did not directly attribute these changes to having HF choosing to refer more frequently to their advancing age. None of the participants discussed financial consequences although one person had the expense of moving to a more manageable home.

For carers, the condition had consequences for both the patient and themselves. The daughters of two of the participants could relate HF symptoms to physical limitations, mental wellbeing and social isolation. All carers expressed a feeling of responsibility to ensure their relative was well cared for despite having their own health concerns or family commitments.

5.2.3.5 Control and curability

The domain of cure and controllability describes beliefs about whether the condition can be cured or kept under control and the degree to which the individual plays a part in achieving this. The majority of participants discussed control with only one participant discussing the possibility of a potential cure for the condition in the future:

Potential for cure

One participant expressed a belief that while they understood HF to be a progressive condition there might, in the future, be potential for a permanent cure:

> *"I don't think it will be cured but what they are doing now in, what do they call it gene therapy, growing muscles and all the rest of it who knows?"* [P04]

This particular participant however was aware of the seriousness of the advanced stage of their own HF. The following example indicates that they were conscious that the treatment they were currently receiving was not a cure:

> *"The cardiologist had given up on me and sent me home and according to my own doctor he thought he had done all he could so sent me home to die"* [P04]

Perceived control:

All participants discussed their strategies for dealing with ill health. For some participants the condition had potential to deteriorate however there was a perceived lack of ability to influence this:

> *"Well my heart may get worse but then you have no control over that"* [P01]

While not always referring specifically to their heart failure however some of the participants felt that they had potential to maintain their health or at least find appropriate treatment:

> *"I mean I am doing my best to be healthy"* [P08]

> *"Whatever you have got there seems to be a treatment for it you know"* [P01]

When discussing control participants often referred to their symptoms and the actions they took to control these:

> *"I have a heart that is half working. I have got a pacemaker that is assisting and if I don't do too much I am ok"* [P04]

> *"I do get a bit breathless but I just walk slower to cope with that"* [P04]

> *"I stop there and take a spray it is ok then and I can carry on"* [P02]

For some participants however while they could identify actions they could take to improve their condition they had not always managed to do so:

"Well I know what I should be doing, stopping smoking, just take life at a gentler pace" [P03]

Like the participants the carers in this sample did not discuss cure for heart failure. Control was described in terms of how their relative managed on a day-to-day basis as well as the taking of medicines. One participant described how their mother tried to mask the condition from her family:

"Mum was showing off that week, she was trying to create a difference between somebody she perceived to be always ill (and herself), because she doesn't like being ill my mum, I thought that was so interesting, she put on a face, and she did it so successfully but behind the scenes you know, she will hide it, she will hide it but she can't hide it all the time with us because we see her at different times"

All carers discussed things what they did in order to maintain social contact and maintain independence, both seen as important in order to ensure health was managed:

" We try at least once a week like today we go at least a Wednesday and maybe a Saturday we go out and spend a while out, ok we don't do much we just go to the market or whatever but it is better than just sitting staring at the walls in the house" [C03partner]

"We are trying to get her to do kind of conversions in the house, she wants to stay. We are trying to say you know the house is not really suitable for her, it's a great family house you know but the bathroom, she is on diuretics, the bathroom is halfway up the stairs" [C04daughter]

Avoidance coping

Within this sample the most regularly discussed control mechanism was refusing to focus on the condition or in ill health:

"Oh I just say oh I am not gonna let it bother me" [P06]

"I was inclined to think oh I have got heart failure I might no live a long time, I dinna want to die yet and it just gets worse and worse so you are better no thinking oh it, that works for me. I think the more you know the

more you worry... I dinna want to worry about what is gonna happen" [P07]

This coping strategy was also identified by carer who felt that their relative coped better with the condition by not questioning health care professionals about prognosis or management of their health conditions:

"I think she would rather it was unknown, unknown definitely" [C04daughter]

In summary while the majority of participants did not discuss cure, there appeared to be an acceptance that their condition would deteriorate over time, something they felt they had little control over. Control of HF symptoms appeared possible through lifestyle modifications however, refusing to focus on the condition appeared to be a common coping strategy employed by the participants. Support from carers (both practically and emotionally) was identified as important elements to enable participants to maintain control and live independently.

5.2.3.6. Treatment Beliefs

Treatment beliefs is an extension of the CSM and refers to the beliefs held about the necessity and concerns about treatment. In terms of this sample group treatment for HF revolved around taking prescribed medicines. One participant referred to having a pacemaker inserted which had helped their HF, while several discussed how a previous heart bypass had improved their heath.

Beliefs about treatment necessity:

Among the participants there was a general belief that effective treatment is available:

"Whatever you have got there seems to be a treatment for it you know" [P01]

The belief that medication works is an important facilitator for adherence. Most participants in this study held the view that medicines were necessary:

"There is no alternative, there is nothing else you can do….. I depend on them (medicines)" [P02]

"It's stopping it getting worse really I mean that's why I am taking them" [P08]

However as far as HF medication was concerned, only the diuretic medication was identified as having a direct physical effect:

"He gave me a tablet to stop my, to stop water building up on my heart and that helped" [07]

Carers also expressed the belief that medication was necessary when discussing both medication required by themselves as well as the HF participants:

" Well I personally I take my (medicines), well of course I have been told to take them but also I don't want to ever regress, to ever you know, my condition to get worse and go back to where I was before" [C04daughter]

However, this belief in the necessity of their medicines was not held by everyone:

"I sometimes wonder if I need to take these tablets or am I just wasting my time and everybody else's time taking them" [P03]

"What stop taking them for good? I don't think it would matter, I don't think there would be any difference. I don't think so" [P06]

While most participants held positive beliefs about treatment necessity they appeared unquestioning about how medicines worked and simply accepted that they did:

"I think they are good, they are good and that is it" [P02]

"Regarding tablets, I take what I am given" [P04]

Participants and cares both described the role of significant others including family and healthcare professionals in their decision making around the necessity of the medicines:

"*I say to my oldest daughter I'm taking all these tablets and she says mum, they are keeping you alive"* [P01]

"I keep taking them just because I was told this is what you need to keep your heart going…. Just because the doctor told me" [P05]

"The doctor has told her, he has prescribed them he has told her to take them that's it you just take them that's it" [C04 daughter]

Concerns about treatment:

Apart from the inconvenience of urinary frequency due to furosemide no one identified any current unsatisfactory side effects related to their current treatment:

"The only thing that annoys me really is taking the frusemide, I am on 80 in the morning and 40 at teatime and some days I am never away from the toilet" [P05]

"I do nothing but run to the toilet, you have a drink, you have to go to the toilet" [P07]

Two participants did however recall previous unpleasant experiences when prescribed ACE inhibitor medication:

"I had one and I got dizzy, the room was spinning around so I said oh I am not taking that new tablet you gave me, he says that's alright so the doctor changed it" [P06]

"That one (Ramipril) has been put down because I was feeling dizzy with the higher one and I actually fell once with it" [P07]

While one participant was concerned about the side-effects caused by their statin and asked their doctor to have a trial without them:

"One of them wasn't agreeing with me, I mean if you touched me I was sore you know, really sore and then one woman that I know she said I bet you are on statins" [P08]

This one participant was the only one to express concerns that medication did have the potential to do harm:

"The less medication I take the better I like it cause I think everything that you put in your body has some good or bad effects on you" [P08]

Adherence Beliefs

When discussing their beliefs around the need for medications several participants could identify a consequence of poor medication adherence in other medical conditions they had or they had witnessed in other family members:

" I am remembering he said if he missed it or he was late with it he used to get a splitting headache you know and he knew then that he needed to take the medication" [P08]

However with regard to their HF, participants did not perceive any negative consequence for medication non-adherence. While participants appeared happy to take the medication they did not associate poor adherence with changes in health condition for HF. While most participants did not see any negative consequences for missing the medications now and again, most felt they were needed for long-term control:

"If I missed them for a day I don't suppose it would make a difference, if I missed them for a week probably, if I stopped them longer than that then yes (negative consequences) [P04]

"I have been on them tablets for that long it's in my system I don't think taking them, forgetting to take them that once would do any harm." [P05]

One participant recalled a time when they had forgotten to take their medicines describing the belief that there had been no consequence for this accidental non-adherence:

"Yeah and I didn't feel any different for not taking them" [P04]

Finally one carer who had spent several years receiving kidney dialysis before receiving a kidney transplant described how missing her antirejection medication would result in significant negative consequences for her health. This carer felt her mother could not place the same importance on her own medication as non-adherence to HF medication would not result a critical illness:

"I don't want to ever regress to ever you know my condition to get worse and go back to where I was before so but mum has never really gone through a sort of a mean I know a heart attack is critical illness but a really critical illness like the situation I was in" [C04daughter]

In summary, this sample of patients with HF perceived treatment for the condition mainly as the taking prescribed medications. Participants believed that the mediation was doing them some good, however not everyone believed in the efficacy of their drug regime. Significant others played a part in reinforcing beliefs with trust in the doctors prescribing and family support both being important. Concern around side-effects focused mainly on urinary frequency, a consequence of diuretic therapy, however some participants were able to discuss examples of medicines they had previously been prescribed and how they had dealt with perceived side-effects.

5.2.3.7. Medication knowledge

When describing their current drug regime there was a lack of knowledge or understanding regarding their medication among participants, with little understanding about why it had been prescribed.

"No I wouldn't remember what half of them are for I just keep taking them." [P05]

"I can't even remember the names of them now" [P03]

"I dinna look at the name I just look at the colour and the boxes" [P07]

<u>*Sources of information:*</u>

Some participants claimed they made an attempt to read information sheets enclosed with the medicines:

"I am still reading them because I forget what they are about and I look at them and I think what am I taking that for? What's a Beta Blocker anyway? So I have got to read it again because it doesn't sink in" [P08]

Only one carer discussed what she thought was the importance of reading the information leaflets:

"she is not taking them (medicines) blindly, just because someone tells you. She reads all the information for you know the side-effects, so she

is not taking them without questioning but I think that is a good thing" [C01daughter]

Although patient information leaflets attempt to inform patients about their prescribed medication, the information supplied appeared in some instances to add to concerns:

"When I opened this this thing I went in the name of God… it was like terrible things could happen to you, you could bleed from your eyes, bleed here, bleed there. Yeah and some of it is quite scary stuff I pictured blood spurting all over the place [P01]

"I come home and read them and sometimes they frighten you. It says don't take if you have got heart problems" [P07]

For one carer the lack of clear information passed from the prescriber to her mother had been frustrating and she had thus made attempts to educate her mother herself:

"this is a beta-blocker" but it wasn't made clear why it was needed you know, to a lay person, I mean I knew what a beta-blocker was but I don't think, I think medical people tend to talk in medical language so then when I was filling up mums box I made her you know, we read the script and I said you know this is your know to regulate your heartbeat from going too fast that is what has been making you tired and puggled" [C04daughter]

Health Literacy

When asked about names of medications on their current prescription list nearly all participants were unable to state either the name or the correct dosage without prompting. Participants often attempted the names with varying success:

"Well in the morning I take me, oh god, what old folk used to call the water tablets, ben or bendofluazide or something like that… I take a zoda something this tiny wee one, when I start taking I take that and eh Primazole or something Brisa it begins with a B" [P01]

Understanding around the role of each medication and the associated condition was also limited. Where participants could identify medications limited understanding led them to be simply described them as being “for the heart” or “the diabetes”.

Knowledge on side-effects of particular medications was extremely limited. For one participant the urinary frequency was such an inconvenience he has attributed it to all of his medicines:

> *“That is for water, yeah cause there is water on the heart. That’s for to make us go to the toilet to pee…they are all for that”* [P06]

In summary knowledge of medical reasoning around medication prescribing was poorly understood by this sample of patients with HF. The majority of participants could not easily say the names of their HF medications or describe in any great detail the reason they had been prescribed the medications. While several of the participants could associate certain medicines with their related medical conditions they could not however expand on the necessity for each medication. This lack of knowledge around reasons for prescribing led to a lack of association with medication side-effects. That the doctors had felt the medicines were required was deemed sufficient reason for adherence.

No one in this sample of HF patients expressed any desire to be given any more knowledge than they currently held. Several participants stated that they had in the past read the supplementary patient information sheets to improve their understanding of their medications, but this had caused alarm for one particular person.

5.2.3.8. Medication Adherence

All participants in this sample of older HF patients felt they managed their medication well. The carers in this sample also held this belief:

> *“She deals with them quite well em because she stayed here so I can see here whole daily routine and she has explained to me how she works her system…. She seems to be on top of what’s what, what each one if for and when she takes them so I am quite impressed”* [C01daughter]

However while the majority of people claimed to adhere to their medications there were admissions that full adherence was not always achieved:

> *"Regarding tablets, I take what I am given*" [P04]

> *"The majority of the time I take them but I haven't taken todays"* [P03]

Facilitators to adherence:

When discussing how medications where taken the majority of participants explained how they each organised their drug regime. While some participants used pill-dispensing boxes, others choose to store the medicines in a visible place.

Taking medicines at the same time daily as part of a routine appeared important in facilitating adherence:

> *"I put them beside my bed sitting for the morning so as soon as I step out of bed I take them… I have it down to a fine art, you just need a system*" [P01]

> *"I put them in the middle of my kitchen table and when I am sitting at my breakfast I am looking at it"* [P07]

Even if it meant not directly following the specific instructions given for each medicine:

> *"The medicines are already there - in the morning before breakfast, afternoon and all that. I don't care about all that, I take them all at once. If I take it when they said and I am not at home I won't take it, they are left out. This way I use the tablets every day"* [P02]

This belief that the taking of medications at the specifically prescribed time was not important was repeated by this participant's carer during their own interview:

> *"Anytime he can take it. So if he is not taking it in the morning he can take it at night-time"* [C02partner]

While all participants stated they were responsible for their own medication taking, support from significant others was described as a facilitator for adherence by some participants:

> *"Sometimes she tells me have you taken your lunchtime tablets? Eh, she knows fine I haven't. That's her way of telling me I haven't taken them"* [P04]

Access to repeat prescriptions was discussed by several participants. While the close proximity of the doctor's surgery and pharmacy ensured medication was always available for one participant, the inconvenience of repeat medication running out at different times in the month was cited as a barrier to adherence for another:

> *"I am very good at picking them up, well it's just across the road so it is convenient….just drop the prescription of at the doctor, they forward it to the chemist for me and I go to the chemist and pick it up" [P08]*

> *"I would forget to take them if I haven't ordered them quick enough because they dinna all run out at the same time…that's the only thing, you just don't get them all at the same time" [P07]*

Facilitating the ordering and collection of prescriptions was therefore identified by carers as something they had to assist with to ensure adherence to medications continued:

> *"Occasionally she will say oh I have only got one of, oh I have run out of that so you say oh mum why didn't you say and we will rush off and try and get her tablets from the doctors"* [C01daughter]

> *"I am still keeping an eye on that, I don't let her order. I am doing the checking and the ordering"* [C04daughter]

<u>*Barriers to adherence*</u>

Forgetfulness was a reason given for non-intentional non-adherence by several participants:

> *"I don't know how old folk manage, you forget… Other times the lunchtime ones are still there at teatime"* [P04]

> *"Invariably it's because I have forgotten and the day has gone by and suddenly it's a bit late to start taking them now you know, I have seen me actually at the stage of taking my morning tablets in the middle of the afternoon"* [P03]

> *"Well Sunday morning I forgot to take them, they are still there…Just stupidity on my part because it's a thing I take on a regular basis, twice a day I take tablets"* [P05]

Intentional non-adherence was described by several participants and carers. This usually related to the taking of diuretics in order to avoid unwanted side-effects:

> *" A couple of times she hasn't taken them, like on a Wednesday when we go up to the clinic"* [C04daughter]

One participate however described previous occasions when he deliberately withheld his medication to assess their necessity:

> *"Sometimes I would try to stop them one or two and I felt something wrong with me. I start them again it is ok. To me then I need that."* [P02]

While this example shows the participant identified a negative consequence of non-adherence, others reported no consequences of non-adherence to medication:

> *"And I don't feel any different for not taking them"* [P04]

While participants in this sample all described a daily routine which facilitated adherence this custom did not always guarantee medications were taken as prescribed:

> *"You just forget because you are taking them day in day out. You would think it would become a habit but it doesn't"* [P04]

> *"I can afford to relax with them because I take them regular as I rule so I think if you miss one day it wouldn't bother you"* [P06]

The potential for physical limitations to affect medication adherence was discussed by one participant who stated that they had difficulty removing the medications from the packets:

> *"Sometimes it is hard to get them out of the packets…..I have got arthritis in my hands you see, if I dinna manage I need to get my daughter to come up and do it" [P07]*

In summary self-reported adherence to medication in this sample of HF patients was good. All participants described the routine for medication taking they had adopted in order to assist in adherence. Despite the adoption of habit-forming behaviour adherence was not always achieved.

Forgetfulness was the main reason given for non-adherence. This may have been as a result of the lack of direct association of medications with physical symptoms or due to an absence of any meaningful consequence of non-adherence. Intentional non-adherence occurred infrequently and was mainly related to the withholding of diuretics in order to facilitate a trip out of the home.

5.2.3.9. Doctor / Patient relationships:

While the initial themes of this study were based around the CSM the relationship between patients and health care professionals, particularly doctors, emerged as a highly important theme running through all of the interviews.

In the main participants talked positively about their experiences with medical staff. Trust in decision making and a good therapeutic relationship both appeared to have influence on motivation for adherence to medicines. The transfer of knowledge around both condition and medications was also discussed by both participants and carers.

Trust in doctors' decision making and knowledge:

Participants appeared to have a high level of trust them to make decisions regarding health and medication prescribing:

> *"I got all that treatment you know, I'm so grateful and I do trust them all" [P01]*
>
> *"Oh no I put a lot of stock into the doctor I think he knows what he is on about oh I would trust him completely"* [P06]
>
> *"Well if he gives you a tablet, well it must be right" [P07]*

One participant described how this trust in doctors was reinforced by family:

> *"My daughter, she says if the doctor tells you to take it take it, he wouldna be telling you to take it if you didna need it" [P07]*

Carers also described trust in GP's however one suggested this might be a generational theme:

> *"she is of the era that would never question the GP quite a lot of them are like that, what the GP says is gospel, especially her GP, she thinks he is wonderful"* [C04daughter]

Some participants held the belief that doctors have greater knowledge and therefore in a better position to make decisions regarding health:

> *"You have to understand that they have all this education... They haven't gone and studied all these years for nothing… [P08]*
>
> *"I just tell him I have a problem, I can't discuss anything, I don't know much about it"* [P02]

This trust in the doctors' knowledge resulted in participants taking prescribed medications even if you didn't agree initially with their recommendations:

> *"You have to give it a chance, even if you think what a load of tosh"* [P08]

However not everyone was willing to follow all of their doctor's recommendations:

> *"I don't have to take any insulin I am happy with the tablets. He (the doctor) asked me for eight years to take insulin and I have said no"* [P02]

There was an unwillingness to question doctors about healthcare decisions or to burden them unnecessarily. Participants in general could see no reason why anyone would question the actions of the doctor*:*

> *"I would be happy to say I don't agree with that but I haven't ever needed to"* [P05]

Therapeutic relationship:

Patients described the importance of having a relationship with their healthcare professionals - particularly their GP's and hospital doctors - valuing their input, especially when they had been acutely unwell:

> "*It's important that some-one sits down and explains what has happened to you and what that means for you. To answer any questions, you may have"* [P04]

Being made to feel they were part of the decision making regarding their health was important for some:

> *"I think I am very lucky with the doctors along there, no they really are good you know they do explain what they are doing…. he would actually say oh I am not sure about that and would look it up, and he would actually turn the screen and you know… let you see what was on the screen as well you know, taking time to share that if you like with you, that's important because it makes you feel as if you are a wee bit in charge of your own health" [P08]*

However not all participants felt that doctors always engaged positively:

> *"The last time I saw a young doctor she did (listen), others, I think they had made their decision before they come to the bed"* [P04]

While on carer expressed the belief that the treatment being offered may not always be appropriate:

> *"They don't want to do anything for him because they are watching his age"* [C02partner]

Participants expressed positive feelings regarding their GP. Accessibility and approachability were themes describes by participants:

> *"He was always good to me, always attentive to his patients…he treats you as if you really matter"* [P01]

While one participant recalled the therapeutic effect of a recent visit from the heart failure specialist nurse they could not recall the content of what had been discussed within the consultation:

> *"She reassured me because I felt better when she came…I canna remember (the content of discussion), no I can't remember" [P06]*

Transfer of knowledge

As previously stated causation and illness identity were poorly understood by most of the participants who found difficulty in recalling who had informed them of their diagnosis.

> *"She says he is the heart failure (doctor) and you are now under his care, you have got heart failure, which was news to me and I don't even know what that entails to be honest with you"* [P01]

This problem with being able to recall important information regarding health and treatment plans was also highlighted by a carer who described their own feelings with regards to accompanying her mum to the doctor:

> *"she definitely didn't say now its really important, you must take this every day... There was nothing as definitive as that. I mean even if they give them a leaflet to take away and read you know afterwards because I think well certainly people of my mums age, well even I do it in front of a doctor, I always you know if it was something serious I always took my husband, I would never challenge the consultant you know but my husband would ask the questions"* [C04daughter]

In this example the daughter felt that information relating to the treatment had not been communicated effectively by the doctor. This reluctance to ask questions or challenge the doctor was expressed by the majority of participants and may account for the overall lack of understanding around the condition.

Limited knowledge, the use of terminology and being under the care of different specialist doctors caused confusion for one carer and their relative:

> *" I am not sure of the exact differences but he said no I am not a heart failure consultant. He is a cardiologist and I think for my mum and for Joe Blogs it is quite hard to know the difference between the two"* [C04daughter]

However when information regarding health was communicated effectively it could make a positive difference to understanding the condition. The following example describes one carer's positive experience of information being transferred successfully.

> *"just before he died he was in ward 15 and this very very fantastic staff nurse em explained to us what was happening… so he explained how the heart not working affected the kidney and I remembered that so I now I know the swelling blah blah blah is related to your heart not functioning properly.. That was the first time that someone had actually explained it and explained it very visually and very simply"*

In summary trust in doctors' decision-making regarding treatment of the condition was high among the participants in this sample. These patients with heart failure valued their relationship with their healthcare professionals, particularly their doctors, and trusted them to make the correct health management choices on their behalf. Feeling included in the decisions made some participants feel they had some control over their life however not all participants chose to follow the health or treatment advice given to them and information given regarding their heart failure was not always retained.

5.3. Discussion

The aim of this qualitative study was to explore what beliefs are commonly held around HF and its management by older patients with HF and their nominated carers and to examine how these beliefs might interrelate with medication adherence. In this study the CSM of illness representation was used to conceptualise medication adherence.

Illness perceptions are influenced by knowledge, beliefs and attitudes. Within this sample of older HF patients most participants could be identified as having a knowledge deficit, this despite interaction from doctors and in some cases from HF nurse specialists. In the main participants in this study lacked a clear understanding of what HF was, why they had developed the condition and what implications this had for them. Participants rarely used the label "heart failure" throughout their individual interviews and failed to connect symptoms to the condition.

Overall, patients with HF in this sample did not demonstrate a clear understanding of the timeline, causes or consequences of heart failure. While participants were vague about the progressive nature of the condition itself the

majority expected their health to worsen over time. This expected deterioration was described in terms of overall general health and was attributed to advancing age or co-morbid disease.

This difficulty with identity is consistent with results reported by other studies in this area [371]. Problems in differentiating HF from other cardiac conditions was described by Field et al with participants in this study referring to the condition in terms of having a "heart problem" [378]. Difficulty with identity was similarly reported by Horowitz et al [36] who found inadequate knowledge of the causes, symptoms and consequences of HF among their sample. The challenge of determining if symptoms are a consequence of co-morbidities or age appears to be a common thread across all studies and appears to complicate participants' understanding of HF. Where deficits in knowledge around identity of condition and associated symptom control are poor motivation to adhere to medication may be reduced.

Only one participant in this current study appeared to have a good understanding of the condition. This participant, the only one to routinely use the term heart failure throughout the interview, had advanced heart failure and was receiving palliative care input to manage their symptoms. Several recent hospital admissions with exacerbation of HF and ongoing support from a Heart Failure Liaison Nurse may have contributed to this improved level of knowledge. While recent hospitalisation has been associated with increased adherence to medication in patients with HF [43] there is no conclusive evidence that increased contact with healthcare professionals' leads to increased knowledge in this patient group. Unlike others in the study this participant made associations between medication and symptom control and could describe how medication had been previously changed in order to manage their HF successfully. In addition this participant stated they had themselves, on occasion, made medication changing suggestions to the HF nurse. In a study by Chen et al [403] health literacy, was directly linked to knowledge of HF.

Where participants identified HF they were unclear about it being a chronic progressive condition although overall they expressed an accurate illness

trajectory indicating that they expected their health to deteriorate over time. Similar difficulties identifying HF as a chronic condition have been reported elsewhere [291].

Failed communication and knowledge transfer between healthcare professionals and patients which contributed to a poor level of understanding of HF was another common theme in this study. A previous study by Reid et al [379] found similar issues including a lack of communication commencing at diagnosis with patients unable to recall healthcare professionals actually giving them an exact diagnosis. This scenario appears to have been mirrored in this current study with participants having difficultly recollecting who had given them their initial diagnosis. Indeed, one participant recalled being advised they must have HF while declaring their current medication regime when applying for travel health insurance. Another participant claimed they had simply received an unannounced appointment in the post for an outpatient appointment at the HF clinic.

Where participants did recall being consulted about the condition retention of information was limited. A previous study by Blackman & Sahebjalal [404] concluded that explanations for cardiac conditions offered by doctors were considered inadequate by 40% of patients who also identified excessive use of terminology. In the main doctors' overestimated patients understanding of terms such as echo, leaky heart valve and the term heart failure itself. Similarly while several participants in this current study used terminology such as "ventricle" or "valves" or "chambers of the heart" it was clear these terms were simply being recalled but had not been clearly understood.

Most participants in this sample lacked a clear understanding of why they had developed heart failure. Given that the majority of heart failure diagnosis can be attributed to coronary heart disease only one participant related their condition back to their angina and previous CABG. While all eight participants in this sample referred back to previous heart attacks, coronary bypass surgery, hypertension, angina or implantable cardioverter defibrillators the majority did not explicitly identify these as cause for their condition. While several participants expressed concern that they may suffer a future sudden

life-threating episode most did not view their heart failure as a life threating condition. This belief that HF is non-life threatening has been identified previously and associated with the similar intermittent, non-adherent behaviour demonstrated by participants in this current sample [298].

Stress, particularly due to employment was identified as causation for HF by several participants and was cited as reason for partaking in previous risky behaviours known to increase the risk of heart disease. Stress has been identified as a perceived cause in other cardiac conditions, some of which were cited as co-morbid conditions by the participants in this current study. While stress can be both cause and consequence of HF it was found to be attributed to symptoms of the condition in the study by Horowitz e al [36].

All participants in this study reported classical symptoms of HF including fatigue, dyspnoea and oedema however these were not always interpreted as symptoms relating to the condition. This deficit in association between the condition, symptoms and medication has been reported elsewhere [183, 376, 379]. Many participants isolated symptoms and attributed them to other illnesses such as COPD, diabetes or peripheral vascular disease, unaware they were also related to their heart. When discussing other medical conditions however participants seemed to have a greater depth of understanding readily connecting symptoms to other illnesses, such as relating chest pain to angina and heart disease.

Several of the participants in this current study referred to depressive illness, either currently or at some time in recent history. A previous meta-analysis on medication compliance concluded that depressed patients were at significantly higher risk of treatment non-adherence than those without depression [231]. While it is difficult to determine if depression is causative or consequential in heart failure a relationship between depression in heart failure and negative beliefs on compliance has been previously identified [405].

Living with HF requires the patients to face multiple challenges including symptom control, complex medication regimes and reduced functional ability. Participants in this study described several different coping mechanisms. For

dealing with physical and functional limitations all described the adjustments they had made in order to maintain independence.

Several participants described feelings of fear and anxiety when discussing their HF with avoidance described by some as a coping mechanism. Choosing not to focus on the condition could be seen as an attempt to cope with the situation and maintain 'normal' life. While this strategy has previously been identified as one of four coping strategies by Buetow et al [406] a review of self-care in HF concluded that avoidance or denial of the condition resulted in reduced self-care capabilities [407].

In this study the participants described the management of HF mainly in terms of medication taking. Here participants expressed beliefs that effective treatments were available and necessary. Participants routinely believed that the medication was doing them some good however there was a commonly held belief that absolute adherence to their regime was not crucial. It may be that this belief stemmed from an absence of meaningful consequence of non-adherence. Perception of risk [408] and belief in necessity of treatment [195] are directly associated with medication adherence. Overall participants in the study held the belief that no direct harm would be caused as result of their medications being omitted occasionally. Given this belief and the absence of a direct link direct between medication adherence and positive symptom control the admission of occasional non-adherence in this sample is unsurprising. While participants in this study could not directly link symptom control to medication taking direct association between medication adherence and positive symptom control is however possible in HF populations as evidenced by studies carried out by Wu and Granger [167, 382].

Dowell & Hudson [409] identifies three groups of medication users: passive; active and rejecters, two of which could be used to describe the participants in this current study. The majority of the participants could be described as passive. They took their medication regularly despite not having a full understanding of their condition or indeed of the medications themselves. Belief in prescribed medications in this sample of patients often stemmed from a trust in the knowledge of the prescriber rather than any personal knowledge.

Several participants indeed cited motivation for adherence as stemming from the desire to follow the directions of the doctor. In this passive group of medication users control of the individual's condition had been handed, in the main to the prescribing healthcare professional.

Two participants in the study could be described as "active" medication users. Both of these participants, while having trust in their medical prescriber were able to draw from past experiences in order to either make suggestions regarding medication changes to their healthcare provider or adapt their medication regime to accommodate themselves and their symptoms. No-one in this current study could be identified as rejecters.

All participants denied persistent non-adherence. Where previous concerns regarding medications had occurred all had been addressed successfully with their doctor. Current concerns around side-effects focused mainly on urinary frequency, a consequence of diuretic therapy however some participants were able to discuss examples of medicines they had previously been prescribed and how they had dealt with perceived side-effects. This dissatisfaction with diuretic therapy is not a new finding. Van der Wal et al [405] sampled over 950 HF patients of which 57% cited the consequence of taking of water pills as the biggest barrier to adherence.

While not one of the initial a priori themes the doctor patient relationship was a significant theme running through all the interviews. Participants valued highly their doctors and trusted them with decisions regarding their health. In the main participants gleaned their knowledge from their GP and used terms such as "attentive", "good rapport", "taking time", "trust" and "educated" when referring to their doctor. These traits have been previously identified as facilitators to adherence by Simpson et al [169] who emphasized the need for healthcare providers to display genuine concern for patients' well-being while being knowledgeable and able to answer questions.

A "blind faith" in the decision making of doctors within the HF population has been documented elsewhere [410]. In a study by Stromberg et al [187] participants described similar beliefs to those in this current study in that patients stated that they took their medications as prescribed because that was

what the doctor had instructed. While several participants indicated they would question the doctors reasoning none had felt the need to do so in relation to their heart failure. One participant responded that they would not question their doctor because they did not feel they had the appropriate level of knowledge about the condition to do so. There was only one example in this study of someone who had refused to follow the doctor's advice. This was however in relation to diabetes and not their HF. In this instance the participant believed they had sufficient knowledge about their health and condition and believed that the self-care practises they had adopted were sufficient to control the diabetes.

Holt et al highlighted the importance of communication with healthcare providers with 64% of their sample group of older adults reporting that positive relationships can contribute to better adherence [245]. While doctors have one to one opportunities to discuss medication adherence during initial diagnosis, review consultations and when prescribing medications it was clear from the majority of the participants in this current study information had not been transferred successfully to the patient.

In some instances participants described how significant others played a part in their lives. Family had the ability to facilitate adherence to medication by offering both practical help and by reinforcing beliefs in the necessity of medication. The desire to maintain independence and not become a burden on family or doctor appeared to effect behaviour in a positive manner.

It is clear that while the majority of participants in this study certainly lacked knowledge about their condition in the main they held positive beliefs about prescribed medication. When considering the design of an intervention aiming to improve adherence to medication in this population it may be that the timing of transfer of knowledge requires greater consideration. Emphasis should be on delivering knowledge at the appropriate level at an appropriate time while focusing on an individual's personal motivating factors.

Carer' is a professional term and may not resonate with a husband or wife or daughter or son. Informal care is simply 'happening' and not identified as a particular set of tasks Additionally people who had been nominated as an

informal carer did not feel it was their place to discuss the health or treatment of their loved one. In one case a nominated carer declined as they felt inadequately knowledgeable about their relative's health.

5.4. Limitations of the study

This explorative qualitative study has a number of noticeable limitations:

- Overall the majority of participants who volunteered for this study were relatively stable with limited input from specialist healthcare professionals. While several patients demonstrated an inability to recall being given a clear diagnosis of their condition it is impossible to determine the accuracy of this claim. Given the methods employed within this study it is not possible to know whether clinicians had previously discussed a new diagnosis of HF with patients or their informal carers at either initial or subsequent follow up consultations.
- While the original aim of the study was to recruit an informal carer along with each HF patient enrolled in the study this proved extremely difficult. In total only four carers agreed to participate in the study. The lack of carer participation therefore limits the voice of family and informal carers within the study.
- The decision to conduct a formal assessment of mood using the HADS, a quantitative measure, was taken as it was deemed important to identify formally any evidence of mood disorder given the link between HF and depression. It is acknowledged that while the HADS is successfully used as a screening tool at an individual level in clinical practice the usefulness of the data collected in this study is extremely limited due to the very small sample size and number of participants who agreed to complete. Additionally its inclusion at the end of the interview may have some impact on the scores given that participants had been engaged in discussions which may have evoked upsetting thoughts.
- Given the age group and frailty of the participants enrolled in the study member checking was not performed on any of the participant transcripts potentially placing some limitations on the overall

trustworthiness of the results. During the data collection phase several compromise suggestions regarding the best approach to participant validation of the data were considered. Firstly while it would have been possible to send out a partial section of the transcript to participants for review the researcher felt this may have caused confusion for the participants regarding where the text fitted into the broader interview discussion. Secondly while it would have been possible for the researcher to physically return to each participant and review the text in a more interactive way this was not possible due to time restraints.

- Thematic analysis was conducted on all transcripts without disaggregating the data into those who had a nominated a carer enrolled in the study and those who did not. The decision to analysis the data in this way means it is impossible to determine the possible impact of informal carers on an individual's experience of living with HF or their management of the condition.

5.5. Conclusion

This chapter has described the methodology and results of a qualitative study undertaken to explore beliefs around HF and its management with an aim to identifying which commonly held beliefs predict medication adherence. This study concluded that knowledge of both condition and medication was poor amongst this sample of older HF patients. In the main health literacy was low and while participants felt that overall medication was beneficial association between treatment and symptom control was poor.

Participants described both non-conforming non-intentional and intentional non-adherence. A wish to remain independent and a belief in the healthcare professionals' ability to manage their condition and prescribe appropriate treatment were the main reasons given for adherence.

Previous randomised controlled studies in HF populations have attempted to improve adherence to medication by purely focusing on improving the knowledge of their patients [341, 352, 356]. These studies reported no positive effect from the intervention. As discussed in previous chapters improved adherence has been shown to be possible in studies which contained multi-

component interventions. The results from this current study highlight the need for healthcare practitioners to use language which can be easily understood at a time when information is likely to be retained by this population.

While increased knowledge has been shown to improve self-care skills generally, the importance of patients' beliefs and preferences should not be underestimated. By focusing on the individual rather than the population personal motivational factors can be incorporated into adherence-enhancing interventions which should combine a number of strategies including information, reminding and reinforcement.

Following the analysis of the results of this qualitative study emergent themes were used to guide the outcome measurement tools used in the quantitative observational study. This thesis continues with a description of how the themes of condition identity and its impact on day-to-day life; health literacy; beliefs about medications; quality of life, and doctor patient relationship were investigated further.

Chapter 6. Quantitative Study Phase

The previous chapter described the exploratory phase of this PhD undertaken to explore HF and adherence to prescribed treatment from the patient and informal carers' perspective. The results were used in the design of an observational study that aimed to quantify the association of a broad range of factors (including attitudes, opinions and behaviours of older HF patients) with medication adherence. Such an approach complements the findings from the qualitative work.

This chapter contains the study design, methodology and results of this observational study, concluding with the discussion of these findings. Given that this quantitative phase of the PhD was designed to measure which modifiable risk factors where most closely linked to adherence to medication the two main aims of the study were:

1. To assess adherence to ACE inhibitor and Furosemide medication in a sample older patients with heart failure.
2. To establish which factors are associated with non-adherence to medication in older patients with heart failure.

6.1. Observational Study Design

The study was a prospective observational study approved by East of Scotland Research Ethics Service (EoSRES) committee (Ref Number ES/15/0200) on 22nd December 2015. It comprised a single visit either within Tayside Institute Cardiovascular Research (TICR) research facility at Ninewells Hospital, or at the participants own home if this was preferred by the participant. Participants were asked to nominate one informal carer who was asked to complete and return a questionnaire.

6.1.1. Training and Preparation

Background research was undertaken on quantitative questionnaire design and delivery. In an attempt to reduce the burden on the participants, eight of the nine questionnaires were compiled into one easy to follow booklet with the exception of the Montreal Cognitive Assessment (MoCA) which was to be

administered separately. The questionnaire order was carefully considered to ensure there were natural break points during the study visit when the participants could take a rest and restart when able. Font size was maximised to make the questionnaires as easy to read as possible without excessively increasing the number of pages.

In order to gain an understanding of the time it would take to complete the questionnaire, respondent fatigue and identify other potential other constraints the booklet was piloted with three older people. Following the pilot stage the booklet was fine-tuned with some minor adjustments (see appendix I for questionnaire booklet).

6.1.2. Study Population

Community dwelling people aged 70 and over resident in the NHS Tayside health board area with a history of HF (see figure 6.1 for inclusion and exclusion criteria) were recruited from the community via the Scottish Primary Care Research Network (SPCRN) or via the Scottish Health Research Register (SHARE).

INCLUSION CRITERIA

- Community dwelling people aged 70 years and over with a diagnosis of chronic heart failure according to the European Society of Cardiology (ESC) guidelines
- Patients with New York Heart Association (NYHA) class II to IV symptoms
- Patients currently prescribed both ACE inhibitor and oral Furosemide.
- Nominated informal carers of the participants described above

EXCLUSION CRITERIA

- Unable to give written informed consent
- Residing in Nursing home or Residential Home Environment
- Currently receiving daily visits from district nursing service to administer medications
- Currently enrolled in another trial, or within 30 days of completing another trial

Figure6.1: Observational Study inclusion and exclusion criteria

6.1.3. Participant Selection and Enrolment

Initial recruitment of study participants was conducted through SPCRN. However, following slower than expected recruitment from primary care it was decided to open recruitment to potentially suitable participants currently registered on the SHARE database. Following an amendment to the study protocol a submission to the EoSRES committee was made and approved on 8th September 2016.

6.1.3.1.SPCRN

The SPCRN, a network funded by the Chief Scientist Office of the Scottish Government, aims to act as a framework to co-ordinate national research activity in primary care. The network is operationally managed at a regional level by five nodes based in Aberdeen, Inverness, Edinburgh, Glasgow and Dundee.

Research active general practices were invited to join the study by staff employed within the Dundee node. Using the practice IT system and the study inclusion / exclusion criteria a SPCRN research officer produced a list of participants who were potentially eligible for the study. The list was reviewed by one of the practice GP's to exclude any patients who they deemed unsuitable to enter the study because, for example, they had recently been diagnosed with a serious illness, or had been recently bereaved.

An invitation letter and reply slip (appendix J) along with a Participant Information Sheet (PIS) (appendix K) and a stamped addressed envelope were sent from the GP practice to all the patients who were potentially eligible. After reading the PIS, those individuals who wished to know more about the study were asked to respond by returning the reply slip.

Reply slips were collected by the SPCRN team and forwarded to the principal investigator (PI) on the study who subsequently contacted all respondents by telephone. During this initial contact a brief outline was given of the purpose of the study and details of what involvement in the study would entail. Eligibility was also checked and potential participants were encouraged to ask questions

at any point during the phone call. If happy to participate in the study a mutually agreed date was arranged to carry out the study visit.

6.1.3.2. SHARE

SHARE is a NHS Research Scotland initiative created to establish a register of people interested in participating in health research. Since inception in 2011 SHARE has recruited over 200,000 people across Scotland who have agreed to allow SHARE to use the coded data stored in NHS computer records to check whether they might be suitable for health research studies [411].

Following ethical approval the completion of an online application a search for potentially suitable participants was carried out by the SHARE team. Potential participants were identified, and provided with details of the study by telephone, email or letter by members of the SHARE team. Those who expressed a wish to know more about the study gave consent to have their contact details passed to the research team for further information.

At this point the study PI contacted potential participants by telephone. During this initial call a brief summary was given of the purpose of the study and details of what participation in the study would involve. Eligibility was also checked and potential participants were encouraged to ask questions at any point during the phone call. If appropriate, a PIS was sent by either post or email and details of further contact arranged. Once sufficient time had lapsed contact was made again to discuss any queries and arrange the study visit if applicable.

6.1. Informed Consent

Regardless of recruitment site, all those who agreed to participate in the study and attend the study visit gave verbal consent during the initial telephone contact for the study PI to review their hospital notes in order to further assess eligibility and document past medical history. Written informed consent was obtained from each participant at the beginning of their study visit (see appendix L for observational study consent form)

6.1.5. Observational Study Outcome Measurements

All visits for the study were carried out either in the participants own home or within the study rooms at TICR, Ninewells Hospital. Taxi transport was provided if required. (See table 6.1 for the study matrix of visit activities). During the pre-visit phone call all participants were instructed to take all their medications as normal on the day of the visit and to bring along an up to date record of all current medications.

Inclusion / exclusion criteria were re-examined at the beginning of the study visit to confirm suitability for study entry.

6.1.5.1. Demographic information

In order to assess their possible effect on HF medication, social support and demographic information were collected during the initial stage of the study visit. For each participant, characteristics such as ethnicity, gender, age, home circumstances and marital status were recorded in the case report form (CRF). As previously discussed there is currently no conclusive evidence to support either age or gender as factors for non-adherence in this population while living alone has been associated with an increased risk of non-adherence to medication.

A meta-analysis of literature looking at the effect of social support on adherence to medical treatment reported a modest increase in adherence levels amongst those who were married or and living with another person [188]. Lack of social support has also been cited as a factor for non-adherence. Several studies have examined the role played by family and significant others concluding that support from family and friends was important for taking medicines and following medical advice in HF. With this in mind those carers nominated by participants were given invited to participate. An invitation letter (appendix M); a Carers Participant Information Sheet (appendix N) and a Carers Consent Form (appendix O) was given to the HF patient to pass on to their nominated carer.

	Pre-visit call	Study visit	Postal	Post visit
Inclusion/Exclusion Criteria	✓			
Verbal Consent	✓			
Informed Consent		✓		
Demographics		✓		
Medical History	✓	✓		
Measurement of Adherence to Medication:				
Direct adherence assessment: Blood sample for serum ACE I and/or urine sample for furosemide		✓		
Adherence self-report assessment: Morisky Medication Adherence Scale (MMAS)		✓		
Retrospective prescription filling data: Assessed by dividing the total number of HF medication dispensed by the total number of days the medication was prescribed in the previous 12 month period				✓
Predictors of Adherence:				
Functional status: SPPB		✓		
Medication burden: list of current medication		✓		
Symptoms of condition: NYHA class		✓		
Record of Recent Hospitalisations		✓		
Comorbidity: Charlson comorbidity index		✓		
Deprivation Level: Scottish Index of Multiple Deprivation (SIMD)		✓		
Beliefs about Medication Questionnaire (BMQ)		✓		
Illness Perception questionnaire (IPQ-R)		✓		
Cardiac Self-efficiency Scale		✓		
Cognition: Montreal Cognitive Assessment		✓		
Mood: Hospital Anxiety and Depression Scale (HADS)		✓		
Health Literacy Assessment		✓		
Carers beliefs: Carers Questionnaire			✓	
Quality of Life: Kansas City Cardiomyopathy questionnaire (KCCQ)		✓		
Satisfaction with doctors' communication: Medical Interview Satisfaction Scale (MISS-21)		✓		

Table6.1: Observational Study matrix

6.1.5.2: Measurement of Adherence to Medication

According to Lam et al [129] any medication adherence measure should be both reliable and flexible whilst remaining low cost and practical. Given that there is no one 'gold standard' tool to determine medication adherence levels, the use of a multi measure approach may help compensate for recognised weaknesses of individual measures [129]. While objective measurements usually involve the detection of a marker in a body fluid such as blood or urine, indirect measures may include prescription filling dates, tablet counts, interviews or diaries as well as therapeutic and preventive outcome measures [112]. In order to accurately assess measurement of adherence to medication, the following adherence measures were used:

a) Direct methods for assessing medication adherence:

Adherence to ACEi

According to current SIGN guidelines all patients diagnosed with HFrEF should be prescribed ACEi medication [1] which are now an accepted part of the routine management of patients with HF and commonly prescribed amongst this group of patients.

One direct method of assessing that a particular medicine has been taken involves the detection of the drug or its metabolite in a biologic fluid [122]. Serum ACE (SACE) is already commonly measured in hospital laboratories as a way of assisting with the diagnosis of sarcoidosis, a disease in which SACE activity is elevated. ACEi suppress the activity of SACE – in most cases to undetectable levels. SACE activity has therefore been used in HF patients to identify non-adherence with ACEi therapy [412]. In previous research conducted by Struthers et al, SACE activity <6.5u/l was reported to give a predictive accuracy of 81% that adherence to ACE I treatment was > 85% [412].

While the measurement of SACE may provide high predictive accuracy for identifying poor treatment adherence trace presence of a particular drug simply confirms that the patient has taken a dose recently [122]. As previously discussed it cannot however quantify the way the medicine has been taken or assess adherence over a period of time. A 5ml sample of venous blood was collected from each participant in a gold vacutainer. Following collection all

samples were delivered to the Core Laboratory at Ninewells Hospital, Dundee for analysis. SACE was measured by monitoring the alteration in absorbance at 340nm of the hydrolysis of furylacrylolylphenylalanylglycylglycine (FAPGG) to FAP and GG on the automated Advia 2400 chemistry system (Siemens, UK). All results were returned within 24 hours with a cut of <6.5u/l taken as adherent to medication.

Adherence to Furosemide

Despite the advances in treatment of HF over the for 20 years with the introduction of drugs such as ACEI, angiotensin receptor blockers (ARBs) and beta-blockers diuretic therapy remains part of routine management in the majority of patients with HF [413]. Diuretics inhibit the reabsorption of sodium or chloride at specific sites in the renal tubules and have been shown to show diuretics improve both mortality in patients with HF [414] as well as relieve congestive symptoms and fluid retention [415].

Due to their potency and ability to maintain their diuretic effect loop diuretics such as furosemide and bumetanide are the most commonly used class of diuretic therapy in HF [416]. Following oral administration of furosemide the onset of diuresis usually occurs within 30 minutes to 1 hour with optimum effect after around 1–2 hours. In patients with HF however pharmacokinetics of loop diuretics are altered resulting in a prolonged time to peak concentration [417].

Given that furosemide is much more commonly prescribed than other loop diuretics, and that approximately 50% of the oral dose of furosemide is excreted unchanged in the urine, furosemide was selected as a suitable HF drug suitable to assess adherence.

All participants were asked to provide a sample of urine obtained within six hours of taking their morning medication which was transferred into two 1ml urine aliquots before being stored in a locked laboratory in a -20^{o}C freezer. Following the last participant visit all samples were analysed in the Biomarker and Immunoassay Biomarker Core Laboratory, University of Dundee using the assay Neogen Furosemide ELISA kit Product# 104219-1 [Lexington, KY, USA] which is designed for the screening of trace quantities of Furosemide and /or other metabolites in human urine, blood or oral fluid. The intra assay variation

of optical density of duplicate samples was found to be 7.1% on the first plate and 11.8% on the second with intra assay variation on quality control (n=6) 5.2%.

Indirect methods for assessing medication adherence

While adherence monitoring methods which asses the level of medicine or metabolite in blood or urine are considered to be more robust than indirect methods, variations in metabolism mean that there are also limitations to these direct methods of adherence assessment [127]. While assessment of both SACE and urinary furosemide levels offer an indication of adherence to HF medication on the day of the study visit it is important to highlight that these direct methods may indeed result in a biased measure of patient's medication taking behaviour as results refer only to the days of sample collection [418].

As previously stated in this thesis indirect methods to assess adherence to medication are commonly utilised and can be either objective, such as pill counting, or subjective, such as participant self-report.

Self-Reported Adherence

Self-report measures have the benefit of being inexpensive acceptable to patients and easy to administer. However, methods such as structured interviews and patient diaries are open to the potential for inaccurate patient recall or the reporting of an overly high estimation of adherence in order to please healthcare providers [419]. Factors such as the relationship between the healthcare professional and the patient, the time frame used to recall behaviour and the wording of questions have been identified as having a potential effect on both accuracy and validity of self-report measures [124].

In order to minimize the limitations of self-report methods and to standardise the measurement of adherence to specific medication regimes, structured self-report questionnaires have been designed and validated against other subjective and objective measures [129]. While several questionnaires exist no one tool has however been identified as being "gold standard" or deemed appropriate for every setting [420]. Prior to the selection of a self-report measure for use within the study several questionnaires were considered:

The Brief Medication Questionnaire (BMQ) is a questionnaire consisting of three sections designed to detect repeat and sporadic non-adherence; assess beliefs about medication and identify difficulties in remembering medication-taking behaviour [421]. One notable limitation of the BMQ is that it requires the production of a comprehensive list of medication regimens the completeness of which may pose difficult for those patients with recall deficits if the medications are not to hand [422].

The Medication Adherence Questionnaire (MAQ) is a structured, 4-item self-report questionnaire originally developed to measure medication adherence to antihypertensive treatment by Morisky et al. In the original study researchers reported that participants scoring high on the MAQ were significantly more likely to have their blood pressure controlled compared to those who scored low on the scale ($r=0.58$; $P<0.01$) [423]. Additionally the MAQ is noted to be adaptable, quick to administer and validated in a broad range of conditions [424].

The Morisky Medication Adherence Scale (MMAS-8) is an 8-item questionnaire based on the MAQ with the addition of items focusing on medication-taking behaviours. The questionnaire has been specifically designed to avoid the 'yes saying' bias where patients only offer positive answers to a series of questions regardless of their content [425]. The new scale has been determined to have higher reliability compared to the 4-item MAQ scale (Cronbach's $\alpha= 0.83$ vs 0.61) [423, 425].

The MMAS-8 has been validated in patients with a range of chronic diseases. In HF it has been used to assess medication adherence in several studies [368, 370] where the term "antihypertensive medication" had been substituted for "heart failure medication". In a previous cross-sectional study conducted among an older hypertensive population, the MMAS-8 was reported to be significantly associated with non-adherence determined by pharmacy fill adherence, correctly classifying ≥ 75% of patients as being adherent or not [426].

Each item on the questionnaire measures a specific medication taking behaviour, not a determinant of adherence behaviour. A dichotomous

response choice of "yes" or "no" is requested for the first seven items while the last item adopts a 5-point Likert response ("never", "rarely", "sometimes", "often" or "always"). Following scoring guidelines reported elsewhere [420, 425], each no response was scored as "1" and each yes response scored as "0" with the exception of question 5 where the scoring is reversed. For item 8, the Likert score was rated from "0" to "4" with the number divided by four before the value of the eight responses is summed. Unlike other scales which have recommended cut off values for adherence the MMAS-8 ranks the the degree of adherence as low, medium or high instead of defining an absolute cut off. Given its previous validation within the HF population the MMAS-8 was chosen as a measure of medication adherence self-report for the purposes of this thesis.

While self-report questionnaires should be completed by patients themselves this may pose difficulties for some older patients and those with low levels of literacy. While all participants were asked to complete the questionnaire themselves, the questions were also read out to the participants if they requested this in order to clarify what was being asked. The degree of adherence was determined according to the score resulting from the sum of all the correct answers: high adherence (eight points), moderate adherence (6 or 7 points) and poor adherence (< 6 points) previously used in other studies [427, 428]

Despite the use of a validated questionnaire designed specifically to reduce bias it is important to view the results of the self-report measure in relation to the other primary outcome measures. In a study reporting on self-report adherence verses MEMS, Nieuwenhuis et al assessed adherence to ACEi/ ARB medication in HF patients where medication adherence measured by the MEMS was reported to be significantly lower than self-reported adherence (76% v 100%) [121].

Computerised Pharmacy Records

Computerised prescribing records and computerised pharmacy dispensing records can be used to provide an indirect assessment of medication adherence. First developed in the 1980s these measures have become more

widely available with the greater availability of electronically recorded, routinely collected clinical data, and have been shown to correlate with a broad range of patient outcomes in patients with CAD [429]. In a longitudinal study assessing the accuracy of computer pharmacy records in patients with HF who were prescribed beta-blockers dispensing records reported adherence as 97.8% ± 11.8% (range 58.1-128.6%) compared to MEMS adherence which was reported as 97.1 ± 7.3% (range 58.1-103.9%) [430].

While both computerised prescribing records and computerised pharmacy dispensing records have previously been used to assess medication adherence the disadvantage of computerised prescribing records is that they only report the prescribing of a medication, not whether that the patient has taken it to a pharmacist to be dispensed. For the purposes of this thesis prescription refill records taken from computerised pharmacy databases were used to obtain estimates of adherence, thus overcoming this limitation of prescribing records.

Computerised pharmacy data containing all medications issued for each participant during the 24 months preceding enrollment into the study were obtained from the Health Informatics Centre (HIC) at University of Dundee. HIC hosts various linkable health data for the population of Tayside and Fife including community dispended prescribing, laboratory tests, hospital stays and deaths. To protect confidentiality, data can only be accessed through a restricted, secure IT environment, where the data handler is given secure remote access to carry out their analysis.

Medication adherence to HF specific medication was calculated as the proportion of days covered (PDC), based on the total number of days supplied for each class of medication divided by the observation time interval. Patients were classified as “nonadherent” based on a PDC <0.80.

6.1.5.3. Predictors of adherence

As many as 200 factors have been hypothesized to influence adherence and these factors can be classified as either intentional or unintentional [431]. Such a high number of factors could not be included in one observational study, especially where numbers of participants are limited. The results from both the

systematic review and the qualitative study were examined to identify the following determinants as possible factors to adherence in this population warranting further assessment.

1. Comorbidity and medication burden

In order to assess the burden of co-morbid disease and medication on adherence the following information was collected:

I. Past medical history, obtained from the medical case notes and patient self-report. This included dates of diagnosis (if known) and whether the condition was currently an on-going problem.

II. A list of concomitant medications to assess medication burden. Participants were asked the following:

   a. Their understanding of each medication currently prescribed

   b. To identify the reason they believe it had been prescribed,

   c. To describe any associated side-effects experienced and

   d. Their understanding of the likely duration of prescribing.

   e. To describe their usual routine for medication taking identifying any visual cue or prompts or medications used to aid adherence

III. To access the effect of multi-morbidity on adherence, The Charlson Comorbidity Index (CCI) was calculated for each participant. The CCI was originally developed as a prognostic indicator for patients with a variety of medical conditions and is currently the most extensively validated measure used to assess the prognostic impact of multiple chronic illnesses [432]. The CCI score was calculated for each participant using the assigned weighting score for each of the 19 categories of comorbidity. Each condition is assigned with a score of one, two, three or six depending on the risk of dying associated with this condition. The final CCI score was calculated simply as the sum of weighted values ranging from 1 (only HF present) to 30 (extensive comorbidity) and recorded in the CRF. Given that all participants were aged 70 years or over no score was attributed to age.

2. Symptoms of condition

As determined by the literature several studies have shown a relationship between presence of symptoms and adherence to medication [164, 1710, 172] thus worthy as consideration as a factor for adherence in this population. While dyspnoea is identified as a classic symptom of HF it is important to highlight that it is also a symptom commonly found in the general population. Not all patients with HF experience dyspnoea, while this symptom may be present for a host of other cardiac and non-cardiac reasons [433].

Another symptom commonly associated with HF is fluid retention occurring as a compensatory response to poor cardiac output. An excess of fluid leaks out of tissue space as a result of hydrostatic pressure and the osmotic process usually ending up in the ankles due to gravity. If this fluid continues to build up it may be forced higher into the sacrum and abdomen (ascites). Ankle oedema in HF is bilateral and described as 'pitting' to pressure [16].

The most commonly used classification system for HF is the New York Heart Association (NHYA) functional classification system which provides a four stage classification of symptoms relating to everyday activities and quality of life. This classification system has been in use since 1902 and provided a common language for clinician communication before objective measurements of cardiac function were available. It is a simple practical method to assess if someone has improved or worsened and has been widely used in both clinical practice and clinical trials. It is not however without its problems. The lack of standardized criteria in assigning an NYHA class has been criticised - the scale is highly subjective relying as it does on patient self-reported information leaving it open to bias. Overall there is little evidence for the reliability, or reproducibility, of the NYHA classes, leaving a serious gap in the literature [434].

Importantly, the NYHA classification may be difficult to assess in patients with some co-morbid conditions such as respiratory disorders or in people with physical function limited by other conditions. It may be difficult to determine if people with severe arthritis, or with conditions such as Parkinson's disease, are limited by these or by the HF. This can be a particular problem in older people, who often don't complain of being breathless but choose to limit their

activity before they become breathless.

All patients were examined for evidence of ankle oedema. Where oedema was not present at the time of the study visit participants were asked to report on any history of leg swelling as well as describe any activities which may result in episodes of shortness of breath. NYHA class was reviewed at the study visit and recorded in the CRF.

3. Record of recent hospitalisations and contact with health care professionals

Healthcare utilisation has been identified as a possible factor for adherence to medication in patients with HF. A systematic review carried out by Oosterom-Calo et al reported on a limited number of studies assessing adherence across different aspects of healthcare utilisation. While a positive association between adherence and institutionalisation was reported the evidence regarding outpatient visits and number of healthcare professionals seen was found to be inconsistent [43].

All participants were asked to recall hospital stays of 24 hours or more within the previous 12-month period as well as all contact made with healthcare professionals. Hospital case notes were checked to validate this self-report and establish any stays or appointments which the participant had forgotten. A record detailing all hospital stays along with relevant healthcare related contact was detailed in the participants CRF.

4. Deprivation Level

As previous stated, while those who are least deprived on average live longer and are more likely to access specialist medical services such as a HF consultant run clinic there is limited evidence to support the possible effect of deprivation on medication adherence [1610]. Quick and easily accessible, the Scottish Index of Multiple Deprivation (SIMD) [435] provides a relative measure of deprivation based on the methodology developed by the Social Disadvantage Research Centre at the University of Oxford. The index identifies multiple deprivations for 6505 small areas (data zones) across Scotland. They are a combination of 38 indicators across seven domains, namely: income, employment, health, education, skills and training, housing, geographic access and crime. The term ‘deprivation decile’ is used to

represent 10% of a population with a particular level of deprivation therefore, the most deprived decile equates to the most deprived 10% within a population, while the least deprived decile represents the 10% of a population living in the least deprived circumstances.

The Scottish Government Website contains a database of all Scottish postcode areas. Within the database users can enter a postcode for any local authority. Each SIMD decile was identified using the postcode from the participant's home address and recorded on the CRF.

5. Cognition:

In HF, evidence suggests that the presence of cognitive impairment may have a negative effect on adherence [190]. Given the lower age limit for recruitment to this study was 70 years assessment of cognitive function was assessed as a factor for adherence. A review of available screening tests for cognitive impairment identified 39 available tests, 13 of which were deemed suitable for brief assessment in the doctor's surgery or outpatient environment [436]. Of these the Folstein Mini-mental Status Examination (MMSE) was the most widely used. Developed over 40 years ago the MMSE is a 30-point questionnaire focusing primarily on language and short-term memory, while briefly touching on other cognitive domains such as aphasia, apraxia and agnosia [437]. The MMSE has however not only proven to be insensitive to early changes in these domains it does not examine executive function and has been found to be insensitive to the detection of mild CI [438]. Furthermore, the MMSE is copyrighted causing alternatives assessments to be sought.

The Montreal Cognitive Assessment (MoCA) is a single page 30-point screening tool which is available to use free without permission. The test has been validated for use in both the community and academic setting. Detecting a broader range of cognitive deficits that MMSE (which is heavily weighted to orientation), the MoCA has been reported to be better at identifying executive dysfunction, particularly important in those with vascular disease. A longitudinal study comparing the effectiveness of the MMSE and MoCA in 50 older patients found poor correlation between the mean test score for MMSE and the MoCA (26.5 vs. 22.2) with a Pearson's correlation co-efficient between

scores of 0.695 ($p<0.003$) The study authors concluded that the MMSE lacked sensitivity to milder cognitive deficits, was influenced by age, gender, educational level and socio-economic status and thus did not perform well as a screening tool for mild cognitive impairment.

Commencing with an assessment of executive function, the test can be completed in around 10 minutes and comprises of assessment of the following eight cognitive domains: orientation to time and place; short term memory recall; visuospatial ability; working memory, attention and concentration; executive functioning and language [(439)]. In the initial study establishing the MoCA, the control group had an average score of 27.4 out of a possible 30 compared with 22.1 in those with mild cognitive impairment. Those diagnosed with Alzheimer disease recorded an average score of 16.2. For this current study the following cut off ranges were used to grade severity: 18-26 = mild cognitive impairment, 10-17= moderate cognitive impairment and less than 10= severe cognitive impairment.

For the purposes of this thesis the MoCA was chosen as a measure of cognition. All participants where guided through the assessment following collection of the demographic and background data with the overall score out of 30 calculated and reported in the participants CRF.

6. Illness Perception:

When faced with a new diagnosis of a condition individuals develop a pattern of beliefs in order to manage that illness. The majority of published studies focusing on patients perceptions of illness are based on the self-regulatory model of Leventhal et al [(440)] which proposes that representations both cognitive and emotional are generated and that these illness perceptions directly influence both an individual's emotional response to the illness and their coping behaviours such as medication adherence [(441)].

Identifying and modifying an individual's perception of illness has been shown to improve outcomes in patients following MI as well as other conditions such as diabetes. The Illness Perception Questionnaire (IPQ) was developed to provide a quantitative assessment of the five components of illness representation [(442)]. The Revised Illness Perception Questionnaire (IPQ-R)

extended the original scale by increasing the number of domains to seven [443]. The control dimension was split into personal control and treatment control while a cyclical timeline dimension and an overall comprehension of illness dimension were incorporated.

The IPQR and the IPQ-R have both been used with a wide variety of patient groups including those with asthma [444], post myocardial infarction [445] in atrial fibrillation [446] and hypertension [447]. Overall it has demonstrated good internal reliability and predictive validity [448]. In HF the IPQ-R has been used to assess the relationship between illness representations, treatment beliefs and self-care [2931]. In this study the questionnaire was adapted to make the questions specific to the HF population and reported internal reliability of α=0.74. In relation to medication adherence, the IPQ-R was utilised by Molloy et al who reported beliefs about HF to be directly associated with adherence to ACEi medication [44].

For this current study perceived identity of HF was assessed using a list of 15 possible symptoms detailed on the initial part of the IPQ-R. Each participant was asked if they had experienced any of the listed symptoms and whether they perceived each of the symptoms as being as a result of having HF. Each symptom is rated using a yes (1) no (0) scale, thus the higher the score, the greater the number of symptoms experienced or perceived to be related to HF.

For each of the remaining questionnaire domains participants were asked to rate their response to a number of statements on a 5-point Likert scale. In addition to the domains discussed above, the questionnaire also examines the patient's perception of the causes of their illness. The questionnaire lists possible causes, with the opportunity for the participant to identify any other cause not listed.

Personal understanding about the illness and positive beliefs about the controllability of the illness are indicated by the recording of high scores on the personal control, treatment control and coherence dimensions. However high scores recorded on the identity, timeline, consequences, and cyclical dimensions represent strongly held beliefs about the number of symptoms

attributed to the illness, the chronicity of the condition, the negative consequences of the illness, and the cyclical nature of the condition.

For the purpose of this thesis the IPQ-R was adopted to assess beliefs around the condition of HF. All participants were guided through the questionnaire and encouraged to complete all parts if possible. Reponses where transferred into an Excel spreadsheet to enable the calculation of individual scores for each of the seven domains.

7. Self-Efficacy:

As stated earlier in this thesis the belief in one's ability to carry out a task and achieve the desired result has been identified as a predictor of behaviour. According to Bandura because self-efficacy is concerned with perceived capability any measurement tool looking to assess the construct should adopt questions phrased in terms of 'can do' (judgment of capability) rather than 'will do' (a statement of intention) [448]. Additionally assessment of self-efficacy can only relate to behavioural factors over which people can apply some element of control. Bandura himself developed a standardised measurement tool used to rate confidence in performing a task which included a 100-point scale, divided into 10-unit intervals however this format was not based on any empirical evidence. Alternative formats of the initial measurement tool have been used subsequently including a rating scale that consists of choices from 1 to 5 or 1 to 4, or a simple yes / no format [449].

Historically, studies of self-efficacy in patients with cardiovascular disease have focused mainly on its role in cardiac rehabilitation however several systematic reviews having been published addressing self-efficacy strategies to improve exercise in patients with HF [301] and self-efficacy and educational Interventions in HF [304]. The Cardiac Self-Efficacy Scale (CSES) is a self-report inventory developed to examine the role of self-efficacy in patients with coronary disease. In completing the questionnaire respondents are asked to rate their confidence with knowing or acting on statements using a 5-point Likert-type scale ranging from not at all confident, to completely confident [450]. Each item can also be rated as not applicable. A score is acquired by summing

the responses to each element before dividing the total by the number of rated items. Items rated as not applicable are not included in the averages [451].

The CSES has been shown to be a reliable measurement of self-efficacy in patients with a history of CHD**.** The original authors divided the CSES into two subscales - controlling Symptoms (SE-CS 8 items) and maintaining functioning (SE-MF 5 items). On initial testing both sub scales demonstrated excellent internal consistency reliability Cronbach's alpha =0.90 for SE-CS and 0.87 for SE-MF. Controlling for a selection of baseline variables, the CSES also demonstrated good convergent and discriminant validity significantly predicting physical function, social function, and family function [452].

Despite the CSES being developed initially for use in patients with CAD where day-to-day symptoms do not usually fluctuate as they may do within the HF population, the initial evaluation study by Sullivan et al comprised of a sample of whom 30% of the participants presented with LVEF <50%. Since inception the tool has since been successfully used to measure self-efficacy within the HF population [452-455]. For the purposes of this thesis the CSES has been adopted as the measurement of self-efficacy.

8. Medication beliefs:

As previously discussed non-adherence behaviours can be categorised as either non-intentional or intentional, the latter arising when a patient makes a deliberate decision not to take their treatment as instructed. While theoretical models such as the HBM and the TRA have previously demonstrated a relationship between adherence and perceived barriers, they do not consider health-related decisions to be a dynamic process [40].

Research conducted with patients with a variety of long-term conditions suggests that the key beliefs influencing patients' common-sense evaluations of prescribed medicines can be grouped under two categories: perceptions of personal need for treatment (necessity beliefs) and concerns about a range of potential adverse consequences [456].

Over the past decade, a number of studies have been conducted using the the Beliefs about Medicines Questionnaire (BMQ), a validated tool developed by Horne and Weinman to measure medication beliefs related to taking

medications for chronic conditions [457]. Comprising of two sections, the questionnaire examines firstly the beliefs about medications specific to the individual themselves (BMQ-specific) followed by a section relating to beliefs around medication in general (BMQ-general). The questionnaire has been devised to enable one section to be used either in conjunction with or independently of the other.

The BMQ-specific is a 10-item scale comprising of two 5-item subscales assessing firstly an individual's beliefs about the necessity of prescribed medication (Specific-Necessity) followed by their concerns about any negative effects resulting from taking their medications (Specific-Concerns). Participants are asked to rate each item on a 5-point Likert scale ranging from 1 – strongly agree to 5 – strongly disagree. Each subsection is then summed giving each a score ranging from 5 to 25. A higher score on the specific-necessity subscale indicates a stronger belief in the necessity of the medication while a higher score on the specific-concerns subscale indicate stronger concerns around the taking of medications [458].

The BMQ-General comprises two 4-item sub-scales assessing beliefs that medicines are harmful (General-Harm) and that medicines are overused by doctors (General-Overuse). Items are again scored using a 5-point Likert scale before being summed resulting in possible score of 4 to 20. Higher scores indicate stronger beliefs about the corresponding concepts in each sub-scale, i.e. the higher the score the more negative beliefs about medicines held.

In the original questionnaire development the researchers carried out replication of the tool across different illness samples and demonstrated an acceptable degree of stability. It is therefore suggested that each individual aspect of the tool represents a 'core theme' underpinning common representations of both specific and general medications thus suitable to be used across different disease specific populations [457].

A recent meta-analysis reported on studies using the BMQ to examine perceptions of medication in patients with long term conditions [456]. Across 94 studies, stronger perceptions of necessity of treatment was associated with higher adherence, OR=1.74, [95% CI 1.57 to 1.93], p=0.0001, and fewer

concerns about treatment, OR=0.50, [95% CI 0.45 to 0.56], p<0.001. The association between necessity and adherence as measured by MMAS was OR=1.84, [95% CI 1.31 to 1.86], p<0.001 while association between concerns and adherence as measured by MMAS was OR=0.59, [95%CI 0.43 to 0.82], p=0.002.

In patients with HF, Percival et al utilised the BMQ to identify beliefs held about medication and how these beliefs related to adherence. The authors reported a significantly higher median necessity score in the adherent group v non-adherent group (22.0 vs.19.5, p=0.03). Patients with a strong necessity score also had significantly higher self-reported adherence compared to patients with a strong concerns score (21.5 vs. 18.0, p=0.006) [(195)].

Importantly, beliefs about medicines have been shown to remain stable over time. As part of a study about non-prescribed analgesics Porteous et al used the BMQ-General to compare beliefs about medicines at two time points, four years apart, in 3,000 individuals selected randomly from the Scottish electoral roll. Participants reported beliefs about medication which remained stable over time, irrespective of changes in health status [(459)].

For the purposes of this thesis the BMQ–specific and the BMQ–general have been adopted to assess the beliefs held about medications in this sample of HF patients. All participants were asked to complete both parts of the questionnaire. All sub-scale scores were calculated as described above and entered into the CRF.

9. Measures of Physical Function:

Impaired physical function and impaired exercise capacity are a major source of disability in older people [(1532)]. Measures of physical function have been shown to be accurate indicators of current health status, be predictive of future health and disability, and are useful tools to predict the likelihood of health and social care use in the future [(154)]. As a predictor for adherent behaviour, it is unclear if poor physical function, perhaps as a consequence of symptomatic HF, increases adherent behaviour in an attempt to improve symptoms or conversely whether having to take medication is simply too much of a burden

when physical function is reduced. Function may be assessed by either self-reported questionnaires or by tests of physical performance.

Standardised physical performance tests are commonly used in ageing research and have been found to be positively associated with health status as well as being predictive of outcomes such as hip fracture, nursing home admission and death [155]. Evidence also exists that these tests are suitable for use in non-disabled adults [156] as well as being able to identify those who are at increased risk for the onset of functional dependence [157;158].

The Short Physical Performance Battery (SPPB) is an objective assessment tool for evaluating lower extremity functioning in older persons and has been designed to measure physical performance and decline over time. It was developed by the National Institute on Aging and is freely available for use without permission or the payment of royalty fees. The SPPB predicts long term disability and future institutionalisation [159]. A 4 year prospective cohort study of older, non-disabled older adults found that those with the poorest lower extremity performance at baseline spent significantly more days in hospital (17.7 v 9.7 days) when compared to those who had recorded a high performance even after adjustment for baseline chronic conditions [160]. In a recent study comparing the predictive value for mortality of several different performance measures, the SPPB score emerged as the strongest predictor of mortality in older community dwelling participants with the chair stand subtask showing highest predictive value [161]. The test is easily administered, takes around 10 minutes to complete and can be easily reproduced.

The three-part test was explained fully to each participant and commenced only after they had had the opportunity to rest for 5 minutes. Each part of the test was demonstrated by the researcher before scores were obtained by the participant for each of the three parts: balance testing; gait speed testing and chair speed testing and entered into the CRF under the relevant section. The test focuses on lower limb function using tasks that mimic daily activities and includes balance stands with the feet held in 3 different positions for 10 seconds each; one chair stand followed (if completed successfully) by 5 timed chair stands, ; and finally a timed 4 metre walk to measure gait speed.

Any part of the test either not attempted or not completed by the participant automatically scored a zero and was entered into the CRF while standardised encouragement was offered at various points during the test.

10. Mood

In HF, evidence suggests that negative emotions, particularly depression, may be associated with non-adherent behaviour [225]. The Hospital Anxiety and Depression Scale (HADS) is a self-report scaling system consisting of fourteen items on a 4-point scale (range 0-3). The questionnaire comprises of seven questions for each of the domains of anxiety (HADS-A) and depression (HADS-D) interspersed within the questionnaire. It has been suggested that a sub-score of ≥11 indicates probable presence requiring further management with scores falling between 8 and 10 suggestive of the presence of the stated and further assessment should be carried out [460].

The HADS was initially developed as a screening tool for identifying and quantifying anxiety and depression in patients with physical health conditions. Unlike other scales such as the Beck Anxiety Inventory [461] or Generalized Anxiety Disorder-7 the HADS does not contain somatic symptoms such as headaches, insomnia and fatigue which could be attributed to the participant's physical ill-health [462]. Additionally the HADS correlates well with other measurement tools for anxiety and depression [463].

The HADS, while not a diagnostic tool, has been shown to be a valid and reliable tool used to identify medical patients who may have depression and anxiety [464]. In a systematic review of 71 papers the sensitivity and specificity of HADS-A and HADS-D with a threshold of each subscale of ≥ 8 ranged from 0.7 to 0.9. In a study examining the validity of both the GDS-15 and the HADS within the older HF population the HADS was identified as a valid tool for detecting anxiety and depression symptoms in older HF patients within an outpatient setting.

For the purposes of this thesis the HADS has been adopted to assess mood in the study population. Each participant was instructed to choose one of four possible answers rated on the 4-point scale in relation to their general mood over the preceding month. Once all fourteen questions had been completed

the total score was calculated for each domain by totalling the scores from the respective seven questions. The total scores for each domain (range 0-21) were recorded in the CRF.

11. Carers Beliefs

According to Leventhal et al self-regulation process "does not take place in a social vacuum; rather, it is interpersonal as well as intrapersonal" [286]. The formation of beliefs about illness is therefore strongly influenced by information gathered from peoples' social environment, including of course family members. When presented with a diagnosis of HF therefore patients will begin to develop subjective interpretations of the condition in order to develop an understanding [465].

Research shows that having the support of significant others plays an important part in how an individual manages their illness. In order therefore to be able to fully understand adherent behaviours an awareness of how significant others view the condition and its treatment is important [465]. In a study looking at the degree of similarity between patients post MI and their partner's perceptions of MI, those patients and partners who reported similar positive cure/control beliefs greater change in behaviour related to dietary intake were reported [466].

In this thesis carers beliefs regarding their relatives HF were assessed using the previously described IPQ-R while the BMQ assessed whether the beliefs that carers held around medication had an impact on the adherence behaviours of the participants.

At the end of the participants' study visit, time was allocated to discuss the possible nomination of an informal carer. Those participants who felt able to do so were supplied a carer's pack containing the following: a carers invitation letter (appendix M); a carers PIS (appendix N); an informed consent from (appendix O), both questionnaires and a self-addressed envelope for return of completed documentation. Name and contact details for the study team were also supplied in case any carers wished to discuss the study further.

12. Health Literacy

As previous stated, health literacy has been associated with reduced knowledge of disease, poorer health outcomes and reduced adherence to medication [203-207]. In HF, higher levels of health literacy have been associated with higher levels of adherence [209]. Several screening tools for health literacy currently exist focusing on an individual's ability to read, and in some cases use, numbers. One such test is the Short-Form Test of Functional Health Literacy (S-TOFHLA), which consists of a 36 item reading comprehension test required to be completed within a 7-minute time frame. The S-TOFHLA entails the reading of a health related passage from which words have been omitted. The participant is required to select each appropriate missing word from the multiple-choice list supplied. Scores are categorized as: inadequate (0–16 points), marginal (17–22 points), and adequate (23-36 points).

While the S-TOFHLA has been identified as a reliable and valid measure of health literacy [467] an evaluation of the measurement tool within a population of HF patients reported that a 15 percent correct score improvement was noted when the 7-minute time limit was not enforced. This would mean 25% of participants improving at least one literacy level [468]. The study authors concluded that use of the S-TOFHLA might result in patients with HF being inaccurately categorized as having low or marginal health literacy when the S-TOFHLA time limits are enforced. For these reasons the tool was not deemed a valid measure of health literacy for this study.

Worryingly, given that the only ongoing reinforcement of correct medication taking instructions HF patients may receive is contained on the label of their daily medication one in three older adults are unable to understand the basic usage instructions written on a medicine label [469]. With this in mind functional health literacy was assessed in this study using a brief four item comprehension test based on the instructions given on an over the counter purchased medication. This assessment method has been used and reported on elsewhere including the International Adult Literacy Survey [470].

Participants were invited to read a fictitious medicine label enlarged to A4 size before being asked four questions developed by Bostock et al [469] based on

the conceptual framework that defines literacy as an ability to fulfil goal directed tasks [455]. Each correct answer scored 1 point resulting in a health literacy score of 0-4. Level of literacy was then categorised into high (no errors), medium (one error) or low (more than one error). While neither validation nor performance metrics for the tool are not available, this scoring method has been used previously in a longitudinal cohort study of older adults who reported medium or low functional literacy levels in 32.8% of the 7857 participants sampled. Similarly von Wagner et al classified functional health literacy as being either marginal or inadequate in 30% participants aged >65 years in a population survey carried out in the UK using the TOFHLA [471].

13. Quality of life

HRQoL is an important indicator for assessing the burden of disease or illness on an individual and it is widely believed that patients who adhere to their treatment regimes should experience an improvement in their HRQoL [472]. HRQoL assessment measurement tools may be either generic or disease-specific.

A systematic review of currently available HRQoL tools for CHF, identified seven questionnaires [473]. Of these seven, three disease-specific instruments were recommended above the others: The Minnesota Living Heart Failure Questionnaire (MLHFQ); The Chronic Heart Failure Questionnaire (CHFQ) and the Kansas City Cardiomyopathy questionnaire (KCCQ). While reliability and validity is well documented for both the MLHFQ and the CHFQ some studies have questioned the MLHFQs responsiveness to interventions [474] while the CHFQ has been criticised for being overly complex to administer [475].

The Kansas City Cardiomyopathy questionnaire (KCCQ) is a 23-item, (15 question) disease-specific measurement of HRQoL. The most recently developed of the HF specific HRQoL instruments designed when advantages and disadvantages of the other tools had been identified. The questionnaire has five individual subscales: physical limitation; symptoms; quality of life; social interference and self-efficacy. All items are measured on a Likert scale with 5–7 response options with missing values assigned a score based on an average of the answered items within that domain. Scale scores are

transformed to a 0 to 100 range by subtracting the lowest possible scale score, dividing by the range of the scale and multiplying by 100. An overall higher scores indicates better health status, fewer symptoms, and greater disease-specific HRQoL.

Two summary scores are included to aid interpretability [476]. Firstly the combining of the physical limitation and symptom domains (excluding symptom stability) forms a functional status score. A clinical summary score can be calculated by combining the functional status with the quality of life and social limitation domains with higher scores indicating better symptoms and physical functioning. The original authors reported Cronbach's alphas of 0.93 for the functional status score and 0.95 for the clinical summary score with self-efficacy the only subscale which failed to reach high internal consistency at 0.62.

The KCCQ has demonstrated good overall construct validity. A significant correlation ($r=0.45$, $p<0.001$) has been reported with the health perception scale of the generic 36 item Short form Health Survey (SF-36) while correlation with NYHA class, mortality and hospitalisation has also been reported [476]. A change of 5 points on the scale scores is regarded as clinically important [477].

In a recent prospective cohort study adherence to medication conducted by Marti et al those with good adherence had reportedly higher KCCQ functional status (70.1 ± 24.6 vs. 63.8 ± 22.8; $p=0.011$) and clinical summary (75.3 ± 22.8 vs. 68.6 ± 21.6; $p=0.003$) scores. The authors also reported significantly better scores in several KCCQ domains among patients with good adherence including, physical limitation, symptom frequency, symptom burden, total symptom, self-efficacy, and quality of life scores [478]. Similarly Morgan et al reported significantly worse HF–related health status among patients who self-reported difficulty taking their medications than patients medication difficulty taking medications, independent of other demographic and clinical characteristics (8.0 ± 3.2 lower mean KCCQ summary scores; $P=0.01$) [178].

For the purposes of this thesis the KCCQ was adopted as the measure of HRQoL.

14. Patient – Provider Relationship

A significant theme running through all the qualitative interviews carried out as part of this multi-methods study was the relationship between patient and the healthcare provider. Satisfaction with care is widely evaluated as an outcome measure for medical consultations. However, many questionnaires have been developed for use in single studies thus limiting the information on external validity for most measures [479]. Support for two measurement tools: the Consultation Satisfaction Scale (CSQ) and the Medical Interview Satisfaction Scale (MISS-21) is however documented in the literature [479].

The 18-item CSQ questionnaire is divided into four subscales: general satisfaction (3 items), professional care (7 items), depth of relationship (5 items) and perceived length of consultation (3 items). Respondents are asked to rate each statement using a 5 point Likert scale resulting in an overall satisfaction score ranging from 18-90, with higher scores relating to a greater level of satisfaction. The CSQ was found to be a reliable measure of patient satisfaction with the original author reporting Cronbach's alpha 0.91 for the overall questionnaire with subscales ranging from 0.67 for general satisfaction to 0.87 for professional care [480].

The Medical Interview Satisfaction Scale Medical Interview Satisfaction Scale (MISS-21) was developed in USA as a specific tool focusing on doctor-patient interaction rather than on a general evaluation of doctors or healthcare facility. Originally a 26-item questionnaire with three subscales (cognitive, affective and behavioral) it has evolved firstly into a 29 point MISS before being developed into a simpler Miss-21 item scale adapted for use in British general practice [219]. The assessment comprises of four subscales: distress relief (6 items), communication comfort (4 items), rapport (8 items) and compliance intent (3 items) and respondents are asked to indicate their level of agreement to each statement on a 7-point Likert scale. The MISS-21 has been found to have satisfactory internal reliability (Cronbach's alpha values cited as between 0.67 and 0.92 for subscales) and scores have been found positively to correlate with satisfaction with previous appointments.

A comparison of the MISS and the CQS questionnaires was conducted in nearly 200 patients across eight GP surgeries in Wales. The study authors could not identify one scale as being superior in terms of psychometric terms. The individual scales appeared to be equally acceptable to respondents and although the CSQ produced a slightly wider range of scores than the MISS the distribution of scores was similar with high correlation between total scores for each questionnaire and the subscales within them. For the purposes of this thesis the MISS-21 was adopted as the measurement tool for patient satisfaction with their doctor.

6.1.6. Data Handling

The researcher recorded data for each participant on the CRF during each study visit. CRFs were kept securely within the department of Ageing and Health, University of Dundee.

All data were entered into an Excel spread sheet by the researcher at regular intervals during the study in preparation for data analysis. Data missing from questionnaires were dealt with according to the individual questionnaire instructions and excluded from the analysis of outcome measures.

6.1.7. Data Analysis

All data were analysed using SPSS statistical package (Version 21.0). For each individual test a two-sided p value of <0.05 was taken to be significant for all analyses. Bonferroni correction was used to correct for multiple comparison. Initial analysis of the data confirmed that most were not normally distributed. Patient characteristics and all possible adherence related factors were compared between adherent and non-adherent participants as determined by the primary outcome using Mann Whitney test for non-normally distributed data. Categorical variables were compared using Pearson's Chi-squared test.

6.1.8. Sample Size

Initial sample size calculations, carried out as part of the original doctoral fellowship application, had proposed recruitment of 90 participants to the

study. This preliminary target number of participants was reviewed after discussion with the funder due to limitations in available funding.

To detect effect sizes (Cohen's F^2) of 0.20 in a multivariable linear regression model (equivalent to a moderate effect size), and assuming there are 10 variables in the model, it was estimated that 60 patients would be required to detect this magnitude of effect with 80% power assuming alpha = 0.05.

6.2. Observational Study Results

6.2.1. Recruitment

Recruitment took place between 1st July 2016 and 28th March 2017. The initial criterion for inclusion into the study was current prescription for both ACEi and oral Furosemide medications. The screening of three initial primary care sites indicated that numbers of patients prescribed both medications appeared lower than expected and the potential to recruit 60 participants from the selected locality was low. Following revision of the inclusion/exclusion criteria, permission was obtained from the local Research Ethics Committee to open recruitment to patients who were prescribed at least one of the two medications (rather than both) thus increasing the potential for recruitment.

In total 64 patients agreed to participate and attended the study visit. Following discussion to establish informed consent 4 of the 64 patients decided they did not wish to consent and proceed. These participants were thanked for their time and their study visit was terminated. For those happy to proceed assessment of suitability for study entry was reviewed. Inclusion / exclusion criteria were re-examined prior to all participants undertaking informed consent.

The initial target number of 60 people were recruited and consented and completed the study visit (see Figure 6.2 for CONSORT diagram and participant flow through the study). A total of 44/60 (73%) participants elected to have their study visit within their own home while 16/60 (27%) of participants elected to travel to the study visits all of which were carried out in the TICR study rooms, Ninewells Hospital, Dundee.

6.2.1.1. Recruitment via GP surgeries

Ten of the GP practices approached by the SPCRN agreed to participate with a search of their databases identifying 232 potential participants. All those identified as potentially suitable were contacted by letter and of the 232 letters sent 62 (27%) responded indicating their interest in the study. A breakdown of responses by individual practice is given in Table 6.2.

Practice ID	Number of letters sent	Number of Responses (%)	Number of Participants consented (%)	Reason for non-entry into study
Practice 1	13	3 (23)	3 (23)	
Practice 2	49	11 (22)	10 (20)	Asymptomatic HF (n=1)
Practice 3	43	8 (19)	5 (12)	Asymptomatic HF (n=1) Declined to consent (n=1) Wished to consult with cardiologist (n=1)
Practice 4	18	5 (28)	5 (28)	
Practice 5	11	2 (18)	1 (9)	Episode of acute HF not chronic HF (n=1)
Practice 6	6	4 (67)	2 (33)	Refused to consent (n=1) HF not diagnosed (n=1)
Practice 7	18	6 (33)	2 (11)	Declined to consent (n=3) Currently participant on a RCT (n=1)
Practice 8	19	6 (32)	5 (26)	HF not diagnosed (n=1)
Practice 9	15	7 (47)	4 (27)	HF not diagnosed (n=2) Refused to consent (n=1)
Practice 10	40	10 (25)	4 (10)	Currently participant on a RCT (n=1) Unable to contact (n=1) Asymptomatic HF (n=1) HF not diagnosed (n=3)
Total	**232**	**62 (27)**	**41(18)**	

Table6.2: Breakdown of individual GP practice recruitment

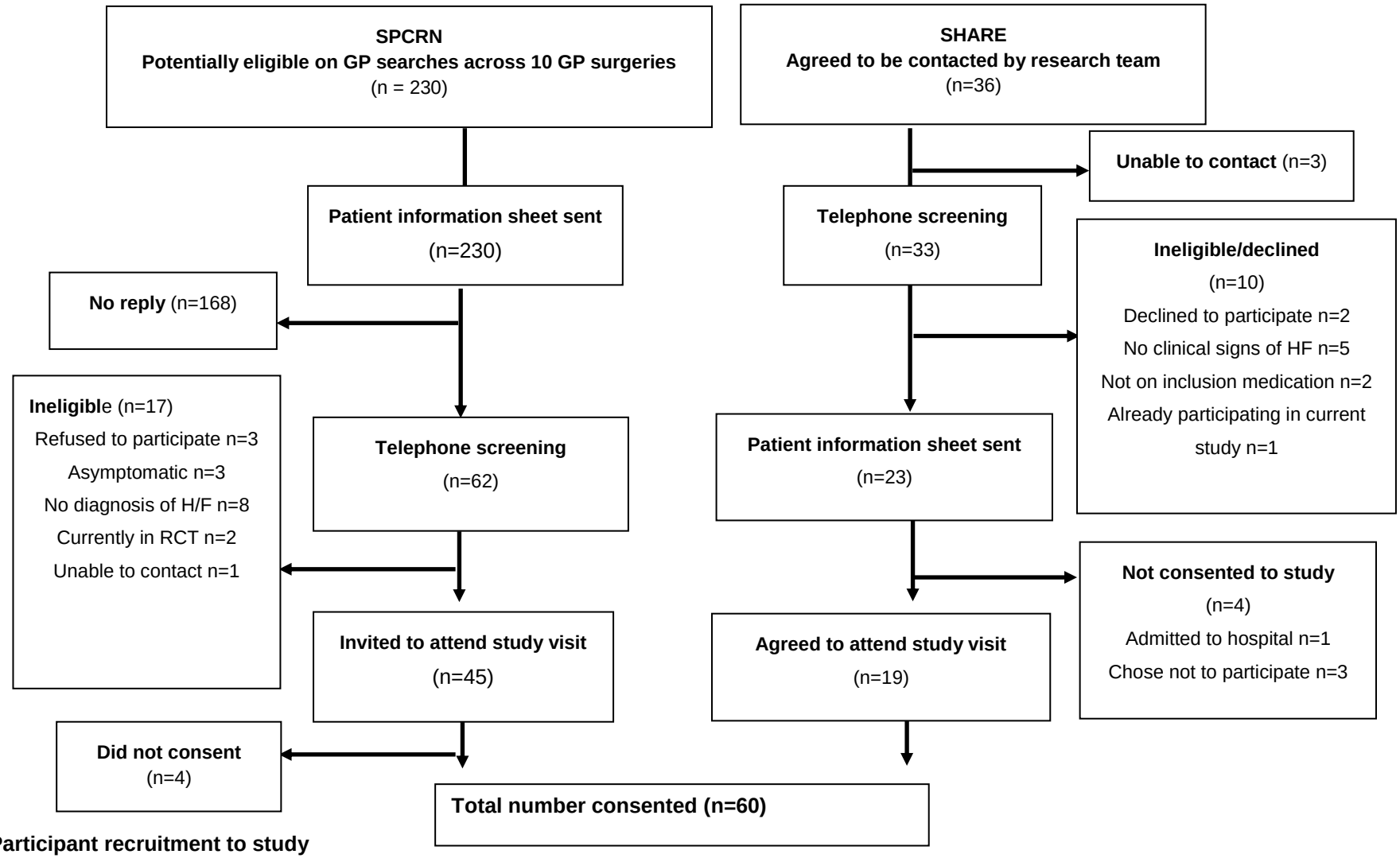

Figure6.2: Participant recruitment to study

6.2.1.2. SHARE recruitment

Permission was granted from 36 potential participants identified from a search of the SHARE register to have their details to be forwarded to the current study team. Despite contact having telephone numbers or email addresses supplied 3 (8%) patients could not be contacted. Of the 33 patients contacted by telephone 23 (70%) agreed to receive a participant information sheet in the post and consider the study further. For the ten who were not sent further information two had declined participation; five had no clinical signs of HF; two were not prescribed inclusion medication while one patient was found to have already participated in the current study. After reading the PIS 19/23 patients agreed to participate, 3/23 declined while one person was admitted to hospital.

6.2.2. Participant characteristics

Participant characteristics were collected on all 60 participants and are shown in table 6.3. Overall participants had a mean (SD) ages of 79 years (5) with 45/0 (70%) being male. While in the main characteristics was found to be similar across both sites of recruitment, those recruited via SPCRN were older, more likely to live alone, less likely to be prescribed a loop diuretic, had lower anxiety scores and had fewer concerns about their prescribed medication.

6.2.3. Adherence to medication

a) Self-Reported Adherence.

59/60 participants completed the MMAS-8 (see table 6.4) with one participant declining to complete the questionnaire. Adherence to HF medication was reported as either high (scores of 8/8); medium (scores of 6 or 7/8) or low (less than 6/8). In total 21/59 (36%) of participants reported that they had forgotten to take their HF medication on occasion, however only 6/59 (10%) reported deliberated non-adherence to HF medications in the two-week period prior to completing the questionnaire.

	Overall (n=60)	SPCRN participants (n=41)	SHARE participants (n=19)	p (SPCRN vs SHARE)
Mean age (years) (SD)	79.4 (4.7)	80.2 (4.5)	77.7 (4.7)	0.05
Male sex (%)	45 (75)	30 (73)	15 (79)	0.63
Past Medical History				
Angina / CABG (%)	16 (27)	8 (20)	8 (42)	0.07
MI (%)	22(37)	12 (29)	10 (53)	0.08
Hypertension (%)	33(55)	21 (51)	11 (61)	0.48
Valvular Disease (%)	12(20)	8 (20)	4 (21)	0.89
Medication Data				
On ACEi (%)	36 (60)	28 (68)	8 (42)	0.05
On ACEi or ARB (%)	46(77)	31 (76)	15 (79)	0.78
On beta blocker (%)	44(73)	29 (71)	15 (79)	0.50
On loop diuretic (%)	44(73)	26 (63)	18 (95)	**0.01**
Median diuretic dose (mg) (IQR)*	40(40-80)	40 (40-80)	40 (40-80)	0.95
Median medications prescribed (IQR) (range 3-19)*	8 (6-10)	6.5 (6-10)	8 (5.4-10.5)	0.10
Medication Adherence aid (%)	27 (45)	17 (42)	10 (53)	0.48
Social History				
Walking aid (%)	19(32)	14 (34)	5 (26)	0.09
Home help (%)	8 (13)	7 (17)	1 (5)	0.21
Lived alone (%)	30 (33)	19 (46)	1 (5)	**0.002**
Median SIMD score (IQR)*	8 (3)	8 (3)	7 (6)	0.51

Table 6.3: Observational Study Participant Characteristics

	Overall (n=60)	SPCRN participants (n=41)	SHARE participants (n=19)	p (SPCRN vs SHARE)
Adherence Determinants				
NYHA status (II / III)	49/11	34/7	15/4	0.71
Record of recent Hospital admission (%)	13 (22)	9 (22)	4 (21)	0.94
Median MoCA (IQR) *	25 (20.5-26.5)	25 (20.25-26.75)	25 (21-26.5)	0.89
Median SPPB (IQR) *	6.8 (3-9)	7.0 (2.25-9)	8 (3-8.5)	0.19
Mean BMQ Specific - Necessity Total (SD) (range 13-25) *	20 (4)	20 (4)	21 (3)	0.31
Mean BMQ Specific – Concern Total (SD) (range 5-18) *	11 (3)	11 (3)	12 (3)	0.02
Mean BMQ General - Overuse Total (SD) (range 4-16) *	12 (3)	11 (3)	12 (3)	0.35
Mean BMQ General – Harm Total (SD) (range 4-15) *	9 (2)	9 (2)	9 (2)	0.63
Median HADS Anxiety (IQR) *	3 (1-6)	2 (1-4.75)	5 (4-6)	**0.01**
Median HADS Depression (IQR) *	3.5 (2-5)	3 (2-5)	4 (2.5-6)	0.35

Table 6.3: Observational Study Participant Characteristics cont.

Threshold for significance for this table is p= >0.002

* Comparison using Mann-Whitney test. CABG, coronary artery bypass graft; MI, myocardial infarction; ACEi, Angiotensin converting enzyme inhibitor; NYHA, New York Health Association; SPPB, Short Physical Performance Battery; MoCA, Montreal Cognitive Assessment; BMQ, Beliefs about Medication Questionnaire; HADS, Hospital Anxiety Depression Scale

Measure	Threshold	Total (%)
MMAS-8 (n=59)	High adherence Medium adherence Low adherence Adherent using cut off value ≥ 6	30 (50) 24 (41) 5 (8) 55 (93)
SACE (n=34)	SACE ≤6.5 U/L	25 (74)
Urinary furosemide (n=38)	Urinary Furosemide present	38 (100)
ACEi prescription data (n=36)	≥80% adherence	34 (94)
Furosemide prescription data (n=38)	≥80% adherence	35 (92)

Table6.4: Medication Adherence Measures

MMAS-8 Morisky Medication Adherence Scale; SACE, Serum Angiotensin converting enzyme; ACEi, Angiotensin converting enzyme inhibitor

When asked to complete the final question detailing how often participants felt they had difficulty remembering to take all their medication 35/59 (59%) reported they never had difficulty while 17/59 (29%) reported occasional difficulty and 7/59 (12%) stated they sometimes forgot to take all their medication. All participants reported that they had taken their heart failure medication the day prior to the study visit and no-one stated they had ever stopped medication or reduced the dose because they felt well. Only 5/59 (9%) of participants reported difficulty in adhering to their treatment plan.

b) Computerised Pharmacy Records

Prescribing data were available on all participants. Participants were assessed as adherent if dispensed prescriptions covered ≥80% of the days the medication had been prescribed. Of 36 participants prescribed ACEi 34/36 (94%) had acquired medication to cover the number of days prescribed while 35/38 (92%) of participants prescribed furosemide acquired enough

medication to ensure adherent behaviour ≥80% of the days the medication had been prescribed. See figure 6.3 for Adherence to ACEi medication reported across measures and figure 6.4 for adherence to furosemide medication reported across measures.

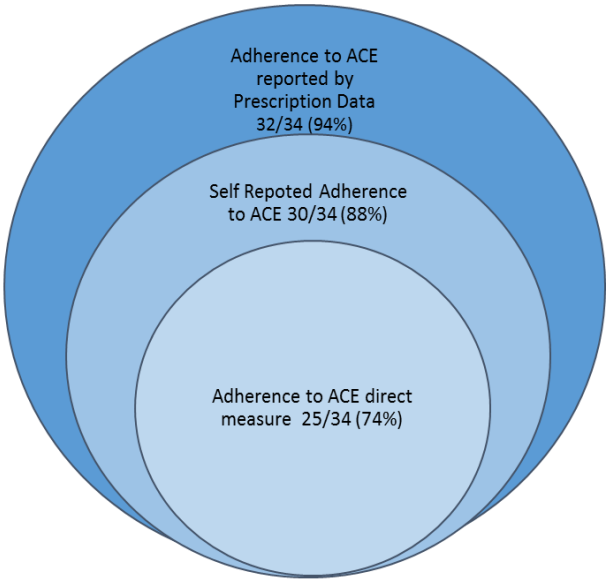

Figure6.3: Adherence to ACEi medication reported across measures

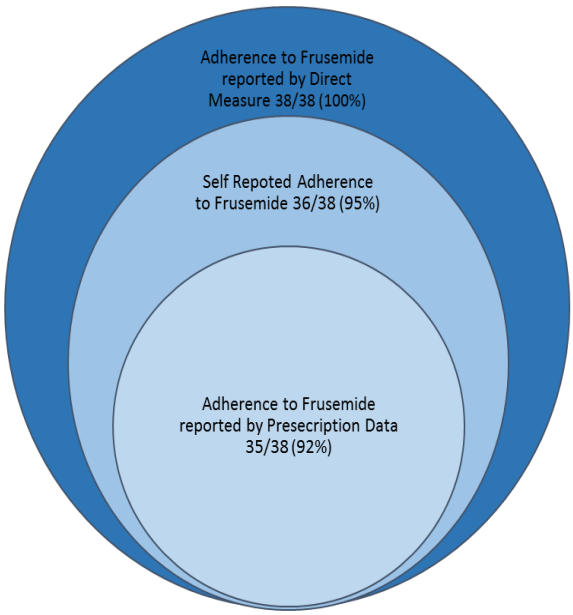

Figure6.4: Adherence to furosemide medication reported across measures

Comparison of Adherence Methods

All methods of adherence where compared using Cohen's kappa. Using Landis guidelines for interpretation of kappa [(481)] agreement between self-reported adherence (were adherence was reported as high, medium or low) and adherence to ACEi was found to be poor, k=0.02, p=0.8. Similar results were reported between adherence to ACEi and self-reported adherence following the introduction of a single adherence cut-off point of six to indicate non-adherent behaviour, k=-0.01, p=0.94.

For prescription data agreement was found to be poor between prescription data relating to furosemide adherence and self-report using both the rating scale (k=-0.002, p=0.96) and the single adherence cut-off point of six to indicate non-adherent behaviour (k=-0.07, p=0.67). For ACE i prescribing data slight to moderate agreement was noted between the prescription data and self-report using the single adherence cut-off point of six (k=0.36, p=0.28) however this agreement was not evident when compared to the initial rating scale (k=-0.01, p=0.61) (Figure 6.5 agreement of adherence to ACE inhibitor & Figure 6.6 agreement of adherence to Furosemide)

Given the similarity in results using both the MMAS-8 adherence rate and the cut off rate of 6, further analyses of the MMAS-8 were conducted using a cut off of 6 to classify adherent behaviour.

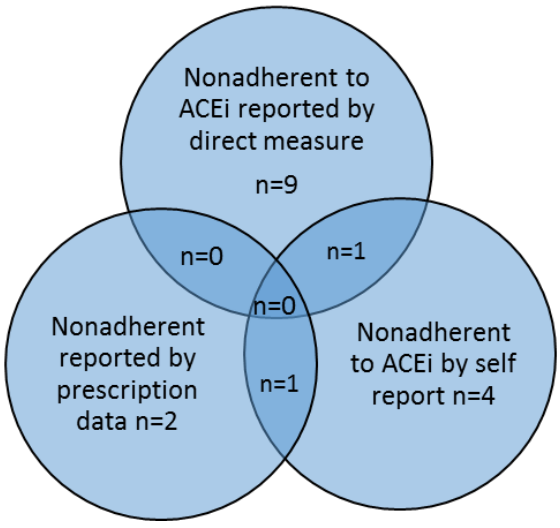

Figure6.5: Agreement of adherence to ACE inhibitor

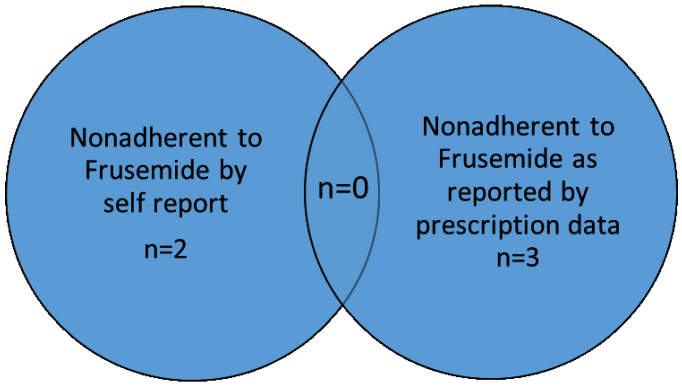

Figure6.6: Agreement of adherence to Furosemide

6.2.4. Predictors of Adherence

Results of univariate analysis of factors associated with adherence can be found in Tables 6.5 and 6.6. None of these participant demographics where found to have a significant relationship with adherence to HF medication.

1. Comorbidity and medication burden

There was no significant relationship between multi-morbidity or number of medications and medication adherence using any of the adherence methods used.

2. Symptoms of condition

NYHA was not a significant factor for adherence to HF medication.

3. Record of recent hospitalisations

Record of hospital stay was not identified as a significant factor for adherence to HF medication.

4. Deprivation

Deprivation was not identified as a significant factor for adherence to HF medication.

5. Cognition

There was no significant relationship between cognition and adherence to HF medication.

	Prescribing data ACE I			Prescribing data Furosemide		
	Adherent (>80%)	Non-Adherent (<80%)	p	Adherent (>80%)	Non-Adherent (<80%)	p
Mean age (yrs.) (SD)	78.8(4.4) (n=34)	82.5 (3.5) (n=2)	0.26	80.5(4.9) (n=35)	78.4(2.1) (n=3)	0.47
Male Sex (%)	26(76) (n=34)	1 (50) (n=2)	0.40	27(77) (n=35)	3(100) (n=3)	0.23
Formal Help at home (%)	3(9) (n=34	1 (50) (n=2)	0.07	6(17) (n=35)	3(100) (n=3)	0.44
Living alone at home	11(32) (n=34)	2 (100) (n=2)	0.33	12(34) (n=35)	2(67) (n=3)	0.26
Median number of medications (IQR)*	6(6-8) (n=34)	9- (n=2)	0.50	9(7-11) (n=35)	8- (n=3)	0.92
Median MOCA score (IQR)*	26 (23-28) (n=33)	26- (n=2)	0.97	26 (20-29) (n=30)	26- (n=3)	0.76
Median HADS Anxiety (IQR)*	3 (1-5) (n=34)	3- (n=2)	0.92	4 (3-6) (n=35)	0- (n=3)	0.01
Median HADS Depression (IQR)*	3 (2-5) (n=34)	3- (n=2)	0.62	4 (3-5) (n=35)	2- (n=3)	0.07
Median SMID rank (IQR)*	8 (6-9) (n=34)	7- (n=2)	0.42	8 (8-10) (n=35)	7- (n=3)	0.47
Median SPPB score (IQR)*	7 (3-9) (n=33)	8- (n=2)	0.86	7 (4-9) (n=30)	11- (n=3)	0.01
Median Charlson Score (IQR)*	3 (1) (n=34)	4- (n=2)	0.76	2 (1-3) (n=30)	3- (n=3)	0.35
Median BMQ Specific– Necessity score (IQR)*	20 (19-23) (n=34)	19- (n=2)	0.54	21(18-24) (n=35)	22- (n=3)	0.23
Median BMQ Specific – Concern score (IQR)*	11 (10-12) (n=34)	14- (n=2)	0.23	10 (10-12) (n=35)	9- (n=3)	0.10
Median BMQ General – Overuse score (IQR)*	12 (10-14) (n=34)	10- (n=2)	0.26	11 (9-14) (n=35)	10- (n=3)	0.27
Median BMQ General – Harm score (IQR)*	9 (7-10) (n=34)	9- (n=2)	0.71	10 (9-11) (n=35)	6- (n=3)	0.06
Median Cardiac Self-efficacy Questionnaire - control (IQR)*	4 (3-4) (n=34)	4- (n=2)	0.86	4 (3-4) (n=34)	4- (n=3)	0.94
Median Cardiac Self-efficacy Questionnaire - maintain(IQR)*	3 (3-5) (n=34)	2- (n=2)	0.32	3 (3-4) (n=34)	4- (n=3)	0.94
Median Health literacy Score (IQR)*	3 (2-4) (n=34)	4- (n=2)	0.38	3 (2-4) (n=25)	3- (n=3)	0.35
Median KCCQ Functional Status score (IQR)*	83 (66-90) (n=33)	64- (n=2)	0.34	80 (72-88) (n=33)	73- (n=3)	0.38
Median KCCQ Clinical summary score (IQR)*	85 (73-90) (n=33)	61- (n=2)	0.17	84 (78-89) (n=33)	85- (n=3)	0.16
Median IPQ-R total symptoms (IQR)*	7 (4-8) (n=32)	8- (n=2)	0.60	7 (6-8) (n=32)	4.0- (n=3)	0.05
Median IPQ-R total symptoms due to H/F (IQR)*	2 (0-2) (n=32)	4- (n=2)	0.47	2 (1-3) (n=32)	2.0- (n=3)	0.24
Median IPQ-R consequences (IQR)*	16 (14-20) n=29	20- (n=2)	0.21	18 (14-20) (n=29)	16- (n=3)	0.16
Median MISS – Overall Satisfaction score (IQR)*	102 (95-122) (n=31)	109- (n=2)	0.50	103 (99-120) (n=25)	111- (n=3)	0.43

Table6.5: Univariate analysis of factors associated with adherence (a)

Data * analysed using Mann-Whitney tests for non-parametric tests. Threshold for significance for this table is p= >0.002

MoCA, Montreal Cognitive Assessment; HADS, Hospital Anxiety Depression Scale; SMID, Scottish Index of Multiple Deprivation; SPPB, Short Physical Performance Battery; BMQ, Beliefs about Medication Questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire; IPQ-R, Illness Perception Questionnaire-Revised; MISS, Medical Interview Satisfaction Scale; MMAS, Morisky Medication Adherence Scale; ACEI, Angiotensin converting enzyme inhibitor.

	Self-reported Adherence			Adherence to ACE I		
	Adherent (MMAS score ≥ 6)	Non-Adherent (MMAS Score <6)	p	Adherent (sACE <6.5)	Non-Adherent (sACE ≥6.5)	p
Mean age (yrs) (SD)	79.2 (4.6) (n=55)	81.3 (7.0) (n=4)	0.41	78.6 (4.2) (n=25)	80.4 (4.0) (n=9)	0.25
Male sex (%)	42 (76) (n=55)	3 (75) (n=4)	0.95	19 (76) (n=25)	7 (78) (n=9)	0.91
Formal help at home (%)	7 (13) (n=55)	1(25) (n=4)	0.49	2 (8) (n=25)	2 (22) (n=9)	0.26
Ling alone at home (%)	18 (33) (n=55)	2(50) (n=4)	0.48	6 (24) (n=25)	1 (44) 2 (n=9)	0.25
Median number of medications (IQR)	6 (6-9) (n=55)	9- (n=4)	0.61	8 (6-9) (n=25)	6 (5-9) (n=9)	0.28
Median MOCA score (IQR)*	26 (23-28) (n=52)	23- (n=4)	0.14	26 (24-28) (n=25)	24 (17-26) (n=8)	0.04
Median HADS Anxiety (IQR)*	2 (1-5) (n=55)	6- (n=4)	0.12	3 (1-5) (n=25)	4 (2-6) (n=9)	0.65
Median HADS Depression (IQR)*	3 (2-5) (n=55)	4- (n=4)	0.70	4 (2-5) (n=25)	3 (1-9) (n=9)	0.57
Median SMID rank (IQR)*	8 (4-9) (n=55)	7- (n=4)	0.26	7 (6-8) (n=25)	8 (5-10) (n=9)	0.34
Median SPPB score (IQR)*	8 (4-10) (n=52)	7- (n=4)	0.79	8 (6-10) (n=25)	7 (6-11) (n=8)	0.76
Median Charlson Score (IQR)*	2 (1-3) (n=51)	2- (n=4)	0.89	2 (1-4) (n=24)	1 (1-3) (n=9)	0.35
Median BMQ Specific – Necessity score (IQR)*	21 (18-23) (n=55)	19- (n=4)	0.31	20 (18-23) (n=24)	19.0 (18-21) (n=9)	0.20
Median BMQ Specific – Concern score (IQR)*	10 (9-12) (n=55)	12- (n=4)	0.28	11 (9-15) (n=24)	11 (10-15) (n=9)	0.76
Median BMQ General – Overuse score (IQR)*	12 (10-14) (n=55)	12- (n=4)	0.99	12 (10-14) (n=24)	12 (10-14) (n=9)	0.79
Median BMQ General – Harm score (IQR)*	9 (7-10) (n=55)	9- (n=4)	0.67	9 (7-10) (n=24)	9 (9-11) (n=9)	0.36
Median Cardiac Self-efficacy Questionnaire - control (IQR)*	4 (3-4) (n=55)	5- (n=4)	0.24	4 (3-4) (n=25)	4 (3-5) (n=9)	0.97
Median Cardiac Self-efficacy Questionnaire - maintain(IQR)*	3 (3-4) (n=55)	3- (n=4)	0.85	3 (2-4) (n=25)	4 (3-5) (n=9)	0.15
Median Health literacy Score (IQR)*	3 (2-4) (n=53)	2- (n=4)	0.10	3 (2-4) (n=25)	2 (2-3) (n=9)	0.09
Median KCCQ Functional Status score (IQR)*	73 (71-90) (n=53)	62- (n=4)	0.30	74 (50-90) (n=24)	86 (77-93) (n=9)	0.12
Median KCCQ Clinical summary score (IQR)*	81 (74-90) (n=53)	66- (n=4)	0.30	79 (65-88) (n=24)	90 (79-95) (n=9)	0.07
Median IPQ-R total symptoms (IQR)*	7 (4-8) (n=53)	8- (n=4)	0.78	7 (5-9) (n=23)	5 (1-7) (n=9)	0.01
Median IPQ-R total symptoms due to H/F (IQR)*	2 (0-3) (n=53)	2 - (n=4)	0.46	2.0 (1-3) (n=23)	0 (0-1) (n=9)	**0.00**
Median IPQ-R consequences (IQR)*	18 (14-20) (n=50)	19- (n=3)	0.73	19 (15-21) (n=22)	14 (13-16) (n=7)	0.02
Median MISS – Overall Satisfaction score (IQR)*	103 (100-120) (n=44)	96- (n=4)	0.15	103 (94-121) (n=21)	102 (97-113) (n=8)	0.84

Table6.6: Univariate analysis of factors associated with adherence (b)

Data * analysed using Mann-Whitney tests for non-parametric tests. Threshold for significance for this table is p= >0.002

MoCA, Montreal Cognitive Assessment; HADS, Hospital Anxiety Depression Scale; SMID, Scottish Index of Multiple Deprivation; SPPB, Short Physical Performance Battery; BMQ, Beliefs about Medication Questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire; IPQ-R, Illness Perception Questionnaire–Revised.

6. Illness Perception:

A total of 57/60 (95%) of participants completed the IPQ-R. A reliability analysis was carried out on the overall questionnaire as well as the individual subdomains. Cronbach's alpha showed the overall questionnaire reached acceptable reliability, α = 0.81 while all subdomains with the exception of consequences demonstrated good internal consistency. Results for each subdomain can be found in table 6.7.

	Number of items	Range	Median (IQR)	Cronbachs Alpha
Timeline acute/chronic	6	16-30	23 (21-26)	0.81
Timeline cyclical	4	4-18	8 (8-10)	0.86
Consequences	6	12-27	18 (15-20)	**0.63**
Personal control	6	12-30	22 (18-24)	0.85
Treatment control	5	5-25	16 (15-19)	0.72
Illness coherence	5	8-25	18 (14-20)	0.81
Emotional representations	6	8-23	13(12-14)	0.80

Table6.7: IPQ-R subdomains

The most common symptoms experienced by the participants where pain 48/60 (84%); breathlessness 48/60 (84%); fatigue 43/60 (77%) and loss of strength 40/60 (70%). Overall the median number of symptoms experienced by participants was 7 (IQR 0-13). Participants attributed only 2 (IQR 0-8) of these symptoms to their HF which was considered by most to be a chronic condition with little variation, and which did not have an overly negative impact on the lives of participants.

While participants reported a relatively good level of personal control over their HF, their beliefs around treatment control appeared less positive. Finally, while

participants felt they had a reasonable level of understanding around their HF it did not evoke strong emotional representations.

The presence of symptoms was found to have a significant association with adherence to medication when assessed using the SACE levels. This effect was found to be significant even when the symptoms were not directly attributed to HF. However, this association was not consistent across the other adherence outcome measures. Of the other IPQ-R domains only consequences of condition was found to have a significant association with adherence. As with symptoms however this significant result was only reported when adherence was measured using SACE and was not consistent across the other measures.

7. Self-Efficacy

All 60 participants completed the cardiac self-efficacy questionnaire. The median control score was 4 (IQR 1). A total of 21/60 (35%) of participants did not however relate their HF medication to episodes of SOB and thus ticked the N/A box. However, the majority of participants (56/60 (93%) reported being either ‘very’ or ‘completely’ confident in their ability to take their heart failure medication.

The median maintain score was 3 (IQR 2). When asked about social activities 21/60 (35%) did not feel confident that they would be able to maintain their usual social activities, however 44/60 (73%) were confident they could maintain their social interaction with their family at home.

There was no significant relationship between self-efficacy and adherence to HF medication.

8. Medication beliefs

All 60 participants completed the BMQ. Participants held strong beliefs in the necessity for the medications they had been prescribed while not showing undue concern for these medications. Participants did not report negative beliefs regarding medication in general. The median overuse score was 12.0/20.0 (IQR10-14) (range 4-16) while the general harm score was 9.0/20.00 (IQR 7-10) (range 4-15).

There was no significant relationship between beliefs in medication either specifically or generally prescribed and adherence to heart failure medication.

9. Functional Status

Almost one third of participants (19/60) required the use of a walking aid to mobilise. The overall median SPPB score was low at 7 out of a possible 12. While the median score for balance was high: 4 out of a possible 4 (IQR 3), the reported median score for chair stands was much lower: 1 out of a possible 4 (IQR 3). On individual testing, worse physical function was found to have significant associations with adherence to medication ($p=0.01$) using the furosemide specific prescribing data. This association however was not significant following correction for multiple comparison and was absent when adherence was assessed using the other outcome measures.

10. Mood

All participants completed the HADS questionnaire. Median HADS scores for both anxiety and depression were within normal range with only 3/60 (5%) of participants recording scores ≥ 11 suggesting the presence of anxiety or depression. Ongoing pharmacological treatment for depression was prescribed for 3/60 (5%) of the participants. No association between depression and adherence to medication was identified across any of the adherence measures used. Using the furosemide specific prescribing data higher anxiety scores were found to have significant associations with adherence to medication in individual testing ($p=0.01$). However, this association was not significant following correction for multiple comparison and absent when adherence was assessed using the other outcome measures.

11. Carers Beliefs about medication and heart failure

In total 21/60 (35%) carers returned completed consent forms and questionnaires. Of these 20/21 (95%) were female with 18/21 (86%) describing themselves as married or partners of the patient with HF. Three respondents identified as daughters. On inspection of the data 13/21

carers responses could be linked to furosemide prescription data, all of which demonstrated positive adherence. Linkage of the ACEi prescription data demonstrated similar results with 13/14 demonstrating positive medication adherence. Further analysis was therefore not appropriate as there was no poor adherence category with which to compare those with good adherence.

Univariate analysis of carers beliefs associated with the self-report data and SACE can be found in table 6.8. There was no significant relationship between carers' beliefs in medication and adherence to HF medication as assessed by the BMQ. Similarly, carers' perceptions of HF did not play a significant factor to medication adherence in this sample.

	Self-reported Adherence			**Adherence to ACE I**		
	Adherent (MMAS score ≥ 6)	Non-Adherent (MMAS Score <6)	p	Adherent (sACE <6.5)	Non-Adherent (sACE ≥6.5)	p
Median Carers BMQ General Harm (IQR)*	8 (7-10) (n=17)	8.0 - (n=3)	0.55	8 (6-9) n=(9)	8 (7-8) n=(5)	0.80
Carers BMQ General Overuse (IQR)*	11 (9-13) (n=17)	11.0 - (n=3)	0.92	10 (8-12) n=(9)	12 (12-13) n=(5)	0.24
Carers BMQ Specific concern (IQR)*	11 (7-13) (n=17)	11.0 - (n=3)	0.42	11 (6-14) (n=9)	11 (9-12) (n=5)	1.00
Carers BMQ Specific Necessity (IQR)*	24 (5) (n=17)	21.0 - (n=3)	0.77	24 (21-25) (n=9)	24 (19-24) (n=5)	0.44
Carers IRQ-R identity (IQR)*	23 (22-29) (n=17)	24. - (n=3)	0.77	23 (20-28) (n=9)	28 (23-30) (n=5)	0.30
Carers IRQ-R consequences (IQR)*	19 (15-21) (n=17)	18 - (n=3)	0.92	18 (16-21) (n=9)	20 (15-20) (n=5)	0.90
Carers IRQ-R personal control (IQR)*	22 (16-27) (n=17)	18 - (n=3)	0.31	20 (15-25) (n=9)	23 (22-23) (n=5)	0.08
Carers IRQ-R Treatment control (IQR)*	17 (15-20) (n=17)	19 - (n=3)	0.77	17 (16-19) (n=9)	20 (17-21) (n=5)	0.24
Carers IRQ-R Illness coherence (IQR)*	21 (15-23) (n=17)	20 - (n=3)	0.84	20 (14-22) (n=9)	20 (19-22) (n=5)	0.52
Carers IRQ-R Timeline cyclinical (IQR)*	8 (5-10) (n=17)	8 - (n=3)	0.42	8 (8-10) (n=9)	8 (5-8) (n=5)	0.52
Carers IRQ-R Emotional Representation (IQR)*	16 (14-20) (n=17)	14 - (n=3)	0.15	14 (13-16) (n=9)	17 (14-19) (n=5)	0.30

Table6.8: Univariate analysis of carers' beliefs associated with adherence

*Data analysed using Mann-Whitney tests for non-parametric tests. Threshold for significance for this table is p=>0.005

BMQ, Beliefs about Medication Questionnaire; IPQ-R, Illness Perception Questionnaire-Revised; ACE I, Angiotensin converting enzyme inhibitor.

Subsequent assessment of both the BMQ and the IPQ-R questionnaires showed the overall questionnaires reached acceptable reliability, α = 0.81 α = 0.88 respectively. However, several of the subdomains of both questionnaires demonstrated questionable internal consistency.

12. Health Literacy

57/60 (95%) of participants completed the health literacy questionnaire. Of those 22/57 (39%) were assessed as low level of health literacy, 17/57 (30%) were assessed as medium while only 18/57 (32%) answered all questions correctly and were thus assessed as having a high level of health literacy. While the majority of participants 55/57 (96%) could correctly identify the maximum number of days the medication could be taken only 32/57 (56%) could identify when they should consult a doctor while 40/57 (70%) could not identify any of the specified conditions for which the described medication should be taken. Similarly 36/57 (61%) participants could not identify conditions of contra-indication.

There was no significant relationship between health literacy and adherence to HF medication.

13. HRQoL

A total of 58 participants completed the KCCQ which demonstrated a high level of internal consistency (Cronbach's α = 0.91). Analysis of data reported no significant relationship between HRQoL as assessed by the KCCQ, and adherence to HF medication.

14. Patient – Provider Relationship

53/60 participants completed the MISS Questionnaire however three of these participants felt unable to complete the compliance intent section as they had not been given treatment at their last consultation. For the 7 participants who chose not to complete the questionnaire five felt they could not recall sufficiently the details of their last medical consultation while two expressed a wish not to discuss their relationship with their doctor. Overall the median overall satisfaction score relating to the last consultation the participant had had with their General Practitioner was 103 out of a maximum score of 147.

The MISS score demonstrated high internal consistency (Cronbach's α = 0.93) in this sample. There was no significant relationship between satisfaction with the doctors' consultation and adherence to HF medication.

6.2.5. Additional analysis

Disappointingly no predictor for adherence was shown to significantly determine adherence to medication when assessed by self-report. Further analysis was conducted using the self-report adherence data as continuous rather than dichotomous data. Results from this supplementary analysis are reported in tables 6.9 and 6.10.

	Correlation between variables
Carer BMQ Specific– Necessity score (n=20)	r_s= 0.10, p=0.69
Carer BMQ Specific – Concern score (n=20)	r_s= 0.13, p=0.58
Carer BMQ General – Overuse score (n=20)	r_s= 0.15, p=0.53
Carer BMQ General – Harm score (n=20)	r_s= 0.15, p=0.53
Carer IPQ-R identity (n=20)	r_s= 0.20, p=0.40
Carer IPQ-R consequences (n=20)	r_s= 0.07, p=0.79
Carer IPQ-R personal control (n=20)	r_s= 0.37, p=0.11
Carer IPQ-R treatment control (n=20)	r_s= -0.05, p=0.82
Carer IPQ-R illness coherence (n=20)	r_s= -0.07, p=0.78
Carer IPQ-R timeline cyclinical (n=20)	r_s= 0.15, p=0.52
Carer IPQ-R emotional representation (n=20)	r_s= 0.17, p=0.49

Table6.9: Correlation of MMAS-8 as a continuous variable and beliefs held by carers

* Data analysed using Spearman's rank correlation coefficient.Threshold for significance for this table after Bonferroni correction p=0.005.

BMQ, Beliefs about Medication Questionnaire; IPQ-R, Illness Perception Questionnaire–Revised

	Correlation between variables
Age (n=59)	r_s=-0.00, p=0.98
Gender (n=59)	r_s= -0.14, p=0.30
Formal Help at home (n=59)	r_s= 0.14, p=0.28
Living alone at home (n=59)	r_s= 0.01, p=0.96
Number of medications (n=59)	r_s= -0.15, p=0.27
MoCA score (n=56)	r_s= 0.21, p=0.13
HADS Anxiety (n=59)	r_s= -0.41, p=0.001*
HADS Depression (n=59)	r_s= -0.21, p=0.12
SMID rank (n=59)	r_s= 0.05, p=0.73
SPPB score (n=56)	r_s= -0.01, p=0.95
Charlson Score (n=59)	r_s= -0.27, p=0.04
BMQ Specific– Necessity score (n=59)	r_s= -0.07, p=0.63
BMQ Specific – Concern score (n=59)	r_s= -0.34, p=0.01
BMQ General – Overuse score (n=59)	r_s= 0.05, p=0.70
BMQ General – Harm score (n=59)	r_s= -0.24, p=0.06
Cardiac Self-efficacy Questionnaire - control	r_s= -0.14, p=0.30
Cardiac Self-efficacy Questionnaire - maintain	r_s= -0.01, p=0.92
Health literacy Score (n=57)	r_s= 0.17, p=0.22
KCCQ Functional Status score (n=58)	r_s= 0.16, p=0.22
KCCQ Clinical summary score (n=58)	r_s= 0.21, p=0.12
IPQ-R identity (n=52)	r_s= -0.12, p=0.38
IPQ-R consequences (n=52)	r_s= -0.09, p=0.52
IPQ-R personal control (n=52)	r_s= 0.13, p=0.36
IPQ-R treatment control (n=52)	r_s= 0.00, p=0.10
IPQ-R illness coherence (n=52)	r_s= 0.15, p=0.30
IPQ-R timeline cyclinical (n=52)	r_s= 0.14, p=0.31
IPQ-R emotional representation (n=52)	r_s= -0.31, p=0.03
IPQ-R total symptoms (n=57)	r_s= -0.23, p=0.09
IPQ-R total symptoms due to H/F (n=57)	r_s= -0.20, p=0.14
MISS – Overall Satisfaction score (n=50)	r_s= 0.14, p=0.35

Table6.10: Correlation of MMAS-8 as a continuous variable and factors associated with adherence

* Data analysed using Spearman's rank correlation coefficient. Threshold for significance for this table after Bonferroni correction p=0.002.

MoCA, Montreal Cognitive Assessment; HADS, Hospital Anxiety Depression Scale; SMID, Scottish Index of Multiple Deprivation; SPPB, Short Physical Performance Battery; BMQ, Beliefs about Medication Questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire, IPQ-R, Illness Perception Questionnaire–Revised.

6.3. DISCUSSION

6.3.1. Summary of Main Findings

The aim of this prospective observational study was to assess adherence to ACEi and Furosemide medication in older patients diagnosed with HF and to identify the key determinants of primary non-adherence in patients with HF. Using multiple, complementary measures, adherence to medication was found to be optimal in this sample of patients; however discrepancies existed between the methods used.

No single determinant was found to consistently predict adherence across the different adherence measures used. For those participants prescribed furosemide, anxiety and overall physical functioning where identified as significant factors for adherence when reviewed against prescribing data. Disappointingly however this association was not significant following correction for multiple comparison or when adherence was measured using the dichotomous self-report adherence data. Similarly, while consequences of condition and evidence of symptoms was found to be a significant factor for adherence to ACEi when assessed using direct methods again this was not consistent with the other adherence measures or following correction for multiple comparison. Interestingly however, when self-report data was analysed as a continuous rather than dichotomous variable, a significant correlation was found with self-reported anxiety. While research within the heart failure population has not previously identified any link between anxiety and adherence to medication, in patients with LVSD, functional ability has been shown to be limited by the presence of anxiety [237] which may have the potential to negatively impact on adherence within this population. Further investigation in this area is therefore warranted.

6.3.2. Recruitment

While the study originally aimed to recruit patients who were prescribed both Furosemide and ACEi this proved difficult and amendment to the study

protocol was necessary to enable the study to meet its aim to recruit 60 older people with a diagnosis of HF. Several factors were likely to have contributed to this difficultly with initial recruitment when both medication required to be prescribed.

Firstly, the participants in this study had a mean age of 79 years and a diagnosis of varying other medical conditions including chronic kidney disease, stroke, postural hypotension, diabetes and chronic obstructive pulmonary disease. The existence of co-morbidities may complicate the management of HF caused in part by the lack of guidance on polypharmacotherapy or due to additional complications of drug interactions and adverse effects [(482)]. While drugs such as ACEi may be considered first line treatment in patients with HFrEF it may be that these medications are withheld in particular cases because of interactions and side effects, particularly in older patients.

The decision to include patients who had a diagnosis of HFpEF in the study meant recruitment was extended to a group of patients for whom prescribed medication may not have necessarily included the medication detailed in the study protocol. While treatment with ACEi is recommended in all symptomatic and non-symptomatic patients with HFrEF there is inconsistent evidence for an improvement in symptoms, morbidity or mortality in those patients diagnosed with HFpEF [(483)].

Diuretic therapy is indicated in all patients with symptomatic HF. While 44/60 (73%) of study patients were prescribed ongoing treatment 5/44 (11%) of these participants were taking bumetanide as an alternative to furosemide which was not measureable with the assay techniques available. For patients who have intolerable side effects with ACEi, ARBs are prescribed an alternative in patients with HFrEF [(484)]. In this study while 46/60 (77%) of patients were prescribed either ARB or ACEi, 11/60 (18%) were in fact prescribed an ARB which would have excluded them if the initial protocol had been retained. In total just over 50% (31/60) of our study participants were prescribed both the medications required by the initial study protocol. Poor potential for recruitment identified by the initial screening of GP practices may have been as a result

therefore of this pattern of prescribing, thus a decision was made to open recruitment to those prescribed either ACEi or furosemide medication.

The low numbers of participants with poor adherence limited the ability of the study to find significant associations on univariate analysis. This fact, combined with the relatively small size of the study, led to the decision not to conduct multivariable analyses. Such analyses would be unlikely to be robust, and would add little to the univariate analyses.

Difficulties with recruitment to research studies, particularly among the older population, are well documented [485]. Despite widening the inclusion criteria, recruitment via GP surgeries continued to prove lower than expected. While response to the GP invitation letters yielded a good (27%) response rate the number of participants suitable for initial approach fell short of expectation. The addition of recruitment from the SHARE register which retains a register of patients' comorbidity and pharmacological treatment enabled a more targeted approach to recruitment which resulted in the recruitment of the target study number. While minimal differences existed between the participants recruited from the two sources these may have had a more significant impact on adherence with a larger sample size.

6.3.3. Adherence to medication

The results from this observational study report ACEi levels comparable with those reported elsewhere. A previous study conducted by Molloy et al assessing adherence to ACEi using similar methods to ours reported serum reported adherence to be 72% compared to the 74% adherence rate in this current study [44].

Results with prescription data are not as consistent. Butler et al [486] reported adherence to ACEi as assessed by prescription data dropping from 77% at 30 days post hospital discharge to 63% at 1 year while prescription data in this current study reported adherence to be markedly higher at 94%. Unlike the participants in our study participants in Butler's study were recruited post hospital discharge when participants may have been prescribed medication as

part of a serious acute event and did not understand the necessity for long term use of these HF drugs.

While it might be expected that participants may have made a conscious effort to take all of their prescribed medication on the day of the study visit (the “toothbrush effect”) this was not the case. While all participants were found to be adherent to their diuretic therapy (a drug known to be selectively withheld by patients due to adverse side effects) on the day of the study visit, lower adherence to ACEi treatment was reported.

One explanation for this may be that patients usually have some understanding that diuretic therapy is associated with their heart condition - both the beneficial effects and side-effects of administration of this treatment are clearly visible. When describing their current drug regime patients frequently identified the need to pass urine as an unwelcome side-effect of their diuretic while many were unable to attribute any notable side-effects to other medications. Participants may have considered that omitting this medication on the day of the study visit may have given the researcher the impression that non-adherence was a regular occurrence effecting the opinion the researcher may have had of them.

Another explanation for the higher than expected adherence to diuretic treatment may have been that the majority of study visits 47/60 (88%) were conducted within the participants own home. Patients often describe delaying or missing doses of their diuretics when they have to leave the house [183]. All participants who elected to travel to the study visit were provided with the option to select a time convenient to them enabling a later appointment time to be set when increased diuresis had subsided but presence of furosemide would still be detectable in the urine.

6.3.4. Predictors of adherence

With over 200 possible factors for non-adherence previously identified this study preselected the determinants identified from both current literature and as a result of conducting a qualitative investigation.

Overall none of the preselected determinant factors proved significant across the adherence measures. Several reasons may account for this. Firstly with such a wide range of determinants being studied it may that the sample size of 60 was insufficient to detect any significant effect played by the determinants measured. Our initial sample size calculation demonstrated an initial estimation of 90 participants however this was revised due to budget constraints. identified

Common across this sample of HF patients was an intention to comply with the advice given at the time of medical consultation. Overall the included participants demonstrated greater adherence to HF medication than had been reported previously with the results from the urinary furosemide measures excluded from the analysis. As a result the low percentage of non-adherent participants may not have been sufficient to detect effect on some of the individual factors for adherence shown to have been significant in other studies.

Despite looking to recruit a sample typical of the HF population some of the preselected factors where difficult to assess. Results from the systematic review had identified hospitalisation as a factor however only 13/60 (22%) of the study population had been in hospital due to an exacerbation of the HF. Overall this was a sample of HF patients whose condition was stable, perhaps as a direct consequence of the high adherence rates reported. Similarly, rates of depression in this sample were less than the 1:5 suggested as representative of the population while participants' socio-economic status was typically higher than the average. It may be that any association between these and non-adherence to medication may have been difficult to identify without a larger, more representative sample size.

Another explanation may be that Scotland has a unique healthcare system. As previously highlighted by the qualitative review no reported studies have been conducted here in Scotland. It may be that the factors for adherence in the locality may differ to those reported in other populations. While factors such as the financial implications of continual long-term access to healthcare providers and the cost of medications cannot be identified in the Scottish population it

may well be that socio-economic; healthcare system and treatment factors are also different from those in other populations.

6.4. Strengths and Weaknesses

6.4.1. Strengths

This observational study has a number of noticeable strengths:

- The study focused its recruitment strategy around community-based HF patients rather than those hospitalised with HF related conditions. Previous to this the majority of studies assessing adherence to medication in older HF populations had been conducted in patients recruited to studies following a hospital admission. The intention of this study was to assess determinants of adherence in a population of stable HF patients who were responsible for their own treatment regime and may have had limited input from specialist services. The vast majority of patients in this study had never required a hospital admission for an exacerbation of their HF. Medication was in the main prescribed by the participants GP or doctor in an outpatient hospital setting where presenting symptoms did not warrant acute hospital admission. As such, the population studied was arguably much more representative of the vast majority of older patients with HF and hence the results should be more generalizable than studies focussing on a smaller, selected population of patients with recent hospitalisation. Understanding and improving adherent behaviour in this large group of patients may go some way to optimising treatment, slowing the progression of the condition and reducing the large number of avoidable hospital admissions experienced by this population of older HF patients every year [138].
- Despite the average age for first diagnosis being 76 years previous studies in this area have focused on HF patients with a lower mean age. This study recruited participants over the age of 70 years, a highly relevant group as HF is more prevalent in later life along with multi-morbidity and polypharmacy.

- Many of the study visits were undertaken in the participants own home which facilitated a more relaxed atmosphere and importantly avoided potentially lengthy travel to the research centre. It is well documented that many patients can be selective with particular medications including diuretic treatment when having to leave their home. In eliminating the need for travel it is likely that the participants adherence recorded on the day was more reflective of their normal routine.
- In order to addresses the well documented limitations associated to adherence assessment methods a triangulated approach was taken. Previous studies within the HF population have demonstrated substantial differences across the different measures of adherence. Smith et al demonstrated a lack of consistent agreement across the different measures of adherence when measuring adherence in a population of HF patients with a mean age similar to that in the current study [(487)]. Self-report was found to have overestimated adherence when compared to other objective measures. Overall, the variation in results, while suggesting that overall adherence was better than previously reported demonstrated poor agreement between the different methods therefore supporting the chosen approach.

6.4.2. Weaknesses

- The candidate determinants were selected based on evidence gleaned from the qualitative study and a comprehensive review of the literature a decision. However, it may be that other determinants play a greater role in adherence to medication for patients with HF than those examined in this study.
- It was not possible to assess the effect of hospitalisation in this study. Data were collected on hospital stays and while 13/60 (22%) of the participants did report an overnight stay in hospital within the preceding 12 months only three of these were directly related to their diagnosis of HF. A larger sample which enabled an approach to patients prior to a

hospital discharge may have demonstrated a link between hospitalisation and non-adherent behaviour.

- Participants who volunteered were relatively stable and appeared to be managing their condition successfully. In general people who respond to observational studies may be more motivated to understand their condition and listen to health care provider's advice. Participants who responded from the SHARE database had previously demonstrated an interest in participating in research studies and may not be representative of the general HF population. In order to fully understand which beliefs which may have an impact on adherence, participation studies require the participation of patients who may have difficulties in managing their medication and are less motivated
- The population recruited to the study was self-selecting, they volunteered to participate in a study which was clear in its objective to assess medication taking. It is more likely therefore that while participants across both the qualitative and observational studies described episodes of both non-conforming non-intentional and intentional non-adherence consent into the study itself may have been less likely in a population for whom intentional non-adherence was an issue. A particular theme emerging from the study was the importance of the patient – doctor relationship. Those with a greater tendency to omit medication may have avoided recruitment concerned that their doctor may look less favourably on them during future contact thus biasing the results in favour of adherent behaviour.
- With such a range of factors being assessed the choice of suitable measurement tools proved difficult. Assessment of validity was conducted for all questionnaires during the selection phase and while some of the included questionnaires used had demonstrated good construct validity when used in other settings it may be that they were less suitable for this population of older patients with HF. While overall Cronbach's alpha for included questionnaires demonstrated good

internal consistency, scores for some of the subdomains were less robust.

6.5. Conclusion

In conclusion this chapter has described the methods and results of the quantitative study. Adherence to ACEi and furosemide medication in 60 older patients with a diagnosis of HF has been reported using a range of different methods for assessing adherence. Possible determinants for non-adherence were assessed. Overall adherence to both HF medications was found to be high however adherence rates differed across the measures used. Surprisingly adherence on the day of the study to diuretic therapy, a drug known to be routinely withheld by patients, was 100%.

As expected with this population the majority of participants were prescribed multiple medications. While participants demonstrated a lack of knowledge around their prescribed medication and their related side-effects many demonstrated a keenness to adhere to their regime and describing the use of pill boxes and reminder stimuli to promote adherence.

Finally no single determinant consistently predicted non-adherence. While several of the determined factors proved significant using one of the adherence measurements this was not consistent across the measures of adherence. A lack of validated tools for measuring factors for medication adherence exist for this population.

Chapter 7: Discussion of Overall Results

The purpose of this chapter is to bring together all of the findings from the studies reported in this PhD thesis and to discuss these results in the context of the existing literature.

7.1. Context of the Study

As set out at the beginning of this thesis HF is an important clinical issue for many older people. A diagnosis of HF can have huge implications for both the patient and their family as well as society as a whole. With an estimated half a million people currently living with the condition in the UK the cost to an already burdened healthcare system is set to increase with more people living into old age and developing long-term conditions such as HF. While there is significant evidence to support the use of medication in the treatment and management of HF, any failure to adhere to prescribed treatment may result in suboptimal benefits producing an exacerbation of these costs on both a personal and economic level.

The original aim of this PhD was to improve understanding around the issue of non-adherence to medication in older people with HF in order to inform the development of an appropriate adherence promoting intervention. While an accurate picture of the level of non-adherence in this population was difficult to establish previous work in the area had concluded that interventions which aimed to improve medication adherence among HF patients had the potential to have significant effects on reducing readmissions and decreasing mortality in this population.

This PhD employed a multi-methods approach conducted in three phases. Phase one involved the undertaking of a systematic review evaluating previously reported interventions aiming to enhance medication adherence in the HF population. The review was followed by a rapid review of qualitative literature exploring potential facilitators and barriers to medication adherence within the same population. Phase two entailed the collection and analysis of qualitative data and aimed to address gaps identified in the published

literature. In total 8 HF patients and their informal carers participated in semi-structured interviews aiming to explore beliefs and understanding around the condition and its treatment. Finally, data from the first two phases was collated and used to select which possible determinants of adherence were to be assessed in a population of 60 older HF patients who were recruited to the observational study conducted in phase three. The key findings from the programme of work are summarised below:

7.2. Main findings

7.2.1 Phase one findings

In order identify which component parts have previously proved successful at improving improve adherence in patients with HF this PhD commenced with the undertaking of a systematic review of current literature. Across the 21 studies included in the review heterogeneity in both the intervention techniques as well as the adherence measurement methodology meant the identification of a reliable and effective intervention was not possible. In addition a number of other notable limitations across the literature were identified including: a lack of representation of older HF patients in research studies; limited long term follow up studies demonstrating positive results and importantly a lack of agreement on either a valid measure of adherence in this population or what constitutes an acceptable level of adherence.

Qualitative literature exploring perceptions and experiences of people with HF in relation to their condition and its management also demonstrated a number of limitations. While individual beliefs and level of personal knowledge were identified as potential factors for adherence in HF patients the exact detail of these beliefs remained uncertain. Again this is even more unclear given the lack of studies focusing on older HF patients who have the added burden of co-morbidity

Despite the study limitations a number of important results were established. Firstly despite literature consistently reporting that adherence is suboptimal not only in HF patients [488] but also among the older population [489] across the studies high levels of adherence were reported at baseline. While it has been

previously documented that adherence levels in research study patients may be uncharacteristically high compared to those seen routinely in clinical practice [490] these results suggest that additional work to establish an accurate level of adherence in this population requires to be undertaken.

Importantly the work contained within the systematic reviews demonstrated that improvement in adherence to medication was indeed possible within the HF population. Improvement in adherence following the delivery of an intervention was noted across 8 of the 21 included RCT's. These results are encouraging offering potential for the future development of a complex intervention drawing on some of the component parts which showed positive results.

7.2.2. Phase Two findings

Following the inconclusive but encouraging results obtained in phase one a qualitative study was undertaken to explore the beliefs held by older HF patients in relation to the condition and its management. In-depth semi-structured interviews with eight older HF patients and their nominated informal carers were conducted with several themes emerging. While health literacy relating to both condition and treatment was found to be low, participants spoke about adherence to treatment in a positive manner with desire to remain as independent emerging as a strong motivating factor for adherence.

For the older HF patients included in the study another important motivator for adherence was the relationship they felt they had with their healthcare professional. Overall participants had a strong belief in the doctor's ability to prescribe appropriate treatment and make appropriate decisions regarding the management of the condition. Participants were in the main identified as "passive" medication users who appeared to have a strong belief in the need to adhere to prescribed treatment plans, this despite an obvious lack of knowledge and understanding.

Adherence was therefore facilitated by having a positive relationship and a high level of trust in the doctor's decision making along with a strong belief in the need for medication. These potential facilitators as well the important

themes of maintaining independent functioning and not become burdensome on informal carers' where key themes in relation to adherent behaviour taken forward to explore further in phase three.

7.2.3. Phase Three findings

In the final phase, an observational study reporting on 60 older patients with HF, adherence to medication was evaluated using a multi-method approach while a wide range of potential facilitators for adherence informed by the worked conducted in two previous stages of this PhD were explored. Adherence to medication ranged from 74% as measured using serum ACE to 100% when adherence was measured using urinary furosemide levels. Given that there is currently no gold standard for measurement for adherence it was important that adherence was measured using a multi-method approach. This study reported serum ACE rates to be similar to those found using this collection method previously in a similar population [44]. Importantly triangulation of adherence outcomes identified consistently high adherence rates not only for the day of the study visit but over the year preceding study consent.

While previous studies have found highly variable levels of adherence the work contained within this PhD was based on the hypothesis that adherence to medication was suboptimal within the HF population [149]. Given that the observational study demonstrated a good level of adherence, with results similar to those previously reported locally, [44] it may be that the significance of poor adherence for older HF patients might not be as great as previously suspected and that non-adherence therefore is not a major problem in this population. It is important to view this assumption with some degree of caution however given that it is based on the results of two local studies both with relatively small sample sizes.

Additionally it is important to remember that these results reflect adherent behaviour in a population of older patients who volunteered to participate in a research study aiming to investigate adherent behaviour. As previously stated those patients with poor adherence are probably less likely to agree participate

in research, therefore the high adherence rates reported here may not be fully representative of the patients found in general populations. While the high levels of adherence are encouraging it is important not to disregard adherence as a problem as it may still remain a problem for a minority of older people.

Factors gleaned from the literature which seemed most relevant along with those emerging from the qualitative interviews were examined further within the observational study. Disappointingly none proved to be a significant factor for adherence in the population of older patients with HF recruited to the study. This finding has significance for future research in this area in that it makes clear that the selection of participants for future studies aiming to improve adherence should not be based purely on these suggested possible factors. Instead the results of this PhD suggest that any future intervention should focus on an individual's personal motivating factors, which may play a more significant part in addressing non-adherence.

7.2.4 Overall context for older HF patients

In order to optimise adherence to prescribed treatments in older HF patients the above results make clear that the traditional view targeting the individual factors thought to influence adherence has potential for only limited success. Before designing an intervention it is important to contextualise how the issue is viewed from the perspective of those living with the condition and managing the treatment. During both the qualitative interviews and the observational study the majority of participants did not feel that HF was having a major impact on their daily life. HF, although correctly identified by most as a chronic condition, was judged by patients to be stable and importantly the majority of patients felt they had a good personal level of control over the condition.

As previously stated, having a high level of self-efficacy has the potential to impact greatly on one's ability to manage self-care tasks like adherence to medication. Older people who feel they have a good level of personal control and confidence in their ability to continue with prescribed treatment may be more likely to follow increasingly complex treatment plans. An acceptance by older patients that their health conditions are going to deteriorate, whether that

is due to them having a good understanding of the condition or simply attributing deteriorating health to the ageing process along with the desire commonly expressed by older people to remain independent and avoid being a burden may potentially aid healthcare professionals to engage patients in accepting these treatment plans.

For older patients with HF it is important to recognise that the condition is not managed in isolation. Indeed for patients over the age of 75 years a diagnosis of HF without co-morbidity is extremely rare [(491)] with the majority of HF patient's requiring to manage a minimum of 5 co-morbid conditions unrelated to a cardiac diagnosis [(492)]. Particularly when compounded by physical and psycho-social deficits co-morbid conditions commonly found in older people such as diabetes mellitus, depression, cognitive impairment, thyroid disorders and skeletal myopathy have been shown to complicate the management of HF in older people. Acknowledgment of the role played by other conditions, in both the development of progression and the successful management of HF is therefore essential to optimise treatment adherence [(493)]. Rather than looking at HF in insolation, a model of care which encompasses concurrent diagnoses has the potential to improve not only outcomes related to HF but other co-morbid conditions and therefore the individual's overall health.

HF is known to encompass a number of nonspecific symptoms which may have emerged over time. For many HF patients other co-morbid conditions such as COPD or arthritis may be perceived to have more of an impact on their daily lives with causal factors for the presence of typical symptoms of HF explained by age or being related to other co-morbid conditions [(291)]. Given that patient knowledge around both HF and treatment is found to be consistently poor but relatively high levels of adherence have been reported [(44)] it may well be that for older people factors other than causation may be important in relation to adherence. Previous research has demonstrated that for some older people there is a practical acceptance that medication is required to allow them to continue "ticking over" [(494)]. Simply put, it may be that a combination of an acceptance of the potential consequences of advancing age along with a belief in the need for treatment or a trust in the recommendations of health care

providers may be more important in enhancing adherence in older patients than developing an understanding of how a specific drug effects symptoms of a specific condition.

Currently around one in three older people live alone [495]. For older people with HF maintaining independence and avoiding becoming burden on others appears to be an important motivating factor for adherence to treatment. Many of the older HF patients recruited to the empirical studies contained within this thesis accepted that while their usual social activities would not be maintained indefinitely social interaction with family would be. Rather than focusing on educating patients using motivational factors such as maintaining independence while establishing positive believes in the need for treatment and improving confidence in being able to manage their own health with appropriate support from significant others may encourage older people with HF to participate in self-care.

7.2.5. Burden of Heart Failure

Modern healthcare increasingly requires patients to take on more responsibility for the management of their conditions which in HF requires ongoing monitoring of symptoms while routinely participating in self-care and complex polypharmacy regimes [496]. For older people this means the burden of living with multiple conditions is likely to increase. Despite the view that conditions other than HF have more limiting factors on daily functioning than HF, living with the condition impacts on an individual's physical, psychological and social well-being with potential consequences for quality of life [497]. Any improvement which can be achieved in the management of symptom burden has the potential to improve overall function in patients with HF positively impacting on levels of independence a factor identified for adherence.

However the burden of illness is not the only consequence of living with a long-term condition. As previously described within this thesis there has been a significant increase in the number of treatment options available for long-term conditions such as HF in recent years. While clinical guidelines such as SIGN 147: Management of chronic heart failure [1] have undoubtedly improved health

outcomes for patients living with long-term conditions they focus on single disease. Given that older patients with HF have an average of three comorbid conditions clinical guideline recommendations offer potential for the number of prescribed treatments to rise without consideration of other comorbidities or how best to prioritise guideline recommendations. [498].

Consequently following disease-centred care not only increases potential for adverse reactions it may also result in complex treatment plans which are uncoordinated and do not consider the individual, their personal preferences or any limitations they may have in regard to their capacity to understand and participate in the management of their conditions [499]. Given that multimorbidity is the norm in older people with HF all treatment associated with the management of HF must be considered in context of patient-centered rather than disease-centered care [500].

Burden of treatment refers to the additional workload placed on patients in order to adhere to healthcare recommendations and to the resources available to patients in order to respond to increase in workload demands [495]. In HF patients require to commit to the undertaking of a life-time of routine tasks such as regular medication taking, symptom monitoring and lifestyle changes. It has been estimated that patients with chronic conditions such as HF have been estimated to spend around 86 minutes per day managing a single condition exclusive of any time allocated to undertake recommended exercise programs [501]. Additionally the extent of this burden can be intensified due to factors including the subsequent prescribing of additional medications and the need to attend regular medical appointments as well as a lack of continuity and poor communication between health professionals [500].

For older patients with HF the presence of co-morbidities may mean that balancing workload and individual ability can be particularly difficult. When considering medication adherence therefore rather than simply focusing on health at a condition specific level it may be more useful to look an individual's interaction with health and how well their treatment plan for all co-morbid conditions fits into their life [502]. Minimally disruptive medicine (MDM) is an

approach which looks impose the minimum treatment burden possible in order to achieve the goals an individual has set for their health [503].

In order to enable patients to undertake an increased personal role in their health the MDM model proposes that two strategies are necessary: firstly, the right care needs to be identified and secondly we need to enable that care to happen. While it is clear that specialist medicine plays an important role in the prescribing of treatment for older people with HF the complexity of regimes prescribable for all co-morbid conditions undoubtedly has potential for high levels of treatment burden in this population. An alternate model of care which is designed around a team of co-ordinating healthcare professionals who sees the patient on a regular basis may be better placed to manage care reducing the potential for repetitive outpatient appointments while overseeing and rationing the prescribing of treatments.

In order for burden of treatment to be reduced healthcare professionals require not only an overview of the treatments necessary for each diagnosed condition but a clear understanding of the work involved in managing treatment regimes. Importantly treatment needs to be holistic and viewed firmly from the patient context for older people. A constant theme running through the work contained within this thesis is the importance placed on the relationship between the healthcare professional and the patient. For older people with HF developing this relationship has potential to improve treatment adherence not only through the development of trust but through the ability to improve knowledge and understanding of treatment while ensuring that treatment regimes remain appropriate and within the patient's capabilities.

7.3. Conclusion

The work contained within this PhD has gone some way to advance the understanding of adherence to medication in older people with HF. It sought to establish a better understanding of which factors play a role in determining adherent behaviour with a view to establishing which components would make the make the greatest contribution towards improving adherence and health outcomes, for older patients with HF.

Despite the increasing availability of new medications available for the treatment of HF it is clear that an improvement in health may be gained from improving adherent behaviour to current medical treatments rather than adding to the overall burden of treatment. However, research looking to address medication adherence in older patients with HF is still limited in both quantity and quality. There remains no consensus on what would be classed as the minimum acceptable level of adherence in this population. While many studies have evaluated the effect on health-related outcomes for many of the drugs currently prescribed for patients with HF it may well be that 100% adherence is not required to achieve acceptable treatment results.

It is the recommendation of the author of this thesis that any future research should attempt to explore multi-component interventions, acknowledging patients' beliefs and preferences and incorporating them into adherence-enhancing interventions which combine a number of strategies including: the adoption of a holistic rather than condition specific approach; the transfer and reinforcement of appropriate knowledge at an appropriate time and addressing patient capability issues. However, by focusing on optimal strategies for the comprehensive management of the patient with HF rather than the isolated effects of single drugs or on the individual factors deemed responsible for non-adherence interventions can be developed which ensure that the already heavy burden of living with HF is not increased.

Finally, by empowering patients healthcare professionals must also accept that patients ultimately have the choice in whether they adhere to the healthcare advice they are given. While interventions have the potential to improve adherence outcomes they will not work for everyone therefore it is important that individuals are empowered to adhere in order that they are in a position to make an informed personal choice and not just because we want to achieve 100% adherence rates in treatments without firm evidence that this is necessary.

Chapter 8: Implications for Future Research

The impetus for this PhD was to gain an understanding of adherence in older patients with HF in order to establish the framework for a future intervention aiming to improve adherence medication in this population. This chapter concludes the thesis by summarising the implications that the results from this study have for future work. An overview of the proposed content of a future intervention aimed at improving medication adherence in older people living with HF will be discussed.

8.1. Proposed content of a future intervention

No single, simple intervention has consistently proven effective in improving adherence to medication in the HF population. Further research therefore needs to focus on exploration of a multi-component intervention. However, in designing an intervention containing several interacting component parts, consideration should be given to the level of complexity which may have an impact on the feasibility and cost-effectiveness of implementing such a solution in clinical practice.

The intervention proposed in this chapter uses the guidance developed by the Medical Research Council (MRC) for the development and evaluation of complex interventions as an underlying framework [504]. The framework describes four main stages: development; feasibility; evaluation and finally implementation (see figure 8.1). The work contained within this thesis has gone some way to address the ‘development’ stage of the MRC framework; the next step is the establishment of a working group to complete the design of a theoretically-based intervention prior to preliminary testing in a pilot study.

In the initial stages of intervention development, a working group made up of a range of stakeholders will review the knowledge gleaned from this PhD to establish a working protocol detailing a full description of the intervention and its component parts. The stakeholder group will need to include multi-professional representatives with specialist knowledge of HF, of behaviour change technique, plus both patients with HF and carers of those with HF.

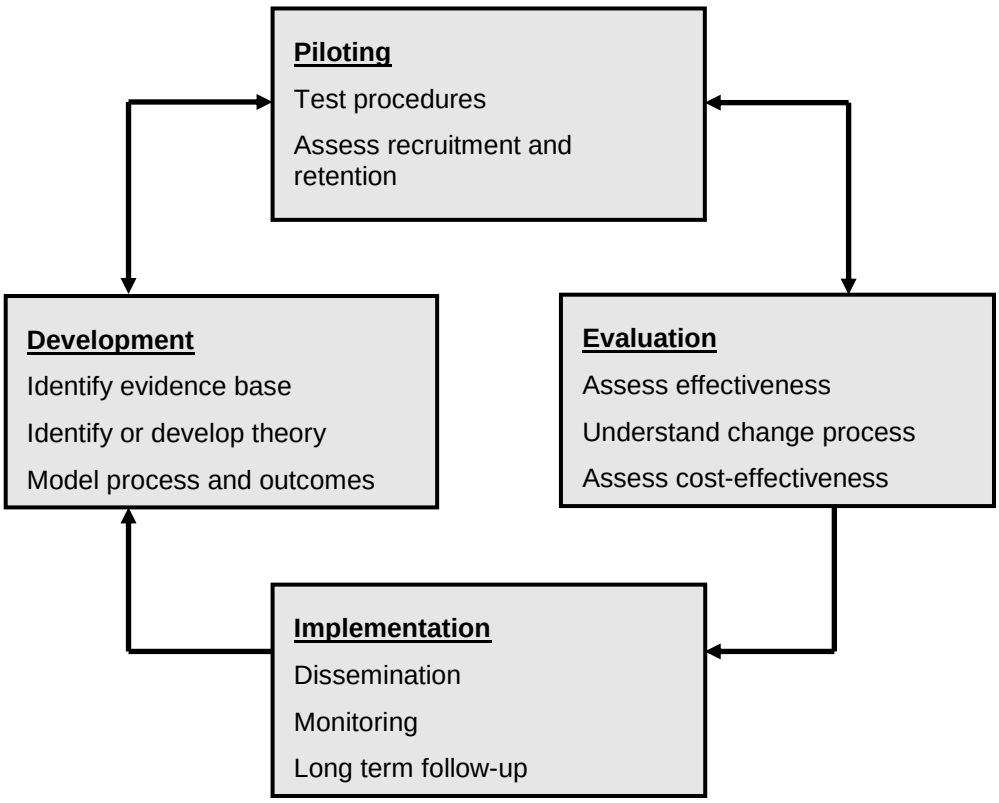

Figure8.1: Elements of the MRC framework adapted from Craig et al 2006 [504]

8.1.1 Theoretical grounding of the intervention

When considering the development and evaluation of a complex intervention theory is considered a central component by the MRC framework [505]. The use of theory is likely to improve the success and generalisability of interventions [506], and underutilisation of theory in many of the previous studies in the field of adherence has resulted in guidance of limited usefulness.

Previous adherence interventions in the HF population have focused primarily on specifics such as the relationship between healthcare provider and patient [360, 362, 365] or on improving knowledge around self-care and treatment of disease [354, 368], and these interventions have in the long-term been mostly unsuccessful. More recent studies have increasingly utilised self-regulatory and social cognition models including the Common-Sense Model utilised within this thesis. However, while these models focus on the beliefs held by

individuals as well as their ability to follow advice and may offer valuable insight into what might underpin non-adherence they may be rather limited in their usefulness to guide any change in the nonadherent behaviour itself [507].

The numerous techniques used to bring about behaviour change have been classified and incorporated into a taxonomy of behaviour change [508]. Following a synthesis of 19 pre-existing frameworks Michie et al developed the Behaviour Change Wheel (BCW), a single interface which provides a framework for intervention development incorporating a theory of behaviour, intervention functions and categories of policy. At the heart of the BCW sit the three components Michie et al propose are required in order to bring about a change in behaviour:

1) (C) the physical and psychological *capability* to perform the behaviour including necessary knowledge and cognition
2) (O) the social and physical *opportunity* to perform the behaviour which include all the factors which lie outside the individual and
3) (M) *motivation* or the cognitive processes such as decision making as well as habit and emotion responses.

Known as the COM-B model of behaviour change the model proposes that while each of these three components have the ability to effect behaviour directly behaviour is part of an interacting system involving all three. Importantly the interaction between these three components may explain why a recommended behaviour (such as adherence to medication) is not employed (see figure 8.2). Interventions therefore must aim to change one or more components in such a way the result is a new system minimising the risk of the behaviours reverting back.

Given that the COM-B model sits at the centre of the BCW, once barriers and facilitators to these components have been established the BCW includes a selection of nine intervention functions which can be selected. Recently, the COM-B model has been used to identify factors associated with self-care behaviours in patients with HF [509].

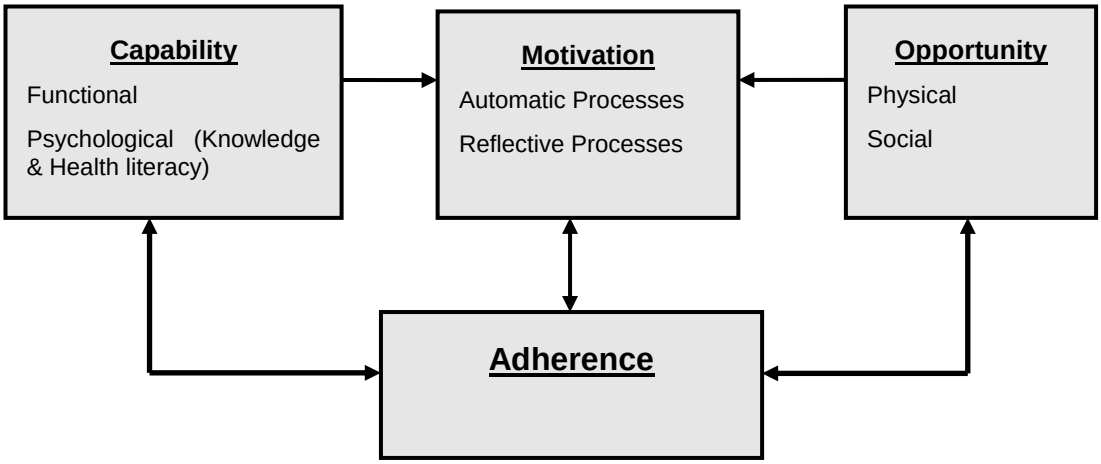

Figure8.2: application of COM-B model to adherence adapted from [492]

As a starting point to guiding the selection of the specific effective interventions required to implement this proposed complex intervention the COM-B model developed by Michie et all will form the basis for development [493]. Within this thesis the use of the Common-Sense Model has enabled factors underlying adherence to medication in older HF patients to be defined. These factors, alongside the facilitators and barriers to adherence described by HF patients within both the qualitative study and qualitative review reported in this thesis can be easily mapped to the COM-B model (see table 8.1).

In a recent article Jackson et al suggested that the COM-B could be applied to medication adherence emphasising its inclusion of automatic processes, system level factors and the specificity of its components as offering a positive basis on which appropriate interventions could be developed [492]. Using the findings of this period of PhD study, the following section proposes the likely component parts of any such intervention.

8.2. Essential components of the intervention

8.2.1. Study Population

While the results from this thesis suggest that the majority of people may in fact adhere to their HF medications literature it is important to identify those

COM-B model	Domains of the Common-Sense Model - Illness Representation	Facilities and barriers to medication adherence
Capability	*Identity* – Comprehension of condition and understanding of management *Cues/control* – beliefs about physical ability to undertake management of conditions. Ability to organise and execute management plan	• Ability to use memory aids and adapt regime when necessary • Forgetfulness / cognitive function • Assistance from others
Opportunity		• Availability of medication • Complexity of regime • Availability of social support • Access to continued relationship between Healthcare professional and patient
Motivation	*Identity* – Perception of condition and associated treatment *Cause* - Perception of cause of illness *Timeline* – Perception of chronic/acute nature of condition *Consequences* – Beliefs about the condition, symptoms, associated management and potential outcomes *Cues/control* – Beliefs about self-efficacy and efficacy of treatment	• Maintaining independence and avoiding hospitalisation • Avoidance of being a burden on others • Belief and trust in healthcare professionals

Table8.1: Mapping of CSM and identified facilitators and barriers to adherence to the COM-B Model

patients who may gain most benefit from any planned intervention. The aim of such an intervention would be change the health trajectory for HF patients who have poor understanding of HF and its management or HF patients whose adherence is known to be low and therefore are potentially at high risk of exacerbation of the condition. Targeting this group would also provide the most

scope to change the underlying behaviours and motivations that underpin adherence. The intervention would aim to target patients newly diagnosed with the condition in order to help establish a good level of understanding around the condition and its management at the earliest stage possible. In addition the intervention could also target those with a recent hospitalisation for HF where adherence has been identified as suboptimal thus providing a 'teachable moment' for behaviour change.

8.2.2. Core components

It is clear from the results of this study that any proposed intervention requires to be tailored to the needs of each individual while not creating additional treatment burden for those already managing multiple disease. During the initial stages the working group will utilise the BCW to complete the design of the intervention, but based on the work contained in this thesis several core components are suggested (see figure 8.3 for proposed components).

- Educational component delivered at first contact and continued throughout intervention delivery.
- Participation in a series of home based person centred interviews enabling the development of a personal action plan incorporating:
    - Linking personal motivating factors with symptoms and treatment of all ongoing medical conditions.
    - Identification and proposed management of social, physical and psychological barriers to adherence
- Involvement of significant others for the individual including family and medical practitioner.

Figure8.3: Essential components of proposed intervention

As discussed in chapter three of this thesis interventions which are focused purely around an educational component do not have the ability to improve adherence to medication. However, improving knowledge around both condition and prescribed treatment has been an integral part of those interventions which successfully improved adherence to medication within the HF population.

During the empirical studies conducted as part of this PhD study most older patients with HF chose to have the researcher conduct their study visits within their own home. Conducting interviews within the home environment has obvious benefits. Not only is it important that patients feel at home in order that a full assessment of social, physical and psychological barriers to adherence can be undertaken and a management plan proposed but the patient's own home environment may be more conducive to promoting discussion around all co-morbid conditions rather than the focus being primarily on the management of HF which, as previously stated, is often not felt to be of great importance to patients.

As identified during the qualitative interviews while older people with HF live with symptoms of the condition these are often related to other conditions. When discussing how health effects daily lives other conditions were often seen as more problematic having a greater impact on daily living. Development of a personal action plan will enable a holistic approach and enable the intervention to be tailored to the specific needs of the individual pulling on the motivational factors unique to each individual.

Finally, the important role played by carers and family is central to the success of the intervention. While factors such as living status or carers beliefs did not have a significant effect on adherence during the observational study during the qualitative interviews the patients desire to avoid becoming burdensome on loved ones was clear. This desire to remain functionally independent coupled with a desire to avoid burdening either relatives or medical practitioner should be incorporated into the design of the intervention.

8.2.3. Intervention Delivery

The qualitative and observational studies described earlier in this thesis reported that many patients are unclear about when they received a diagnosis or who told them of the diagnosis. Therefore early engagement and reinforcement of the diagnosis at the time of initial diagnosis has the potential to help overcome this lack of understanding. Consulting with potential participants at their first clinic appointment and engaging them in the intervention by giving them the educational pack with follow-up shortly after the first visit may go some way to establish a memory of diagnosis, while regular follow-up in the one year period following this diagnosis would potentially reinforce existence of the condition particularly when symptoms may have been initially been contributed to other conditions or ageing.

While it has been highlighted that several trials looking to improve adherence in the HF population have been undertaken by pharmacists it may be more practical to consider that this role may be undertaken by a specialist nurse or Advanced Nurse Practitioner who has the necessary knowledge and skills. A significant finding of the study was the importance placed on the relationship participants had with their doctor. Establishing a positive link between the study and the participants' doctor may help with reinforcement of adherence. The supply of an education pack focusing specifically on the new HF diagnosis would be issued at the first clinic appointment which could further aid reinforcement of both diagnosis but also the link with medical staff.

Currently it is already routine practice across many HF services information to supply information regarding the condition. Modifying this information could by including material around adherence could help both increase knowledge but help open discussion around adherence. In addition while information may be supplied to those attending specialist clinics there is a need to deliver this information to people who are not currently seen by HF services. This is particularly important for older people, who may receive the diagnosis from geriatricians, general medical services, or GPs, and are not always involved with HF specialist services.

Finally, while the intervention looks to address specific factors within each of the three components of the COM-B model an important element of the intervention will be enabling the individual to establish a feedback loop between capability, opportunity and motivation positively influencing adherence to medication.

8.2.3.1. Addressing Capability

In order to take into consideration both the psychological and physical capabilities of the study participants an important consideration for the delivery of this intervention is the “right time, right place” question. Delivering the intervention in the participants own home may enable an accurate assessment of the current barriers and facilitators to adherence however, a degree of flexibility is required to enable patients wish to engage with the intervention elsewhere to do so. A review of the patient’s current medication taking regime will potentially allow simplification of the regime but will also facilitate an assessment of health literacy and the development of an individualised plan on how to overcome barriers to adherence such as reduced cognitive function.

Education alone is not sufficient to improve adherence. Nevertheless, sufficient knowledge of HF and the purpose of the medications is likely to be a necessary component of an intervention. An educational element within this proposed intervention would focus on supplying information based not only on HF but tailored to include the other medical conditions experienced by the patient. By encompassing all the conditions which are important to the patient, the education component may go some way to enabling the patient to manage often complex regimes with competing effects and harms. This improved all-round health knowledge may also allow an increased understanding of the specific signs and symptoms of deterioration in their HF which may previously been wrongly associated to other conditions potentially enabling patients to seek medical guidance before the condition deteriorates significantly.

Towards the end of the intervention the inclusion of a personal reflection on each individual’s health trajectory since initial diagnosis may help place the condition in context for the patient. This reflection may not only help HF

patients place the condition in context but may once again reinforce the diagnosis and need for ongoing management.

8.2.3.2. Addressing Motivation

Studies which have shown some effectiveness in improving self-care and adherence in patients with HF have included the a positive relationship with health care providers, promoting self-efficacy; identification of a link between HF and symptoms; family or carer giver involvement and are individualised and responsive. A focus on personal motivating factors will be an essential component of the intervention with interviewing tailored to avoid extra burden of treatment.

During the home visits, person-centred interviewing will seek to establish the individual's perception of the condition, their prognosis and the beliefs they hold about the medications they have been prescribed. During the one-to-one interviews, participants will be encouraged to explore their own motivation for medication adherence. These motivational interviews will enable the patient to establish a meaningful association between symptoms, their condition and medication, over time, this focus on personal motivational factors alongside positive reinforcement will allow the patient to develop realistic expectations of their own health trajectory and adopt increased responsibility for their own health and treatment. The option for inclusion of family and informal carers in the person-centred interviews will be actively encouraged given their importance as highlighted by the findings in this thesis.

8.2.3.3. Addressing Opportunity

The proposed intervention will also focus on factors which offer the individual both physical and social opportunities to improve adherence to medication. Interlinking with the other domains of the COM-B model, the intervention will include assessment of the external factors which may impact on adherence. Conducting the interviews in the participants own home will enable an assessment of individual's physical environment identifying facilitators and barriers and planning ways to maximise the value of facilitators whilst planning ways to circumvent barriers. Advice on reminders e.g. pill boxes, medications

diaries, use of prescription services shown to be of value in other studies [156] can be added as part of the individual action plan at this stage.

Finally, linking with the motivational domain, the intervention will include family and significant others including members of the healthcare team. This will aid in the identification of relationship factors such as the influence of family, friends and importantly the patient's own doctor which have been shown to be important in influencing how patients with HF think about both their condition and its management.

8.3. Pathway to future testing and study

Finally, when considering the development of a complex intervention it is important to consider the interplay between: development, piloting, evaluation and implementation of interventions as described by the MRC framework [489]. In order to facilitate the examination of the proposed intervention within a full RCT the author proposes the following iterative pathway as the route to future testing and study (see figure 8.4).

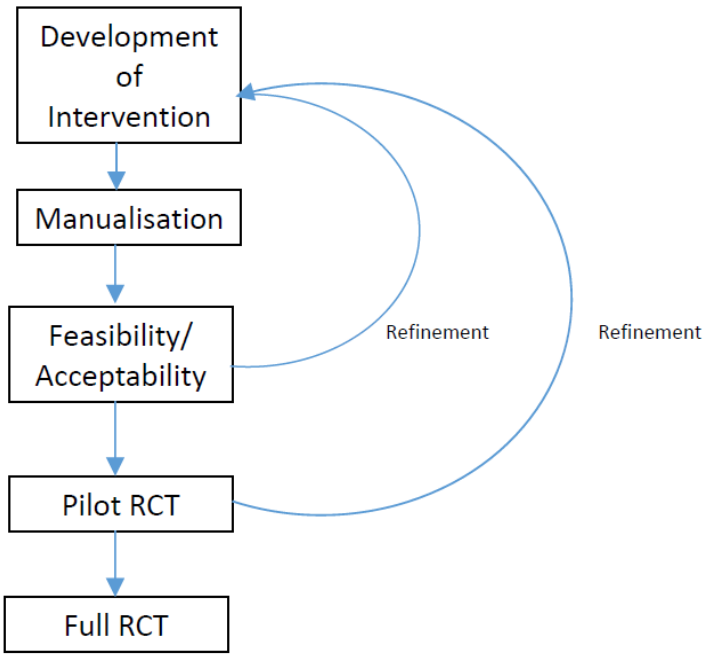

Figure 8.4 Pathway as the route to future testing and study

Firstly the intervention development will be undertaken as described above. Once the component parts have been agreed by all stakeholders and manualisation has occurred a non-randomised study, conducted on a series of HF patients, is proposed. This feasibility study will involve the collection of both qualitative and quantitative feedback which will allow adherence to the intervention to be evaluated and inform refinement of the intervention design. Following any necessary modification the intervention will be trailed in a small pilot RCT. This study will aim to test the intervention in the same way as would be done for the main trial with adherence to the intervention as the main outcome. Again process outcomes would be collected to further refine the intervention.

Finally the intervention will be examined as part of a multi-centre RCT. At this stage likely outcomes would be adherence to medication, symptom management, QoL, and hospitalisations. Additionally, process outcomes to determine if that the intervention was actually used by participants would also be conducted.

This chapter has described the proposed content of a future intervention aimed at improving medication adherence in older people living with HF. Following the MRC framework for complex interventions the COM-B model has been selected as the theoretical underpinning for the intervention development. The specific targeting of newly diagnosed HF patients, those with poor understanding of the condition as well and those whose adherence is known to be low would aim to help establish a good level of understanding around the condition and its management.

The following concluding chapter contains a brief personal reflection on my journey through this doctoral programme of work.

9. Personal Reflection

The motivation for the development of this PhD was a desire to investigate which modifiable factors were associated with poor adherence to medication in older patients with HF with a view to developing a theory-based intervention. This experience has taken me in a surprising direction. While my previous experience undertaking RCT's in older people had equipped me with basic quantitative research skills this period of study has enabled me to explore adherence using multi-methods.

Over the last five years I have developed a grounding in the principles of systematic reviewing, developing my skills not only around literature searching but also in critical appraisal and the synthesising and disseminating of results. My knowledge and skills within this area continue to develop and are used daily as part of my new teaching role.

The inclusion of a qualitative study helped fill in many of the gaps that had been missing in previous research I had conducted. The experience has enabled me to challenge my own perceptions and develop a reflexivity previously missing from my research. Overall, I have developed a confidence and belief in my abilities previously missing.

The undertaking of a study looking to understand something as complex as adherence has been extremely rewarding. My journey has brought me into contact with older HF patients who despite having limited knowledge or understanding of their condition or treatment are managing to live with multi-morbidity and polypharmacy. It has been a privilege to meet with both patients and carers who were all most generous in the sharing of their personal stories. It is clear that a desire to remain as independent as possible and not become a burden on those around them was an important factor motivating most the people I came in contact with. Despite not finding any conclusive results around which modifiable factors are associated with poor adherence in HF I remain convinced that there is a need to develop and test a theory-based intervention within this population. My work over the next few years will continue the journey started with this PhD.

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Appendix A

Protocol for systematic review of Interventions to Enhance Adherence to Medications in Patients with Heart Failure

V1.0 30/03/15

Background

Heart Failure (HF) is a major cause of disability, hospitalisation and death, particularly amongst older people [1]. It currently affects approximately 900,000 people in the UK. Despite improvements in the prevention and treatment of HF the prognosis remains poor with a median survival following a first episode of decompensated HF being 2.3 years for men and 1.8 years for women [2]. The annual cost of heart failure to the NHS is estimated to be 4% (direct costs of 1.9%) of the total NHS expenditure, with hospitalisation being the predominant cost component.

The improvements, which have been achieved in symptoms and mortality, are due in large part to the prescribing of effective medications such as angiotensin-converting enzyme inhibitors (ACEi), beta-blockers and spironolactone. While there is clear evidence that these medications improve survival and reduce hospitalisation rates due to HF, there is also evidence to suggest that adherence to medication is sub-optimal in chronic heart failure

(CHF) patients, especially amongst older HF patients [1, 3]. This non-adherence to medication remains a significant barrier to optimising outcomes for those with CHF and so presents a modifiable target for intervention.

In observational studies poor adherence to medication is associated with worse outcomes for CHF patients. Strategies to improve adherence to drug therapy in CHF has the potential to both improve health outcomes and reduce the burden on the health budget. One of the largest studies of adherence in CHF patients found that only 80% of patients with a prescription for ACEi at hospital discharge actually filled the prescription in the following 30 days, with this rate dropping further to only 60% of prescriptions being refilled at 12 months [4]. The Candesartan in Heart Failure: Assessment of Reduction in Mortality and morbidity study (CHARM) concluded that adherence was independently associated with improved clinical outcome, even in the placebo group [5] . This relationship between adherence and improved outcomes in all-cause mortality, even to placebo, suggests that adherent behaviour itself is associated with clinical outcome and highlights the requirement to find ways to improve medication adherence.

In the last few years there have been a number of studies published showing that simple well-specified behaviour change strategies that could be incorporated into routine nursing care can increase adherence to medications in a number of conditions. These include patients with Type 2 diabetes [6] and in a recent Chief Scientist Office (CSO) funded study of patients following stroke [7]. The potential for these kinds of interventions has not been examined

in the context of chronic heart failure, which has similar e.g. complex regimens, but also unique challenges e.g. a distinct symptom profile.

This systematic review is an update on the systematic review carried out by Molloy et al [8] and published in 2012. Given that available evidence is generally dynamic and evolving, incorporating additional studies into the current review will ensure that the best available evidence will be available.

Objectives

To systematically review the evidence from randomised controlled trials of interventions to enhance medication adherence in patients with chronic heart failure.

Design

Types of studies

- Randomised controlled trials where treatment was compared to a usual care or a clearly justified comparison group
- The intervention strategy clearly had a primary or secondary aim to increase adherence to heart failure medication
- Self-administered medication adherence (i.e. medication not administered by a health care professional) was measured as an outcome by either –
    - pill count
    - electronic monitoring
    - refill or prescription records
    - self-report

- biochemical measures of drug ingestion specific to heart failure medication

Types of participants

Studies enrolling adults >=18years, with a clinical with a diagnosis of heart failure (confirmed by a physician) will be eligible.

Types of interventions

Any intervention designed to enhance medication adherence including the following**:**

- Patient Education and Information (such as face to face oral, written material, visual aids or mailed instructional materials)
- Intensified Patient Care (including direct patient contact interventions or telephone / tele monitoring programs)
- Complex Behavioural Approaches
- Simplification of the Drug regimen (either pill number or dose timing)

Control groups or treatment as usual groups should either have received no intervention or 'usual care' and have similar demographic characteristics to the intervention groups. Treatment as usual includes 'usual' dosage medication regimens.

Exclusion criteria

1. Interventions not aimed at enhancing adherence to heart failure medication.

2. Interventions to enhance medication adherence in other chronic diseases.

3. Interventions not directed at patients (e.g. education of healthcare professionals about the importance of adherence).

4. Studies that do not report the results in full (e.g. conference abstracts), where further information (sufficient to make a fair appraisal of the methodological quality and results of the study) are not available from the authors.

5. Non-randomised studies

Primary Outcome

Adherence to medication including any definition of adherence noting how this was defined and measured in each study.

Search strategy

A comprehensive search strategy will be used to retrieve all relevant RCT of medication adherence in heart Failure. The following electronic databases will be searched:

Medline (start date to end March 2015)

CINAHL (start date to end March 2015)

Embase (start date to end March 2015)

Cochrane Central Register of Controlled Trials (start date to end March 2015)

PsychInfo (start date to end March 2015)

Google Scholar (for grey literature)

Controlled Clinical Trials.com

NHS elibrary

There will be no restrictions on language or publication status

Search terms:

Databases will be searched using the same search criteria as used by the author of the previous review (see appendix)

Hand-searching:

Reference lists of all retrieved articles will be screened to identify any additional publications. Where necessary, we will contact the authors of relevant articles.

Selection of Studies.

Two reviewer authors (RF and MW) will independently pre-screen all search results (titles) for possible inclusion. Each reviewer will then indicate whether

I. A citation is relevant (i.e. appears to meet the inclusion criteria)
II. A citation is clearly not relevant
III. A citation gave insufficient information to make a judgement.

All discrepancies will be were resolved by discussion and consensus.

Abstracts for all potentially relevant titles will be obtained and the process repeated.

We will seek full-text paper copies of all potentially relevant abstracts (categories I and III). Any discrepancies will be resolved by consensus, overseen by a third review author acting as arbiter.

A detailed PRISMA flowchart will be formulated in which the characteristics of the excluded studies will be presented.

Quality assessment of studies

As recommended by the Cochrane Reviewers Handbook studies will be assessed for adequate sequence generation and allocation concealment (selection bias), the presence of blinding in outcome assessment (performance and detection bias), and whether reporting of losses to follow-up and intention-to-treat analysis were specified (attrition bias) using a standardised quality checklist.

The two review authors (RF & MW) will independently assess the risk of bias in each of the included studies, with any disagreements resolved by discussion and consensus. Assessment will be presented in a Risk of Bias table using criteria suggested in the Cochrane Handbook. For each study a summary assessment will be made for the primary outcome (high, low or unclear risk of bias). The GRADE system will be used to assess the quality of the evidence for the primary outcome across studies and a Summary of Findings table will be produced.

Data extraction

Both authors (RF and MW) will collect data from all papers independently using the standardised data extraction form (see appendix 2). Both reviewers will extract details concerning:

e) Study characteristics: including study design, inclusion/exclusion criteria; recruitment procedures used (e.g. details of randomisation, blinding)

f) Patient characteristics: including age, gender, ethnicity, severity of illness, co-morbidities; current medication, as well as number of participants in each characteristic category for intervention and control group

g) Intervention and setting: including setting in which the intervention is delivered; method of delivery; description of the intervention and control; duration of treatment period; sample size and description of co-interventions if relevant

h) Outcome data/results: including outcome names; measurement tool or method used for outcome measures; length of follow-up number and/or times of follow-up measurements; number of withdrawals, exclusions, deaths or recorded hospitalisation and results of study analysis

Key findings relating to adherence will be compiled in a 'summary of findings' table

Data analysis

We will conduct a narrative synthesis of the included studies. We will examine interventions designed to enhance medication adherence, classing them into the same 4 main categories used in the initial review:

- Patient Education and Information
- Intensified Patient Care
- Complex Behavioural Approaches
- Simplification of the Drug regime

Clinical and methodological heterogeneity across the included studies will be evaluated by comparing the characteristics of participants, interventions and study designs. If study interventions and outcomes are sufficiently similar we will consider pooling the data statistically via meta-analysis. If there is sufficient cope we aim to identify the specific behaviour change techniques used in each study using a behaviour change taxonomy.

Meta-analysis

Due to the wide range of possible interventions and outcomes it is not expected that there will be scope for meta-analysis. However if studies are sufficiently homogeneous in terms of design and measurement of adherence meta-analysis will be conducted in Revman software using random effects models. Continuous variables will be aggregated using inverse-variance analyses; odds ratios will be combined using Peto odds ratio analyses. Heterogeneity will be assessed using the I2 statistic, and possible publication bias will be assessed by means of funnel plots and application of Egger's test.

Sensitivity analyses

In the event that meta-analysis is deemed appropriate, sensitivity analyses will be conducted. These will include, but not be limited to:

- Omitting studies with a high risk of bias
- Subgrouping studies into those with self-reported adherence vs objectively measured adherence

Missing / incomplete data

If the presented data are insufficient or missing, we will attempt to obtain additional information from the authors of the included studies by personal communication. If we do not receive correspondence from the authors, we will analyse the available data.

Reporting

The results will be reported according to the current PRISMA guidelines

Review Registration

The review will be registered on the PROSPERO database of systematic reviews

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8. Molloy GJ, O'Carroll RE, Witham MD, McMurdo MET. Interventions to enhance adherence to medications in patients with heart failure: a systematic review. Circulation Heart failure. 2012;5(1):126-33.

Systematic Review Protocol – Search terms

((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomized[tiab]) OR (placebo[tiab]) OR (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab])) NOT (animals[mh] NOT humans[mh]))

AND

((Patient compliance[mh]) OR (Treatment Refusal[mh]) OR (Patient Dropouts[mh]) OR (Attitude to health[mh]) OR (Patient satisfaction[mh]) OR (adher* OR nonadherence* OR non-adherence*) OR (compliance* OR noncompliance* OR non-compliance*) OR (refusal OR refuse) OR (dropout* OR drop-out*)) AND ((heart failure[mh]) OR (heart failure[tiab]) OR (cardiac failure[tiab]))

Appendix B

Systematic review of Interventions to Enhance Adherence to Medications in Patients with Heart Failure

Data Extracted by:	**Date**
Checked by:	**Date**

Study ID: *(surname of first author and year first full report of study was published)*

Report IDs of other reports of this study *(e.g. duplicate publications, follow-up studies)*

General Information

Report title
Report author contact details
Publication type
Study funding sources
Possible conflicts of interest
Notes

Methods

	Description	
Primary Outcome		
Population description		
Country / Setting		
Method/s of recruitment of participants		
Ethical approval needed/ obtained for study	☐ Yes ☐ No ☐ Unclear	
Informed consent obtained	☐ Yes ☐ No ☐ Unclear	
Type of study	Randomised Controlled Trial	☐ Yes ☐ No ☐ Unclear

Study Characteristics	Inclusion criteria
	Exclusion criteria
Notes	

Risk of Bias assessment

Domain	Risk of bias Low risk ☐ High risk ☐ Unclear risk ☐	Support for judgement
Random sequence generation *(selection bias)*	☐ ☐ ☐	
Allocation concealment *(selection bias)*	☐ ☐ ☐	
Blinding of participants and personnel *(performance bias)*	☐ ☐ ☐	
Blinding of outcome assessment *(detection bias)*	☐ ☐ ☐	
Incomplete outcome data *(attrition bias)*	☐ ☐ ☐	
Selective outcome reporting? *(reporting bias)*	☐ ☐ ☐	

Other bias	☐ ☐ ☐	

Other information

	Description
Correspondence required for further study information *(from whom, what and when)*	

Inclusion in current Systematic Review:

☐ Included ☐ Not included ☐ For Discussion

Reason for non-inclusion

Participants

	Intervention group	Control Group	Overall
Total no. Randomised			
Withdrawals and exclusions			
Age (range, mean, SD)			
Sex (%)			
Race/Ethnicity			
Severity of illness **e.g. NYHA class**			
Co-morbidities			

Medication			
Subgroup analysis			
Notes			

Intervention

	Description
Description of intervention	
Details of Control/usual care Group	
Theoretical basis	
Duration of treatment period	
Setting	
Delivery including Providers*(e.g. no., profession, training) Integrity of delivery)*	
Co-interventions	
Notes	

Outcomes

	Outcome 1	Outcome 2	Outcome 3
Outcome name			
Timing of outcome measures			
Method and / or unit of measurement			
Is outcome/tool validated?	☐ ☐ ☐ Yes No Unclear	☐ ☐ ☐ Yes No Unclear	☐ ☐ ☐ Yes No Unclear
Notes			

Results

	Intervention		Comparison	
No. Missing participants and reasons				
No. Participants moved from other group and reasons				
No. recorded deaths				
No. recorded hospitalisations				
Outcome 1	Mean Change (SD)	Number participants	Mean Change (SD)	Number participants
	Odds Ratio (95% CI)			
Any other results reported				
Notes				

Results cont.

Outcome _____	Mean Change (SD)	Number participants	Mean Change (SD)	Number participants
	Odds Ratio (95% CI)			
Any other results reported				
Notes				

APPENDIX C

Qualitative Study Protocol

Title: How do older Heart Failure patients manage their medication?

Sponsor	University of Dundee / NHS TAYSIDE
Sponsor R+D Number	2013GR03
Funder	Chief Scientist Office
Funding Reference Number	DTF/13/04
Chief Investigator Principal Investigator	Prof Marion McMurdo Mrs Roberta L Fulton
REC Number	14/ES/0066
Version Number and Date	V1.0 10/04/14

PROTOCOL APPROVAL

How do older Heart Failure patients manage their medication?

Signatures

By signing this document I am confirming that I have read, understood and approve the protocol for the above study.

Prof Marion McMurdo		
Chief Investigator	Signature	Date
Mrs. Roberta L Fulton		
Principal Investigator	Signature	Date

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ABBREVIATIONS

ACEi: angiotensin-converting enzyme inhibitors

CHF: chronic heart failure

CSO: Chief Scientist Office

ESC: European Society of Cardiology

GCP: good clinical practice

HF: heart failure

NHS R&D: National Health Service Research and Development

NYHA: New York Heart Association

REC: Research Ethics Committee

TASC: Tayside Medical Science Centre

SUMMARY

Heart Failure (HF) is a major cause of disability, hospitalisation and death, particularly amongst older people. Prognosis remains poor despite the improvements in prevention and treatment achieved through the prescribing of effective medications. Evidence suggests that adherence to medication is sub-optimal but there is a lack of current data identifying which modifiable factors are associated with poor adherence in older HF patients. This study forms part of a programme of work, which aims to address these issues, culminating in the development of a tailored intervention to enhance medication adherence in older HF patients.

This study is the first stage of this programme of work. This qualitative study will use a purposive sampling approach to recruit up to 12 older HF patients and their nominated carers to participate in a semi-structured interview to explore their understanding of heart failure and medication, along with the perceived drivers and barriers to adherence. The findings of this study will be used, along with information gleaned from the updating of a recent systematic review [1], to guide development of the next phase of this programme of work.

1. INTRODUCTION

Heart Failure (HF) is a major cause of disability, hospitalisation and death, particularly amongst older people [2]. It currently affects approximately 900,000 people in the UK. Despite improvements in the prevention and treatment of HF the prognosis remains poor with a median survival following a first episode of decompensated HF being 2.3 years for men and 1.8 years for women [3]. The annual cost of heart failure to the NHS is estimated to be 4% (direct costs of 1.9%) of the total NHS expenditure, with hospitalisation being the predominant cost component.

The improvements, which have been achieved in symptoms and mortality, are due in large part to the prescribing of effective medications such as angiotensin-converting enzyme inhibitors (ACEi), beta-blockers and spironolactone. While there is clear evidence that these medications improve survival and reduce hospitalisation rates due to HF, there is also evidence to suggest that adherence to medication is sub-optimal in chronic heart failure (CHF) patients, especially amongst older HF patients [2, 4]. This

non-adherence to medication remains a significant barrier to optimising outcomes for those with CHF and so presents a modifiable target for intervention.

In observational studies poor adherence to medication is associated with worse outcomes for CHF patients. Strategies to improve adherence to drug therapy in CHF has the potential to both improve health outcomes and reduce the burden on the health budget. One of the largest studies of adherence in CHF patients found that only 80% of patients with a prescription for ACEi at hospital discharge actually filled the prescription in the following 30 days, with this rate dropping further to only 60% of prescriptions being refilled at 12 months [5]. The Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity study (CHARM) concluded that adherence was independently associated with improved clinical outcome, even in the placebo group [6] . This relationship between adherence and improved outcomes in all-cause mortality, even to placebo, suggests that adherent behaviour itself is associated with clinical outcome and highlights the requirement to find ways to improve medication adherence.

In the last two years there have been a number of studies published showing that simple well-specified behaviour change strategies that could be incorporated into routine nursing care can increase adherence to medications in a number of conditions. These include patients with Type 2 diabetes [7] and in a recent chief Scientist Office (CSO) funded study of patients following stroke [8]. The potential for these kinds of interventions has not been examined in the context of chronic heart failure, which has similar e.g. complex regimens, but also unique challenges e.g. a distinct symptom profile.

A recently performed systematic review of interventions to enhance adherence to medications in patients with heart failure concluded that limited high quality evidence evaluating the effectiveness of specific adherence enhancing interventions currently exists and called for further research to identify the optimum strategies for implementation into clinical practice [1].

In order to address this lack of evidence gaps in existing knowledge need addressed, the aims of the programme of work of which this study forms part are:

a) To understand what are the beliefs which are currently commonly held around HF and its management by older HF patients and their nominated carers

b) To identify which of these commonly held beliefs around HF and medication consistently predict medication adherence and which can be modified

c) To use the information gathered to identify which adherence enhancing strategies could be implemented for evaluation at a later date.

2. RESEARCH QUESTIONS

This qualitative phase of the study aims to answer the following questions**:**

a. What are the beliefs and attitudes older heart failure patients and their informal caregivers hold about their disease and its treatment?

b. What are the barriers and drivers to medication adherence for heart failure patients?

3. STUDY DESIGN

The methodology for this qualitative study follows the framework approach based on work developed at the National Centre for Social Research by Ritchie and Lewis [(9)]. This approach, widely used in healthcare research, draws on characteristics of the scientific model while adapting them to suit the nature of qualitative data which is more appropriate for exploring the complexities of health and well-being, assisting the investigator to achieve a deeper understanding of the patient experience [(10)]. The underpinning principles of the framework approach are based on the concepts of interpretivism and reflexivity, balancing them with pragmatism and transparency [(11)]. This approach is in direct contrast to other entirely inductive approaches, such as grounded theory, were the research design is not strictly predefined but developmental in response to the data obtained.

Using this approach the investigator will aim to remain as objective and neutral as possible during the collection, interpretation and presentation of the data while minimising the extent of their influence on the participant. The use of topic guides to facilitate the interview process as advocated by the framework approach will support the investigator to identify patterns within the data. While the investigator recognises that neutrality and objectivity can never be totally achieved the principles of the

framework approach can be used to undertake qualitative data analysis systematically enabling the exploration of the data in depth while simultaneously maintaining an effective and transparent audit trail, enhancing the rigour of the analytical processes, something that some published qualitative studies often lack [10].

Study type: This Qualitative study will comprise of the following:

- Individual semi structured interviews, using structured topic guides, with older heart failure patients taking place within their own home or another nominated site.
- Focus groups, using structured topic guides, comprising relatives or other nominated informed carers of those who have been diagnosed with heart failure.

4. STUDY POPULATION

The study is a single site study (NHS Tayside Area)

Study population:

a) Community dwelling people ages 70 and over with a diagnosis of chronic heart failure according to the European Society of Cardiology (ESC) guidelines and with evidence of left ventricular systolic dysfunction.
b) Nominated informed carers of the participants described above.

Participants will be recruited from the following various sources:

- Secondary care via Heart Failure and Medicine for the Elderly outpatient clinics.
- Secondary care via medical wards in Ninewells Hospital
- Primary care via primary care Heart Failure outpatient clinics.
- Heart Failure nurse liaison service

The use of the above range of recruitment methods will ensure that the study population includes recently hospitalised patients whose heart failure may not be optimally controlled as well as those patients who are being managed successfully within the community.

4.1 INCLUSION CRITERIA

Age 70 years and over

Living in own home or sheltered housing

Existing diagnosis of chronic heart failure according to ESC guidelines:

- Presence of breathlessness or tiredness on exertion or at rest
- Presence of structural heart disease on imaging

Left ventricular systolic dysfunction (on echocardiogram) or other cardiac imaging

New York Heart Association class II, III or IV

4.2 EXCLUSION CRITERIA

Unable to give written informed consent

Residing in Nursing home or Residential Home Environment

Currently receiving daily visits from district nursing service to administer medications

5. PARTICIPANT SELECTION AND ENROLMENT

Patients meeting the inclusion criteria, identified from any of the previously identified sources, will be considered for enrolment in the study:

Participants will be recruited to participate in a one using a purposive sampling strategy as described by Patton [12] chosen to provide the researchers with a detailed picture of living with heart failure by encompassing a range of demographic variables. Using information gleaned from the reading of current literature two key variables have been chosen as selection criteria –

1. Gender
2. Recent hospital admission following an episode of decompensated heart failure.

Evidence exists to show that different views and beliefs are held by men and women regarding their amount of medication use, their adherence to medications, and their likelihood of receiving ongoing medication monitoring [13] while a recent systematic review looking at determinants of adherence to heart failure medication identified that

institutionalisation including hospitalisation was associated with adherence to medication [14].

Potential participants will be identified within the relevant clinic or inpatient areas my members of the medical and nursing team who will supply a copy of the PIS and reply slip or seek permission for a member of the research team to send study information to the potential participants' home address. The potential participant will have the opportunity to consider the study by reading the PIS and respond by returning the reply slip using the prepaid envelope supplied. This will allow the principle investigator to contact potential participants to discuss the study in more detail and establish if they meet the selection criteria by referring to the sampling matrix. All participants meeting the inclusion criteria will be asked to nominate an informal carer to participate in the carer's interview. Those patients unable to nominate a carer will still be eligible to participate in the individual interview should they meet the selection criteria as directed by the sampling matrix.

6. PLAN OF INVESTIGATION

This study aims to ensure that while all main elements are covered diversity is also included to ensure each element can be explored thoroughly. Purposive sampling of eligible participants will be carried out using a sampling matrix. Given the experience within the investigating team with this type of research it is anticipated that up to 12 heart failure patients and 12 nominated carers will be required to achieve data saturation. Recruitment will however cease early should saturation be realised at an earlier point.

Participants selected will be invited to participate in the individual interview and will be given the opportunity to nominate an alternative setting should they not wish the interview to be conducted in their home. Nominated carers will be asked to participate in either an individual interview or a small focus group depending on their preference.

6.1 CONSENT

The Principal Investigator will be responsible for ensuring written informed consent is obtained before any interviews are carried out.

Participants will receive adequate oral and written information – appropriate Participant Information will be provided at least 48 hours prior to potential participation. The oral explanation to the participant will be performed by the Principal Investigator and must cover all the elements specified in the Participant Information Sheet/Informed Consent, The participant will be given every opportunity to clarify any points they do not understand and, if necessary, ask for more information. Sufficient time will be given to each participant to consider the information provided. It will be emphasised that the participant may withdraw their consent to participate at any time without it affecting any medical care in the future.

The participant will be asked to agree to their medical records being inspected by regulatory authorities but understand that their name will not be disclosed outside the hospital.

The Investigator or delegated researcher and the participant will sign and date the Informed Consent Form(s) to confirm that consent has been obtained. The participant will receive a copy of this document and a copy will be filed in the Trial Master File.

6.2 DATA COLLECTION

Prior to commencing the interview the permission will be sought to tape record the interview for transcribing by the investigator at a later date. Patient demographics including age, sex, home circumstances including postcode and formal help at home will be collected along with a list of the patient's current medication. The interview will be conducted using the appropriate topic guide (see appendix) and recorded throughout.

A review of the literature highlighted depression as a common variable in medication adherence thus mood will be formally assessed in all participants with the their permission using a commonly used assessment tool - the Hospital Anxiety and Depressions Scale

Interviews with participants will continue alongside data analysis with the recruitment of participants continuing until data saturation occurs. All interviews will be tape recorded by and transcribed from audiotapes by the principal investigator. . A unique study identifier will be allocated to each participant

6.3 DATA ANALYSIS

Analysis of all the data will be conducted using NVivo software. The principal investigator, in order for familiarisation of the data to occur, will carry out transcribing of the taped interviews. The framework approach is based on thematic analysis and will be used to underpin all data analysis. Thematic frameworking is an interpretive process, which aims to develop meaningful themes representing participants' accounts. The data will be systematically searched and analysised by the investigator to identify patterns.

Using thematic frameworking the investigator will classify and code the data transcribed from the interviews according to key themes, concepts and emergent categories. The categories will be refined through familiarisation with the raw data and the subsequent cross-sectional labeling subdivided by a succession of related sub-themes or topics.

Once a comprehensive list of main and sub-themes has been obtained each one will be charted in a matrix. The response of each research subject will be allocated a row with each column representing a separate subtopic. Finally the investigator will summarise or synthesise the original data from each participant. Importantly the key terms phrases or expressions used by the research participants will be retained as much as possible. Interpretation will be kept to a minimum and material will not be dismissed just because it is not immediately obvious where it should be included in the analysis.

7. INSPECTION OF RECORDS

Chief and Principle Investigators and institutions involved in the study will permit study related monitoring, audits, and REC review In the event of an audit, the Investigator agrees to allow the Sponsor, representatives of the Sponsor or regulatory authorities direct access to all study records and source documentation.

8. STUDY MONITORING

The study may be subject to monitoring by the Sponsor or Research Ethics Committee. No monitoring visit is required prior to study commencement.

9. RISK ASSESSMENT

Risks of study: Occasionally when discussing ill health or life events participants may become emotionally distressed.

Minimising the risk: The investigator is an experienced research nurse with many years' experience dealing with older people with heart failure and has undergone appropriate training.

10. ETHICAL CONDUCT OF THE STUDY

The study will be conducted in accordance with the principles of the good clinical practice (GCP). A favourable ethical opinion will be obtained from the appropriate REC and local NHS R&D approval will be obtained prior to commencement of the study.

11. REGULATORY COMPLIANCE OF THE STUDY

The study will not commence until research sponsor approval, favourable ethics opinion and local NHS R+D approval are in place

12. CONFIDENTIALITY

All transcribed interviews, field notes, reports, and other records will be identified in a manner designed to maintain participant confidentiality. All records will be kept in the allocated secure storage area within Department of Ageing & Health, Ninewells Hospital. Information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the Sponsor, its designee, Regulatory Authorities, or the REC. The Investigator and study site staff involved with this study will not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee will be obtained for the disclosure of any said confidential information to other parties.

13. DATA PROTECTION

All study site staff involved with this study will comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. Access to collated participant data will be restricted to those directly involved with the study.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data that could allow identification of individual participants. Quotations will be anonymised and labeled with participant study numbers only in published documents

13.1 Insurance and Indemnity

The University of Dundee and Tayside Health Board are Co-Sponsoring the study.

Insurance – The University of Dundee will obtain and hold a policy of Public Liability Insurance for legal liabilities arising from the study].

Tayside Health Board will maintain its membership of the Clinical Negligence and Other Risks Insurance Scheme ("CNORIS") which covers the legal liability of Tayside in relation to the study].

Where the study involves University of Dundee staff undertaking clinical research on NHS patients, such staff will hold honorary contracts with Tayside Health Board which means they will have cover under Tayside's membership of the CNORIS scheme.

Indemnity Co-Sponsors do not provide study participants with indemnity in relation to participation in the Study but have insurance for legal liability as described above.

14. STUDY CONDUCT RESPONSIBILITIES

Protocol Amendments, deviations and breaches

The CI will seek approval for any amendments to the Protocol or other study documents from the Sponsor, REC and NHS R&D Office. Amendments to the protocol or other study docs will not be implemented without these approvals.

In the event that a CI needs to deviate from the protocol, the nature of and reasons for the deviation will be documented and submitted to the Sponsor. If this necessitates a subsequent protocol amendment, this will be submitted to the Sponsor for approval and then to the appropriate REC and lead NHS R&D Office for review and approval.

In the event that a serious breach of GCP is suspected, this will be reported to the Sponsor immediately using the form "Notification to Sponsor of Serious Breach or Serious Deviation".

15. STUDY RECORD RETENTION

All study documentation will be kept for at least 5 years. Archiving will take place according to current TASC standard operating procedures.

16. PUBLICATION

The information collected by the study will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing the results of the study.

17. PEER REVIEW

The proposal for this study formed part of a fellowship award which has been subjected to external peer review via the CSO, the funding body.

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APPENDIX D

Participant Identification Number

Title of Project: **How do older Heart Failure patients manage their medication?**

Please initial box

1. I confirm that I have read and understood the information sheet dated 10/04/14 (version 1.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without any medical care or legal rights being affected.
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by regulatory authorities from the University of Dundee or from NHS Tayside, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
4. I agree to the audio tape recording of the interview which will be anonymised
5. I agree to take part in the above study.

Participant name (Block Capitals)	Date	Signature
Person taking consent (Block Capitals)	Date	Signature

APPENDIX E

PARTICIPANT INFORMATION SHEET

How do older Heart Failure patients manage their medication: An Observational Study

Invitation

My name is Roberta Fulton and I am undertaking a project as part of my PhD at the University of Dundee. I invite you to take part in the following study. Before you decide to do so, I need to be sure that you understand firstly why I am doing it, and secondly what it would involve if you agreed. I am therefore providing you with the following information. Please read it carefully and be sure to ask any questions you might have and, if you want, discuss it with others including your friends and family. I will do my best to explain the project to you and provide you with any further information you may ask for now or later. You do not have to make an immediate decision.

Why are we doing this study?

As researchers we are interested in the views that older people with heart failure have about their health, medicines and treatment. We are also interested in your day-to- day experiences living with your medications. The results of this study will help us understand how well people with heart failure understand their condition and how they deal with their treatments. To help us understand these views, we are inviting

you to take part in this study. This knowledge will help other people get the best from their treatments in the future.

We are always interested in the views of your family or those people who care for you. We would like you to suggest someone you think may want to help us. If so, they will be asked to complete a questionnaire relating to heart failure and return it in a free-post envelope. This is also voluntary, and they can say ‘no’ at any time, however you can take part even if you feel you do not wish to recommend a friend or carer.

Why Have I Been Invited?

You have been invited because you are aged 70 years or over and are currently prescribed medication commonly used to treat people with a condition called heart failure. This condition means the heart does not pump enough blood to meet all the needs of the body, usually because the heart muscle has been damaged. This condition is not uncommon; around 900,000 people in the UK have a diagnosis of heart failure, which may result in symptoms such as breathlessness and tiredness. Many people suffering from heart failure are prescribed daily tablets by their doctor to help control their condition. We are asking a minimum of 60 older people with heart failure to participate in the study.

How Will The Study Help Me?

While we cannot promise the study will help you, you may find the opportunity to talk about your experience beneficial. The information we get will help other older people with heart failure in the future, because we will have a better idea of what they understand about their heart condition and medication and how they manage their medication. We aim to use this information to design a programme which may help people with heart failure to manage their medication and condition more effectively in the future.

Do I have to take part?

It is up to you to decide. Participation in this study is entirely voluntary and you are free to refuse to take part or to withdraw from the study at any time without having to give a reason and without this affecting your future medical care or your relationship with medical or nursing staff looking after you. Remember you can take part even if you feel you do not wish to recommend a friend or carer.

What will happen to me if I take part?

If you feel you may be able to help us and complete the enclosed reply slip, I (Roberta Fulton) will telephone you to discuss the study further.

The telephone call

I will first phone you at home to ask you some short questions about your health and current medication. If these questions suggest that the study is suitable for you, we will arrange for you to visit your local hospital. If you would prefer, I can visit you at home or at another place convenient for you.

The study visit

Should you be happy to travel to the hospital we can pay for a taxi or other transport to collect on the day of the visit and take you home again. You may ask a friend or relative to accompany you to the visit should you wish it.

At the visit, which should last around 2 hours, we will go over the study information; you will have the opportunity to ask any questions you want to about the study. If you are happy to take part, we will ask you to sign a consent form. You will be given a copy of this along with this Participant Information Sheet to keep.

At this visit, we will do the following:

- We will take a note of your medicines and medical conditions
- Ask you to provide a small sample of urine, this will be tested for levels of one of the medications if you are currently taking called Furosemide.
- Test your walking speed and balance
- Take some blood (about a teaspoonful), this will be sent to the laboratory and tested for levels of another of the medications if you are currently taking, it may have a name like Ramipril, Lisinopril or Perindopril.
- Ask you to complete nine Questionnaires. These questionnaires relate to your health, medication taking, mood and memory. I can help you to complete these if you wish.

Will my GP know about this research project?

If during your study visit we discover anything we feel your GP should be aware of, we will ask for your permission to share these f indings with your GP.

Will my taking part in this study be kept confidential?

All the information that is collected about you during the course of this study will be kept strictly confidential.

Your research data will be stored using a unique study code which does not identify you. All written information will be kept in a locked filing cabinet in a locked room. Any web-based data will be stored in a secure password protected central database. Only individuals directly involved with the study will have access to this information.

It is a requirement of the regulators that your records in this study, together with any other relevant medical records, be made

available for scrutiny by appropriate monitors from NHS Tayside. This procedure is routine and carried out by fully qualified officials, and data confidentiality is preserved at all times.

At the end of the study the confidential records will be kept for 10 years and then destroyed. The confidential handling, processing, storage and disposal of data are in accordance with the Data Protection Act 1998. Should you change your mind and not wish your information to be stored you may contact the research team at any time and ask that it be destroyed.

We will also ask your permission to allow us access your paper and electronic medical records for a period of five years. This will help us obtain information on your health now and over the next five years to investigate the long-term effects of your treatment.

The blood sample will be sent to the local NHS laboratory for analysis. The result will be stored indefinitely using your name and unique hospital record number within the NHS clinical system and can be made available to specialist doctors for your future health care needs. The urine sample will be stored until all participants have been recruited before being analysed by colleagues at the University of Dundee laboratories. The samples will be destroyed after they have finished analysing it.

What will happen to the results?

The results will be examined by the researchers who have organised the study and a short report will be produced. You will not be identified in this report. The results will be shared with the funder for the study (The Scottish Government's Chief Scientist Office.) The results will then be published in scientific journals. Again, you will not be identified in any journal articles. If you

would like a copy of the full results, please let us know; we will give everyone who takes part a summary of the main results.

Who is organising and funding this research?

The study has been organised by Dr Miles Witham and colleagues at the University of Dundee. The study is funded by the Scottish Government's Chief Scientists Office and sponsored by the University of Dundee and NHS Tayside.

What are my rights?

If you have any concerns about your participation in the study you have the right to raise your concern with a researcher involved in conducting the study or a doctor involved in your care. If you have a complaint about your participation in the study, you should first talk to a researcher involved in the study. However you have the right to raise a formal complaint.

You can make a complaint to a senior member of the research team or to the Complaints Officer for NHS Tayside:

Complaints and Feedback Team

The Business Unit, Level 7, Laboratory Corridors B and F Ninewells Hospital, Dundee DD1 9SY

Freephone: 0800 027 5507
Email:feedback.tayside@nhs.net

In the event that you think you have suffered harm as a result of your participation in the study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation against the University of Dundee or NHS Tayside. If you wish to make a claim, you should consider seeking independent legal advice but you may have to pay for your legal costs.

The University of Dundee maintains a policy of public liability insurance which provides legal liability cover in respect of damages, costs and expenses arising out of claims.

Tayside Health Board is a member of the Clinical Negligence and Other Risks Insurance Scheme which provides legal liability cover.

Who has reviewed the study?

The East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of medical ethics. It is a requirement that your records in this research, together with any relevant medical records, be available for scrutiny by monitors from University of Dundee and NHS Tayside, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

What to do now:

Now that you have read the information sheet, please think about it and discuss it with friends or family if you wish. If you would like to talk to a member of the research team about the study, please contact Roberta on the phone number below or return the reply slip in the self-addressed envelope and Roberta will contact you.

Thank you for reading this Information Sheet and considering taking part in this study.

By returning the form you are only agreeing that the researcher may phone you. You can make a decision on whether to take part after speaking to her

Mrs Roberta Fulton

- **Call on: 01382 383086**

- **E-mail: r.l.z.fulton@dundee.ac.uk**

APPENDIX F

CARERS INFORMATION SHEET

Study title: How do older Heart Failure patients manage their medication?

Chief Investigator: Prof Marion McMurdo

INVITATION

My name is Roberta Fulton and I am required to undertake a project as part of my PhD at the University of Dundee. I invite you to take part in the following study, however, before you decide to do so, I need to be sure that you understand firstly why I am doing it, and secondly what it would involve if you agreed. I am therefore providing you with the following information. Please read it carefully and be sure to ask any questions you might have and, if you want, discuss it with others including your friends and family. I will do my best to explain the project to you and provide you with any further information you may ask for now or later. You do not have to make an immediate decision.

ABOUT THIS RESEARCH

As researchers we are interested in the views that older people with heart failure hold about their health, medication and treatment as well as their experiences of day to day life. The results of this study will help us understand how well informed people with heart failure are about their medical conditions and prescribed treatments. We are also interested in the experiences of relatives or carers of people diagnosed with heart failure. This knowledge will help other people get the best from their treatments in the future.

To help us understand your views, we are inviting you to participate in either a one to one interview with a researcher or a small focus group with other people who also care for someone diagnosed with heart failure. Your may also find that we have already invited someone you know to help us.

WHY HAVE I BEEN INVITED?

You have been invited because you care for someone aged 70 years or over who have had a diagnosis of heart failure. This means their heart does not pump enough blood to meet all the needs of their body, usually because the heart muscle has been damaged. They are not alone; around 900,000 people in the UK also have a diagnosis of heart failure, which may result in

symptoms such as breathlessness and tiredness. Many people suffering from heart failure are prescribed daily tablets by their doctor to help control their condition. We are asking a total of 12 older people with heart failure and 12 nominated carers to participate in the study.

WHAT WILL TAKING PART INVOLVE?

If you feel you may be able to help us, and complete the enclosed reply slip Roberta Fulton will telephone you to discuss the study further. If you are agreeable:

- Roberta will then arrange to either visit you individually at your home or at a place convenient for you or arrange for you to attend a venue where you will be part of a small informal group sharing your views with other people who may be in a similar situation to yourself.
- Roberta will discuss the carers information sheet with you ask you to sign a consent form indicating you wish to take part in the study.
- You will be asked some questions about your understanding of heart failure and its treatment and your opinion on how it impacts on both your life and the person suffering from it.

- Roberta will ask your permission to record the interview so she can listen to it again to make sure we fully understand your views. The researcher will agree a false name with you so that what you say can be quoted later without revealing your identity.
- The interview will last around one hour, everything you tell us is confidential and will not be directly fed back to the person you care for.

HOW WILL THE STUDY HELP ME?

While we cannot promise the study will help you, you may find the opportunity to talk about your experience beneficial. The information we get will help other older people with heart failure in the future, because we will have a better idea of what they understand about their heart condition and medication.

DO I HAVE TO TAKE PART?

No. Participation in this study is entirely voluntary. If you choose not to take part, you do not have to give a reason. You are also free to change your mind at any time without having to give a reason and without it affecting any future medical care.

PRIVACY

We would like to record the discussions. All the information you give is strictly confidential. At the start of the study you will be assigned an identity (ID) number to protect your anonymity. Instead of using your name, the recording and the written copy of the discussions will be stored with a code. The information will be kept in a locked room and held on a secure computer. Only the researchers involved in the study will have access to this information. At the end of the study the recordings and any other identifiable information held on our computer will be destroyed. You will never be identified in any study report or publication.

WHAT WILL HAPPEN AT THE END OF THE STUDY?

The results will help us design the next phase of our research. This will look at how well older people with heart failure manage to take their medication as it has been prescribed. The information we collect will also be used to write up the results from the study as a publication in a medical journal. The Scottish Government, which funds the research, will receive a report of our overall findings. None of your personal details will appear in any report, presentation or publication arising from the research and all collected data will be destroyed 5 years from the end of the study.

WHAT IF THERE IS A PROBLEM?

In the event that something goes wrong and you are harmed during the study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Dundee or NHS Tayside but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

If you have a complaint about your participation in the study you should first talk to a researcher involved in your care. You can ask to speak to a senior member of the research team or the Complaints Officer for NHS Tayside:

Complaints and Claims Manager

Complaints and Advice Team

Level 7, Ninewells Hospital

Dundee DD1 9SY

Freephone: 0800 027 5507

Email: nhstaysidecomplaints@thb.scot.nhs.uk

WHO HAS REVIEWED THE STUDY?

The study has been looked at by an independent group of people called a Research Ethics committee, who are there to protect your interests. The study has been reviewed and approved by East of Scotland Research Ethics Committee. It is a requirement that your records in this research, together with any relevant medical records, are made available for scrutiny by monitors from the University of Dundee and NHS Tayside. Their role is to check that research is properly conducted and the interests of those taking part are adequately protected.

WHAT DO I DO NOW?

Now that you have read the information sheet, please think about it and discuss it with friends or family if you wish. If you would like to talk to a member of the research team about the study, please contact Roberta on the phone number below or return the reply slip in the self-addressed envelope and Roberta will contact you.

CONTACT DETAILS

Mrs Roberta Fulton

Research Fellow

Ageing and Health

Division of Diabetes & Cardiovascular Medicine

Ninewells Hospital

Dundee

DD1 9SY

Telephone: 01382 383086

Email: r.l.z.fulton@dundee.ac.uk

Professor Marion McMurdo

Division of Diabetes & Cardiovascular Medicine

Ninewells hospital and Medical School

Dundee DD1 9SY

Telephone 01382 383086

Thank you for reading this Information Sheet and considering taking part in this study.

By returning the form you are only agreeing that the researcher may phone you. You can make a decision on whether to take part after speaking to her

CARER REPLY SLIP

Study title: How do older Heart Failure patients manage their medication?

CI: Prof Marion McMurdo PI: Roberta Fulton

Yes, I would like to take part in this study, and I am happy to be contacted by the research team to make arrangements

Name:

……

Address:

……

……

Home telephone number(s):

……

Mobile telephone

……

Email address:

……

When would be a good time for us to call?

Morning Afternoon Evening Other (please specify)

APPENDIX G

Carers Identification Number

Title of Project: **How do older Heart Failure patients manage their medication?**

Please initial box

1. I confirm that I have read and understood the information sheet dated 10/04/14 (version 1.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without any medical care or legal rights being affected.
3. I agree to the audio tape recording of the interview which will be anonymised.
4. I agree to take part in the above study.

Participant name (Block Capitals)	Date	Signature
Person taking consent (Block Capitals)	Date	Signature

APPENDIX H

How do older Heart Failure patients manage their medication?

Topic Guide Discussion for interviews with Patients

1. Present Circumstances

- Age
- Current living arrangements including: who lives with them, postcode and area, supportive network, previous occupation?

2. Just to get started, can you tell me a little bit about any medical conditions you have? –

- Names
- How long you have had them,
- What is the prognosis for each of them,

3. Tell me a bit about long you have suffered from your heart condition

(Symptoms; Cause; timeline; consequences i.e. physical social emotional; cure and controllability)

- Can you remember when and who told you about the problem with your heart

- Are you able to describe what you thought when they told you
- Can you explain to me what the problem with your heart actually is
- Are you able to describe to me any symptoms you may have which you feel are related to your heart problem,
- Can you tell me does anything help you with these symptoms?
- Tell me about any regular heath checkups you may be having (who, when what where)
- What effect do these appointments have? If anything

4. Let's focus specifically on your general health for now. When it comes specifically to health issues – what would you say are the biggest problems that you face?

- Which condition do you think is most serious,
- Why do you think that?
- Which condition, if any, causes you more problems than the others
- In what ways does it cause problems?

- Tell me how do you overcome theses problems? Is there anything you do?
- Do any of your medical conditions make you worry, which ones, why

5. Now, let's talk about your medicines for a few minutes.

(necessity & concerns; medication knowledge; social influences; impact of medication on lifestyle)

- Can you tell me a little about the medications you are taking? – Names, dose, how often you take them
- In which way do you think these tablets help your condition?

-

- Sometimes people who take tablets long term say they have problems with their medication. Can you tell me about any problems you may be having with these tablets.
- Would you say any of your medications cause any side effects? – If so which tablets, what are the symptoms, what do you do to deal with these side effects?
- Can you tell me about any issues about taking your medication that make you worry?

6. Overall can you describe to me how do you think your health will affect your life over the next few years?

- Physically, emotionally, financially, relationships with friends and family

7. Are there any questions that you want to ask us, or final words you like to tell me about what health professionals need to know about patients with heart failure or medications that we haven't covered?

How do older Heart Failure patients manage their medication?

Topic Guide Discussion for interviews with Nominated Carers

1. Present Circumstances

- Age
- Current living arrangements including: who lives with them, employment status, postcode and area, supportive network,
- How often they visit xx, hours per week, help they require to give

2. Just to get started, can you tell me a little bit about what you know about the medical conditions xxx has?

- List, Prognosis for each, how long they have had them, how their medical conditions effect the participants life and the carers life.

3. Tell me a bit about long they have suffered from their heart conditions

(Symptoms; Cause; timeline; consequences i.e. physical social emotional; cure and controllability)

- Can you remember who told you that xxx had a problem with their heart
- Are you able to describe what you thought when they told you
- Can you explain to me what the problem with their heart actually is
- Are you able to describe to me any symptoms you may have which you feel are related to their heart problem,
- Can you tell me of anything, which helps xxx cope with these symptoms?
- Tell me about any regular heath checkups they may be having (who, when what where)
- Can you tell me in what way if any these appointments help them with their heart condition

4. Let's focus specifically on xxx's general health for now. When it comes specifically to health issues – what would you say are the biggest problems that they face?

- Which condition do you think is most serious
- Do you think one condition causes them more problems than the others and if so in what way
- Tell me about the things they do to overcome these problems

5. Now, let's talk about xxx's medicines for a few minutes. Can you tell me anything about the medications they are taking? – Names, dose, how often?

(necessity & concerns; medication knowledge; social influences; impact of medication on lifestyle)

- In which way do you think these tablets help their condition
- Sometimes people who take tablets long term say they have problems with their medication. Can you tell me about any problems you may think xx's may be having with their tablets?
- Can you tell me about any issues about their medication, which makes you worry?

6. Overall can you describe to me how you think xx's health will affect their life over the next few years?

- Can you describe to me if in any way, xx's health affects you?
- How do you think their health conditions will impact on your life over the next few years?

7. We have talked about xx health, are you currently having any issues with your own health? Conditions? Medications? Impact on your life? How do you see your own health and personal circumstances impacting on xx over the next few years?

8. Are there any questions that you want to ask us, or final words you like to tell me about what health professionals need to know about patients with heart failure?

How do older Heart Failure patients manage their medication?

Focus Group Topic Guide

- **What does everybody understand by the term 'Heart Failure?'**

- **What treatments are available – medication and others and how well are these managed – what help is available to patients and carers?**

- **What is the day to day effect of heart failure on patient and carers – how does it fit in with other illnesses?**

- **What does the future hold for both patient and family because of heart failure?**

- **What would help and who would deliver this help?**

APPENDIX I

Dear [PATIENT NAME]

RE: RESEARCH PROJECT:

How do older Heart Failure patients manage their medication: An Observational Study.

Your practice is helping researchers at the University of Dundee with this research study, which is funded by the Scottish Health Department. We are writing to you because you are aged 70 years or older and have heart failure, so this study may be suitable for you to take part in.

People with heart conditions are regularly prescribed medications. Dr Witham and his team at the university are looking at the opinions older people with heart failure hold about their health, medication and treatment. They are also interested in people's experiences of managing their medications. The study plans to recruit a minimum of 60 patients from Tayside.

I have enclosed some information on the study for you to read, and I hope that you would consider taking part. If you would like to ask further questions or are interested in taking part please contact the study team directly using the details below.

 Call on 01382 383086

 Return the attached REPLY SLIP in the SAE

 E-mail: r.l.z.fulton@dundee.ac.uk

Your participation is completely voluntary.

With kind regards,

[PI]

APPENDIX J

PARTICIPANT INFORMATION SHEET

How do older Heart Failure patients manage their medication: An Observational Study

Invitation

My name is Roberta Fulton and I am undertaking a project as part of my PhD at the University of Dundee. I invite you to take part in the following study. Before you decide to do so, I need to be sure that you understand firstly why I am doing it, and secondly what it would involve if you agreed. I am therefore providing you with the following information. Please read it carefully and be sure to ask any questions you might have and, if you want, discuss it with others including your friends and family. I will do my best to explain the project to you and provide you with any further information you may ask for now or later. You do not have to make an immediate decision.

Why are we doing this study?

As researchers we are interested in the views that older people with heart failure have about their health, medicines and treatment. We are also interested in your day-to-day experiences living with your medications. The results of this study will help us understand how well people with heart failure understand their condition and how they deal with their treatments. To help us understand these views, we are inviting you to take part in this study. This knowledge will help other people get the best from their treatments in the future.

We are always interested in the views of your family or those people who care for you. We would like you to suggest someone you think may want to help us. If so, they will be asked to complete a questionnaire relating to heart failure and return it in a free-post envelope. This is also voluntary, and they can say 'no' at any time, however you can take part even if you feel you do not wish to recommend a friend or carer.

Why Have I Been Invited?

You have been invited because you are aged 70 years or over and are currently prescribed medication commonly used to treat people with a condition called heart failure. This condition means

the heart does not pump enough blood to meet all the needs of the body, usually because the heart muscle has been damaged. This condition is not uncommon; around 900,000 people in the UK have a diagnosis of heart failure, which may result in symptoms such as breathlessness and tiredness. Many people suffering from heart failure are prescribed daily tablets by their doctor to help control their condition. We are asking a minimum of 60 older people with heart failure to participate in the study.

How Will The Study Help Me?

While we cannot promise the study will help you, you may find the opportunity to talk about your experience beneficial. The information we get will help other older people with heart failure in the future, because we will have a better idea of what they understand about their heart condition and medication and how they manage their medication. We aim to use this information to design a programme which may help people with heart failure to manage their medication and condition more effectively in the future.

Do I have to take part?

It is up to you to decide. Participation in this study is entirely voluntary and you are free to refuse to take part or to withdraw

from the study at any time without having to give a reason and without this affecting your future medical care or your relationship with medical or nursing staff looking after you. Remember you can take part even if you feel you do not wish to recommend a friend or carer.

What will happen to me if I take part?

If you feel you may be able to help us and complete the enclosed reply slip, I (Roberta Fulton) will telephone you to discuss the study further.

The telephone call

I will first phone you at home to ask you some short questions about your health and current medication. If these questions suggest that the study is suitable for you, we will arrange for you to visit your local hospital. If you would prefer, I can visit you at home or at another place convenient for you.

The study visit

Should you be happy to travel to the hospital we can pay for a taxi or other transport to collect on the day of the visit and take

you home again. You may ask a friend or relative to accompany you to the visit should you wish it.

At the visit, which should last around 2 hours, we will go over the study information; you will have the opportunity to ask any questions you want to about the study. If you are happy to take part, we will ask you to sign a consent form. You will be given a copy of this along with this Participant Information Sheet to keep.

At this visit, we will do the following:

- We will take a note of your medicines and medical conditions
- Ask you to provide a small sample of urine, this will be tested for levels of one of the medications you are currently taking called Furosemide.
- Test your walking speed and balance
- Take some blood (about a teaspoonful), this will be sent to the laboratory and tested for levels of another of the medications you are currently taking, it may have a name like Ramipril, Lisinopril or Perindopril.
- Ask you to complete nine Questionnaires. These questionnaires relate to your health, medication taking, mood and memory. I can help you to complete these if you wish.

Will my GP know about this research project?

If during your study visit we discover anything we feel your GP should be aware of, we will ask for your permission to share these findings with your GP.

Will my taking part in this study be kept confidential?

All the information that is collected about you during the course of this study will be kept strictly confidential.

Your research data will be stored using a unique study code which does not identify you. All written information will be kept in a locked filing cabinet in a locked room. Any web-based data will be stored in a secure password protected central database. Only individuals directly involved with the study will have access to this information.

It is a requirement of the regulators that your records in this study, together with any other relevant medical records, be made available for scrutiny by appropriate monitors from NHS Tayside. This procedure is routine and carried out by fully qualified officials, and data confidentiality is preserved at all times.

At the end of the study the confidential records will be kept for 10 years and then destroyed. The confidential handling, processing, storage and disposal of data are in accordance with the Data Protection Act 1998. Should you change your mind and

not wish your information to be stored you may contact the research team at any time and ask that it be destroyed.

We will also ask your permission to allow us access your paper and electronic medical records for a period of five years. This will help us obtain information on your health now and over the next five years to investigate the long-term effects of your treatment.

The blood sample will be sent to the local NHS laboratory for analysis. The result will be stored indefinitely using your name and unique hospital record number within the NHS clinical system and can be made available to specialist doctors for your future health care needs. The urine sample will be stored until all participants have been recruited before being analysed by colleagues at the University of Dundee laboratories. The samples will be destroyed after they have finished analysing it.

What will happen to the results?

The results will be examined by the researchers who have organised the study and a short report will be produced. You will not be identified in this report. The results will be shared with the funder for the study (The Scottish Government's Chief Scientist Office.) The results will then be published in scientific journals. Again, you will not be identified in any journal articles. If you

would like a copy of the full results, please let us know; we will give everyone who takes part a summary of the main results.

Who is organising and funding this research?

The study has been organised by Dr Miles Witham and colleagues at the University of Dundee. The study is funded by the Scottish Government's Chief Scientists Office and sponsored by the University of Dundee and NHS Tayside.

What are my rights?

If you have any concerns about your participation in the study you have the right to raise your concern with a researcher involved in conducting the study or a doctor involved in your care. If you have a complaint about your participation in the study, you should first talk to a researcher involved in the study. However you have the right to raise a formal complaint.

You can make a complaint to a senior member of the research team or to the Complaints Officer for NHS Tayside:

Complaints and Feedback Team

The Business Unit, Level 7, Laboratory Corridors B and F Ninewells Hospital, Dundee DD1 9SY

Freephone: 0800 027 5507

Email: feedback.tayside@nhs.net

In the event that you think you have suffered harm as a result of your participation in the study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation against the University of Dundee or NHS Tayside. If you wish to make a claim, you should consider seeking independent legal advice but you may have to pay for your legal costs.

The University of Dundee maintains a policy of public liability insurance which provides legal liability cover in respect of damages, costs and expenses arising out of claims.

Tayside Health Board is a member of the Clinical Negligence and Other Risks Insurance Scheme which provides legal liability cover.

Who has reviewed the study?

The East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of medical ethics. It is a requirement that your records in this research, together with any relevant medical records, be available for scrutiny by monitors from University of Dundee and NHS Tayside, whose role is to

check that research is properly conducted and the interests of those taking part are adequately protected.

What to do now:

Now that you have read the information sheet, please think about it and discuss it with friends or family if you wish. If you would like to talk to a member of the research team about the study, please contact Roberta on the phone number below or return the reply slip in the self-addressed envelope and Roberta will contact you.

Thank you for reading this Information Sheet and considering taking part in this study.

By returning the form you are only agreeing that the researcher may phone you. You can make a decision on whether to take part after speaking to her

Mrs Roberta Fulton

- **Call on: 01382 383086**
- **E-mail: r.l.z.fulton@dundee.ac.uk**

APPENDIX K

PARTICIPANT INFORMED CONSENT FORM

Study title: How do older Heart Failure patients manage their medication - an observational study.

Chief Investigator: Dr Miles Witham

This form must be completed and signed by the research participant in the presence of Principal Investigator or someone from the research team designated by the Principal Investigator.

		Initials
1. I have read and understood the Participant Information Sheet for the study V1.0, 04-09-15	Yes☐ No☐	
2. I have had the opportunity to discuss the study and to ask questions which have been answered to my satisfaction.	Yes☐ No☐	
3. I agree to my GP being informed of my participation in this study.	Yes☐ No☐	
4. I understand that my participation in the study is voluntary and that I am free to withdraw from the study at any time without having to give a reason and that this will not affect my medical care in any way.	Yes☐ No☐	
5. I understand that relevant sections of my medical notes and data collected during the study may be looked at by the research team or from the regulatory authorities or appropriate staff from the University of Dundee or NHS Tayside, where it is relevant to my taking part in this study. I give permission for these individuals to have access to my records.	Yes☐ No☐	
6. I agree that if I withdraw or I am withdrawn from the study that data already collected can be retained and included in the data analysis.	Yes☐ No☐	

7. I agree that the research team can access my medical records, in both paper and electronic form, to obtain information on my health now and over the next five years to investigate the long-term effects of the study treatment. Yes☐ No☐ ☐

8. I agree to take part in the above study. Yes ☐ No☐ ☐

After initialling the boxes above please now initial the appropriate box below.

This research is approved by The East of Scotland Research Ethics Service REC 2

Name of Participant	**Date**	**Signature**
Name of person taking consent	**Date**	**Signature**

1 copy for participant; 1 copy to be kept in the SMF and1 copy for the original hospital notes.

APPENDIX L

Dear

RE: "*How do older Heart Failure patients manage their medication: An Observational Study"*

Thank you for taking the time to read this information pack about a study that I am carrying out with colleagues at the University of Dundee. The results of this study will help us understand how well people with heart failure understand their condition and how they deal with their treatments. We are also interested in the experiences of relatives or carers of people diagnosed with heart failure.

You have been nominated by [ ] as their informal carer. Your participation is completely voluntary and you are free to decide to take part. Before you decide I would be grateful if you could take some time to read the enclosed participant information sheet.

After reading the information, if you feel you can help please complete the enclosed questionnaire and consent form and return them in the freepost envelope.

If you would like to ask further questions or are interested in taking part please contact me using the details below

☎ Call on: 01382 383086
E-mail: r.l.z.fulton@dundee.ac.uk

With kind regards

Mrs. Roberta Fulton

APPENDIX M

CARER/FAMILY MEMBERS INFORMATION SHEET

How do older Heart Failure patients manage their medication: An Observational Study

Invitation

My name is Roberta Fulton and I am undertaking a project as part of my PhD at the University of Dundee. I invite you to take part in the following study. Before you decide to do so, I need to be sure that you understand firstly why I am doing it, and secondly what it would involve if you agreed. I am therefore providing you with the following information. Please read it carefully and be sure to ask any questions you might have and, if you want, discuss it with others including your friends and family. I will do my best to explain the project to you and provide you with any further information you may ask for now or later. You do not have to make an immediate decision.

Why are we doing this study?

As researchers we are interested in the views that older people with heart failure have about their health, medicines and treatment. We are also interested in people's day-to-day experiences living with medications. The results of this study will help us understand how well people with heart failure understand their condition and how they deal with their treatments. We are also interested in the experiences of relatives or carers of people diagnosed with heart failure. To help us understand your views,

we are inviting you to take part in this study. This knowledge will help other people get the best from their treatments in the future.

Why Have I Been Invited?
You have been invited because you care for someone aged 70 years or over who are currently prescribed medication commonly used to treat people with a condition called heart failure. This condition means the heart does not pump enough blood to meet all the needs of the body, usually because the heart muscle has been damaged. This condition is not uncommon; around 900,000 people in the UK have a diagnosis of heart failure, which may result in symptoms such as breathlessness and tiredness. Many people suffering from heart failure are prescribed daily tablets by their doctor to help control their condition. We are asking a minimum of 60 older people with heart failure and their informal carers to participate in the study.

How Will The Study Help Me?
While we cannot promise the study will help you or your relative personally the information we get will be used to help other older people with heart failure in the future. We will have a better idea of what people understand about their heart condition and medication and how they manage their medication. We aim to use this information to design a programme that may help people with heart failure to manage their medication and condition more effectively in the future.

Do I have to take part?
It is up to you to decide. Participation in this study is entirely voluntary and you are free to refuse to take part from the study without having to give a reason and without and without it affecting any future medical care.

What will happen to me if I take part?
If you feel you may be able to help us please make sure you have read this information sheet carefully. If you would like to

talk to a member of the research team about the study, please contact me on the phone number below.

If you feel happy to participate please complete the enclosed questionnaire and the informed consent form and return them in the freepost envelope supplied.

Will my taking part in this study be kept confidential?
All the information that is collected about you during the course of this study will be kept strictly confidential.

Your responses will be stored using a unique study code that does not identify you. All written information will be kept in a locked filing cabinet in a locked room. Any web-based data will be stored in a secure password protected central database. Only individuals directly involved with the study will have access to this information.

It is a requirement of the regulators that your records in this study be made available for scrutiny by appropriate monitors from NHS Tayside. This procedure is routine and carried out by fully qualified officials, and data confidentiality is preserved at all times.

At the end of the study the confidential records will be kept for 10 years and then destroyed. The confidential handling, processing, storage and disposal of data are in accordance with the Data Protection Act 1998. Should you change your mind and not wish your information to be stored you may contact the research team at any time and ask that it be destroyed.

What will happen to the results?
The researchers who have organised the study will examine the results and a short report will be produced. You will not be identified in this report. The results will be shared with the funder for the study (The Scottish Government's Chief Scientist Office.) The results will then be published in scientific journals. Again, you will not be identified in any journal articles. If you would like a copy of the full results, please let us know.

Who is organising and funding this research?
The study has been organised by Dr Miles Witham and colleagues at the University of Dundee. The study is funded by the Scottish Government's Chief Scientists Office and sponsored by the University of Dundee and NHS Tayside.

What are my rights?
If you have any concerns about your participation in the study you have the right to raise your concern with a researcher involved in conducting the study or a doctor involved in your care. If you have a complaint about your participation in the study, you should first talk to a researcher involved in the study. However you have the right to raise a formal complaint.

You can make a complaint to a senior member of the research team or to the Complaints Officer for NHS Tayside:

Complaints and Feedback Team
The Business Unit,
Level 7, Laboratory Corridors B and F
Ninewells Hospital,
Dundee
DD1 9SY
Freephone: 0800 027 5507

Email: feedback.tayside@nhs.net

In the event that you think you have suffered harm as a result of your participation in the study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation against the University of Dundee or NHS Tayside. Where you wish to make a claim, you should consider seeking independent legal advice but you may have to pay for your legal costs.

The University of Dundee maintains a policy of public liability insurance which provides legal liability cover in respect of damages, costs and expenses arising out of claims.

Tayside Health Board is a member of the Clinical Negligence and Other Risks Insurance Scheme which provides legal liability cover.

Who has reviewed the study?
The East of Scotland Research Ethics Service REC 2, which has the responsibility for scrutinising all proposals for medical research on humans in the UK, has examined this study and has raised no objections from the point of view of medical ethics.

What to do now:
Now that you have read the information sheet, please think about it and feel free to discuss it with friends or family if you wish. If you would like to talk to a member of the research team about the study, please contact me on the phone number below. If you feel you are able to help us please return the enclosed questionnaire and consent form in the self-addressed envelope.

Thank you for reading this Information Sheet and considering taking part in this study.

UNIVERSITY OF DUNDEE

CHIEF SCIENTIST OFFICE

APPENDIX N

CARER/FAMILY MEMBER INFORMED CONSENT FORM

Study title: How do older Heart Failure patients manage their medication - an observational study.

Chief investigator: Dr Miles Witham

		Initials
9. I have read and understood the Participant Information Sheet for the study dated 18-09-15 (Version 1.0)	Yes☐ No☐	
10. I have had the opportunity to discuss the study and to ask questions which have been answered to my satisfaction.	Yes☐ No☐	
11. I understand that my participation in the study is voluntary and that I am free to withdraw from the study at any time without having to give a reason, without any medical care or legal rights being affected	Yes☐ No☐	
12. I agree to take part in the above study.	Yes ☐ No☐	

After initialling the boxes above please now initial the appropriate box below.

This research is approved by The East of Scotland Research Ethics Service REC 2

Name of Participant	**Date**	**Signature**
Name of person taking consent	**Date**	**Signature**

1 copy for participant and 1 copy to be kept in the ISF.

APPENDIX O

VERSION 1.0

NOVEMBER 5 2015

MEDICATION ADHERENCE IN HEART FAILURE QUESTIONNAIRE

STUDY ID _____

DATE COMPLETED ___/___/___

This booklet contains a series of questionnaires relating to your heart failure, medication taking, mood and your relationship with your doctor. It is a compilation of the following commonly used forms:

- Beliefs about Medications Questionnaire
- Illness Perception Questionnaire (Revised)
- Cardiac Self-efficiency Scale
- Hospital Anxiety & Depression Scale
- Morisky Medication Adherence Scale
- Kansas City Cardiomyopathy Questionnaire
- Medical Interview Satisfaction Scale

There are no right or wrong answers, we are interested in your own personal views. Please feel free to ignore any questions you feel uneasy answering.

Roberta is on hand to help you complete the questions should you wish it. Please feel free to take rest periods as you need.

Thank you

The following questions relate to the taking of medicines, there are no right or wrong answers. Please read each statement and place a tick in the appropriate box:

QUESTION 1	YES	NO
Some people have difficulty remembering to take their medications. Do you sometimes forget to take your heart medicine?	☐	☐

QUESTION 2	YES	NO
People sometimes miss taking their heart medications for reasons other than forgetting. Over the past two weeks, were there any days when you did not take your heart medicine	☐	☐

QUESTION 3	YES	NO
Have you ever cut back or stopped taking your heart medicine without telling your doctor because you felt worse when you took it?	☐	☐

QUESTION 4	YES	NO
When you travel or leave home, do you sometimes forget to bring your medication?	☐	☐

QUESTION 5	YES	NO
Did you take your heart medicine yesterday?	☐	☐

QUESTION 6	YES	NO
When you feel well, do you sometimes stop taking or reduce the dose of your heart medication?	☐	☐

QUESTION 7	YES	NO
Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	☐	☐

QUESTION 8

How often do you have difficulty remembering to take all your medication?

Never ☐ Once in a while ☐ Sometimes ☐ Usually ☐ All the time ☐

The following questions are designed to help us know how you feel. Read each item and place a firm tick in the box opposite the reply, which comes closest to how you have been feeling in the past week. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought-out response.Tick one box only for each question

1 I feel tense or wound up:
- Most of the time ☐
- A lot of the time ☐
- Time to time, occasionally ☐
- Not at all ☐

2 I still enjoy the things I used to enjoy:
- Definitely as much ☐
- Not quite so much Only a little ☐
- Hardly at all ☐

3 I get a sort of frightened feeling as if something awful is about to happen:
- Very definitely and quite badly ☐
- Yes, but not too badly ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

4 I can laugh and see the funny side of things:
- As much as I always could Not quite so much now ☐
- Definitely not so much now Not at all ☐

5 Worrying thoughts go through my mind:
- A great deal of the time ☐
- A lot of the time ☐
- From time to time but not too often Only occasionally ☐

6 I feel cheerful:
- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

7 I can sit at ease and feel relaxed:
- Definitely ☐
- Usually ☐
- Not often ☐
- Not at all ☐

8 I feel as if I am slowed down:
- Nearly all the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

9 I get a sort of frightened feeling like "butterflies" in the stomach:
- Not at all ☐
- Occasionally ☐
- Quite often ☐
- Very often ☐

10 I have lost interest in my appearance:
- Definitely ☐
- I don't take so much care as I should ☐
- I may not take quite as much care ☐
- I take just as much care as ever ☐

11 I feel restless as if I have to be on the move:
- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

12 I look forward with enjoyment to things:
- As much as I ever did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

13 I get sudden feelings of panic:
- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

14 I can enjoy a good book or radio or TV programme:
- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

Please rate your confidence with knowing or acting on each of the following statements by ticking the appropriate box.
There are no right or wrong answers. We are interested in your personal views.
How confident are you that you know or can:

QUESTION 1

Control your breathlessness by changing your activity levels.

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 2

Control your breathlessness by taking your medications.

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 3

When you should call or visit your doctor about your heart disease.

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 4

How to make your doctor understand about your concerns about your heart

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 5

How to take your heart medications

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

How confident are you that you know or can:

QUESTION 6

How much physical activity is good for you

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 7

Maintain your usual social activities

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 8

Maintain your usual social activities at home with your family

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 9

Maintain your usual activities at work

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

QUESTION 10

Maintain your sexual relationship with your spouse

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

How confident are you that you know or can:

QUESTION 11

Get regular aerobic exercise (work up a sweat and increase your heart rate

Not at all confident	☐	somewhat confident	☐	moderately confident	☐
Very confident	☐	completely confident	☐	N/A	☐

The following questions refer to your relationship with your GP. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

Please place a tick in one box for each question

QUESTION 1

The doctor told me just what the trouble is :

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 2

After talking with the doctor, I know just how serious my heart failure is:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 3

The doctor told me all I wanted to know about my heart failure:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 4

I am not really certain about how to follow the doctor's advice:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 5

After talking with the doctor, I have a good idea of how long it will be before I am well again

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 6

The doctor seemed interested in me as a person:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 7

The doctor seemed warm and friendly to me:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 8

The doctor seemed to take my problems seriously:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 9

I feel embarrassed while talking with the doctor:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 10

I feel free to talk to this doctor about private matters:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 11

The doctor gave me a chance to say what was really on my mind:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 12

I really felt understood by my doctor:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 13

The doctor did not allow me to say everything I wanted about my problems:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 14

The doctor did not really understand my main reason for coming:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 15

This doctor I would trust with my life:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 16

The doctor seemed to know what he (she) was doing

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 17

The doctor has relieved my worries about my illness:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 18

The doctor seemed to know just what to do about my problem:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 19

I expect it to be easy for me to follow the doctor's advice

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 20

It will be difficult for me to do exactly what the doctor told me to do:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

QUESTION 21

I'm not sure the doctors treatment will be worth the trouble it will take:

Very Strongly Disagree	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree	Very Strongly Agree
☐	☐	☐	☐	☐	☐	☐

Your views about medicines prescribed for you

We would like to ask you about your personal views about medicines prescribed for you. The following are statements other people have made about their medicines.

Please indicate the extent to which you agree or disagree with them by ticking the appropriate box.

There are no right or wrong answers. We are interested in your personal views.

QUESTION 1

My health, at present, depends on my medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 2

Having to take medicines worries me:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 3

My life would be impossible without my medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 4

Without my medicines I would be very ill

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 5

I sometimes worry about long-term effects of my medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 6

My medicines are a mystery to me:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 7

My health in the future will depends on my medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 8

My medicines disrupt my life:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 9

I sometimes worry about becoming too dependent on my medicines

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 10

My medicines protect me from becoming worse:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

Your views about medicines in general

We would now like to ask you about your personal views about medicines in general.

The following are statements other people have made about medicines in general.

There are no right or wrong answers. We are interested in your personal views.

Please indicate the extent to which you agree or disagree with them by ticking the appropriate box.

QUESTION 1

Doctors use too many medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 2

People who take medicines should stop their treatment for a while every now and again:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 3

Most medicines are addictive:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 4

Natural remedies are safer than medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 5

Medicines do more harm than good:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 6

All medicines are poisons:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 7

Doctors place too much trust on medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

QUESTION 8

If doctors had more time with patients they would prescribe fewer medicines:

Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
☐	☐	☐	☐	☐

Health Literacy

This is a made-up medicine label and does not refer to a real medicine. It is often difficult to read and understand instructions on medicine labels. In a moment, I will ask you to read the label quietly to yourself. I will then ask you some questions about what it says. You do not have to memorise the label, as you will be able to look at it while answering the questions.

MEDCO TABLET
INDICATIONS: Headaches, muscle pains, rheumatic pains, toothaches, earaches.

RELIEVES COMMON COLD SYMPTOMS

DOSAGE: ORAL. 1 or 2 tablets every 6 hours, preferably accompanied by food, for not longer than 7 days. Store in a cool, dry place.

CAUTION: Do not use for gastritis or peptic ulcer. Do not use if taking anticoagulant drugs. Do not use for serious liver illness or bronchial asthma. If taken in large doses and for an extended period, may cause harm to kidneys. Before using this medication for chicken pox or influenza in children, consult with a doctor about Reyes Syndrome, a rare but serious illness. During lactation and pregnancy, consult with a doctor before using this product, especially in the last trimester of pregnancy. If symptoms persist, or in the case of an accidental overdose, consult a doctor. Keep out of reach of children.

INGREDIENTS: Each tablet contains
500 mg acetylsalicylic acid.
Excipent c.b.p 1 tablet
Reg. No. 88246

Made in Canada by STERLING PRODUCTS. INC
1600 Industrial Blvd. Montreal, Quebec H9J 3P1

The following questions refer to your heart failure and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

QUESTION 1

Heart failure affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Place an X in one box on each line

Activity	Extremely Limited	Quite a bit limited	Moderately limited	Slightly limited	Not at all limited	Limited for other reasons or did not do the activity
Dressing yourself	☐	☐	☐	☐	☐	☐
Showering/Bathing	☐	☐	☐	☐	☐	☐
Walking 100 metres on level ground	☐	☐	☐	☐	☐	☐
Doing gardening, Housework or Carrying shopping	☐	☐	☐	☐	☐	☐
Climbing a flight of Stairs without stopping	☐	☐	☐	☐	☐	☐
Hurrying or jogging (as if to catch a bus)	☐	☐	☐	☐	☐	☐

QUESTION 2

Compared with 2 weeks ago, have your symptoms of **heart failure** (shortness of breath, fatigue, or ankle swelling) changed?

My symptoms of **heart failure** have become...

Much worse	Slightly worse	Not changed	Slightly better	Much better	I have had no symptoms over the past 2 weeks
☐	☐	☐	☐	☐	☐

QUESTION 3

Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times a week, but not every day	1-2 times per week	less than once a week	Never over the past two weeks
☐	☐	☐	☐	☐

QUESTION 4

Over the past 2 weeks, how much has **swelling** in your feet, ankles or legs bothered you?

It has been...

Extremely bothersome	**Quite a bit** bothersome	**Moderately** bothersome	**Slightly** bothersome	**Not at all** bothersome	**I've had no swelling**
☐	☐	☐	☐	☐	☐

QUESTION 5

Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you want?

All of the time	Several times per day	At least once a day	3 or more times a week, but not every day	1-2 times per week	less than once a week	Never over the past 2 weeks
☐	☐	☐	☐	☐	☐	☐

QUESTION 6

Over the past 2 weeks, how many times has **fatigue** bothered you?
It has been....

Extremely Bothersome	Quite a bit Bothersome	Moderately Bothersome	Slightly Bothersome	Not at all Bothersome	I've had No fatigue
☐	☐	☐	☐	☐	☐

QUESTION 7

Over the past 2 weeks, on average how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times a week, but not every day	1-2 times per week	less than once a week	Never over the past 2 weeks
☐	☐	☐	☐	☐	☐	☐

QUESTION 8

Over the past 2 weeks, how many times has **shortness of breath** bothered you?
It has been....

Extremely Bothersome	Quite a bit Bothersome	Moderately Bothersome	Slightly Bothersome	Not at all Bothersome	I've had No shortness of breath
☐	☐	☐	☐	☐	☐

QUESTION 9

Over the past 2 weeks, on average how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times a week but not every day	1-2 times per week	less than once a week	Never over the past 2 weeks
☐	☐	☐	☐	☐

QUESTION 10

Heart Failure symptoms can worsen for a number of reasons. How sure are you that you know what to do, or whom to call, if your **heart failure** gets worse?

Not at all sure	**Not very** sure	**Somewhat** sure	**Mostly** sure	**Completely** sure
☐	☐	☐	☐	☐

QUESTION 11

How well do you understand what things you are able to do to keep your **heart failure** symptoms from getting worse? (for example, weighing yourself, eating a low salt diet etc)

Do not understand at all	Do not understand very well	Somewhat understand	Mostly understand	Completetly understand
☐	☐	☐	☐	☐

QUESTION 12

Over the <u>past 2 weeks</u>, how many times has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** enjoyment of life at all
☐	☐	☐	☐	☐

QUESTION 13

If you had to spend the rest of your life with your **heart failure** the way it is <u>right now,</u> how would you feel about this?

Not at all Satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
☐	☐	☐	☐	☐

QUESTION 14

Over the past 2 weeks, how often have you felt discouraged or down in the dumps because of your heart failure?

I felt that way All of the time	I felt that way most of the time	I occasionally felt that way	I rarely felt that way	I never felt that way
☐	☐	☐	☐	☐

QUESTION 15

How much does your heart failure affect your lifestyle? Please indicate how your heart failure may have limited your participation in the following activities over the past 2 weeks.

Please place an X in one box on each line

Activity	Severely Limited	Limited quite a bit	Moderately Limited	Slightly Limited	Did Not Limit at all	Does not apply or did not do for other reasons
Hobbies, recreational activites	☐	☐	☐	☐	☐	☐
Working or doing Household chores	☐	☐	☐	☐	☐	☐
Visiting family or Friends out of Your home	☐	☐	☐	☐	☐	☐
Intimate relationships with loved ones	☐	☐	☐	☐	☐	☐

Your views about illness

Listed below are a number of symptoms that you may or may not have experienced since your heart failure, please indicate by circling YES or NO, whether you have experienced any of these symptoms since your heart failure and whether you believe that these symptoms are related to your heart failure

	I have experienced this symptom since my illness		*This symptom is related to my heart failure*	
Pain	Yes	No	Yes	No
Sore Throat	Yes	No	Yes	No
Nausea	Yes	No	Yes	No
Breathlessness	Yes	No	Yes	No
Weight loss	Yes	No	Yes	No
Fatigue	Yes	No	Yes	No
Stiff Joints	Yes	No	Yes	No
Sore Eyes	Yes	No	Yes	No
Wheeziness	Yes	No	Yes	No
Headaches	Yes	No	Yes	No
Upset Stomach	Yes	No	Yes	No
Sleep Difficulties	Yes	No	Yes	No
Dizziness	Yes	No	Yes	No
Loss of Strength	Yes	No	Yes	No

We are interested in your own personal views of how you now see your heart failure

Please indicate how much you agree or disagree with the following statements about your heart failure by ticking the appropriate box.

	VIEWS ABOUT YOUR HEART FAILURE	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE NOR DISAGREE	AGREE	STRONGLY AGREE
ip1	My heart failure will last a short time					
ip2	My heart failure is likely to be permanent rather than temporary					
ip3	My heart failure will last for a long time					
ip4	This heart failure will pass quickly					
ip5	I expect to have heart failure for the rest of my life					
ip6	My heart failure is a serious condition					
ip7	My heart failure has major consequences on my life					
ip8	My heart failure does not have much effect on my life					
ip9	My heart failure strongly affects the way others see me					
ip10	My heart failure has serious financial consequences					
ip11	My heart failure causes difficulties for those who are close to me					
ip12	There is a lot which I can do to control my symptoms					

	VIEWS ABOUT YOUR HEART FAILURE	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE NOR DISAGREE	AGREE	STRONGLY AGREE
	What I do can determine whether my heart failure gets better or worse					
	The course of my heart failure depends on me					
	Nothing I do will affect my heart failure					
	I have the power to influence my heart failure					
	My actions will have no affect on the outcome of my heart failure					
	My heart failure will improve in time					
	There is very little that can be done to improve my heart failure					
	My treatment will be effective in curing my heart failure					
	The negative effects of my heart failure can be prevented (avoided) by my treatment					
	My treatment can control my heart failure					
	There is nothing which can help my heart failure					
	The symptoms of my heart failure are puzzling to me					

	VIEWS ABOUT YOUR HEART FAILURE	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE NOR DISAGREE	AGREE	STRONGLY AGREE
	My heart failure is a mystery to me					
	I don't understand my heart failure					
	My heart failure doesn't make any sense to me					
	I have a clear picture or understanding of my heart failure					
	The symptoms of my heart failure change a great deal from day to day					
	My symptoms come and go in cycles					
	My heart failure is very unpredictable					
	I go through cycles in which my heart failure gets better and worse.					
	I get depressed when I think about my heart failure					
	When I think about my heart failure I get upset					
	My heart failure makes me feel angry					
	My heart failure does not worry me					
	Having heart failure makes me feel anxious					
	My illness makes me feel afraid					

Finally we are interested in what you consider may have been the cause of your heart failure. Again there is no correct answer. We are most interested in your own views about the factors that caused your heart failure rather than what others including doctors or family may have suggested to you.

Below is a list of possible causes for your heart failure. Please indicate how much you agree or disagree that they were causes for you by ticking the appropriate box.

POSSIBLE CAUSES	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE NOR DISAGREE	AGREE	STRONGLY AGREE
Stress or worry					
Hereditary - it runs in my family					
A Germ or virus					
Diet or eating habits					
Chance or bad luck					
Poor medical care in my past					
Pollution in the environment					
My own behavior					
My mental attitude e.g. thinking about life negatively					
Family problems or worries caused my heart failure					
Overwork					
Emotional state e.g. feeling down, lonely, anxious,					
Ageing					
Alcohol					
Smoking					
Accident or injury					
My personality					
Altered immunity					

Finally in the table below, please list in rank-order the three most important factors that you now believe caused YOUR heart failure. You may use any of the items from the box above, or you may have additional ideas of your own.

The most important causes for me:-

1. _____
2. _____
3. _____

THANKYOU

NOTES: