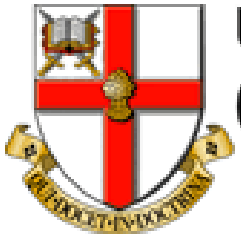

University of Chester

Centre for Exercise & Nutrition Science

MSc
In
Cardiovascular Rehabilitation

Is exercise training safe and effective for ALL heart failure patients: a retrospective service evaluation of a hospital based cardiac rehabilitation programme

By Laura Ann Burgess

Dissertation submitted in accordance with
the requirements of University of Chester
for the degree of Master of Science

September 2010
15,497 words

Acknowledgement

I would like to thank Dr John Buckley and Dr Stephen Fallows, my research supervisors for their support, advice and help throughout, this has been invaluable. Thank you also to Mike Morris for his time and assistance with the data analysis for this work.

Thank you to my colleagues in the cardiac rehabilitation team at the University Hospital of South Manchester and to my wider circle of cardiac rehabilitation physiotherapy colleagues for their interest and encouragement during the number of years it has taken me to complete my Master of Science degree.

I would also like to thank the heart failure clinic staff at the University Hospital of South Manchester for their continued assistance and support in my work with heart failure patients.

Finally I would like to thank my husband Andrew, and my two sons, Michael and Stephen for their patience and understanding over the many years I have had to take time away from them to concentrate on my studies.

Abstract

Is exercise training safe and effective for ALL heart failure patients: a retrospective service evaluation of a hospital based cardiac rehabilitation programme

The main purpose of this study was to investigate whether exercise training is safe and effective for all classifications of heart failure, female and elderly (70 years and above) heart failure patients and also those heart failure patients with significant co-morbidity. Much of the research into exercise training and heart failure has been carried out on middle aged men in NYHA II-III classification of heart failure who have no other significant co-existing conditions. This is not reflective of the population of heart failure patients in general. The cardiac rehabilitation records (n =1000) of heart failure patients who had attended an exercise programme at a hospital based NHS service over a period of ten years were retrospectively evaluated to investigate the safety and efficacy of exercise training. Analysis of baseline statistics and repeated outcome measures were used to investigate the significance of the service and to ascertain where similarities and differences lay with the research.

74% were male, the age range was 17-90 years and 52% of patients had one or more significant co-morbidity. The acute event incidence was recorded at four per 1000 patients. NYHA I patients, female, elderly heart failure patients and those with significant co-morbidity showed significant improvements in functional capacity and quality of life measures with exercise training ($p < 0.05$). However no conclusion on the effectiveness of exercise could be drawn for NYHA IV heart

failure patients due to insufficient recorded data and reduced adherence to exercise sessions for this group. A hospital based exercise programme, therefore may not be the most appropriate setting for the NYHA IV patient.

This study supports previous research of the benefit of exercise training in heart failure but broadens it further to show that exercise is safe for all heart failure patients and is also effective for all heart failure patients with the exception of NYHA IV patients where further investigation is needed.

word count 313

Dedication

This work is dedicated to my late father Kenneth Ewart Holden, 1924-2008

This work is original and has not been previously submitted in support of a degree, qualification or other course.

Signed

Date 18th September 2010

Contents

Glossary and list of abbreviations

Cardiac Rehabilitation	A programme of exercise and information sessions that helps individuals get back to everyday life as quickly as possible following a cardiac event
Co-morbidity	The presence of a disorder or disease in addition to a primary disease or disorder
Functional Capacity	The capability of performing tasks and activities that individuals find necessary or desirable in their lives
Heart Failure	The heart has lost the ability to pump enough blood to the body's tissues for the organs and other tissues to be able to function properly
NHS Code of Practice (Record Management)	A guide to the required standards of practice in the management of records
Rate of Perceived Exertion	A measure of how hard an individual feels their body is working during exercise or activity
VO2 Max Test	A test to determine the maximum capacity of an individual's body to transport and use oxygen

AACVPR	American Association of Cardiovascular and Pulmonary Rehabilitation
HF ACTION	Heart Failure: A Controlled Trial Investigating Outcomes of Exercise TraiNing
HAD scale	Hospital Anxiety and Depression scale
LVEF	Left Ventricular Ejection Fraction
MLHF	Minnesota Living with Heart Failure (Questionnaire)
NACRe	National Audit for Cardiac Rehabilitation
NHS	National Health Service
NYHA	New York Heart Association (classification of heart failure)
SPSS	Statistical Packages for Social Sciences
UK	United Kingdom

List of Tables **Page**

Chapter 1 Introduction and Literature Review

1.1 Incidence

Heart failure affects at least 1% of the population in the United Kingdom (UK), this figure rises to around 7% in the elderly population with the average age of heart failure diagnosis reported to be 78 years old (National Health Service Information Centre for Health and Social Care, 2009). Predictions are that the incidence of heart failure will rise further over the next two decades due to an ever increasing elderly population and an improved survival rate for cardiac disease.

1.2 Background

More than 20 years ago heart failure patients were actively discouraged from performing any form of exercise training. A diagnosis of heart failure was considered to be an absolute contraindication to exercise training, such as that offered by a cardiac rehabilitation programme, as it was believed that exercise was unsuitable and unsafe for patients diagnosed with this cardiac condition (Ponikowski, 2004).

However, over the subsequent years, systematic review of the evidence, such as that undertaken by Rees, Taylor, Singh, Coats and Ebrahim in 2004 for the Cochrane Collaboration, has shown that exercise training for the heart failure patient is effective.

Importantly exercise training for this group of patients is also now considered to be safe as reported by Smart and Marwick (2004) following a systematic review of the exercise evidence.

Additionally there is some evidence to suggest that exercise programmes can reduce

overall mortality in heart failure (ExTraMATCH Collaborative, 2004) and, more recently, evidence to suggest that exercise reduces the rate of hospital admissions for the heart failure patient (Davies et al., 2010).

Therefore exercise recommendations for the heart failure patient have changed remarkably over the last 20 years. The evidence now strongly supports exercise in order to improve quality of life and functional capacity and also to reduce costly heart failure hospitalisation (The National Clinical Guideline Centre, 2010). Exercise training for heart failure is considered to be more effective when it is delivered as part of a comprehensive cardiac rehabilitation programme (National Institute for Clinical Excellence 2003). The Department of Health National Service Framework for Coronary Heart Disease (2000) recommends that cardiac rehabilitation should be considered for the heart failure patient and the European Society of Cardiology (2008) recommends exercise training as part of the lifestyle management of heart failure.

However, despite the evidence that demonstrates the benefit of exercise in heart failure and the service drivers which recommend cardiac rehabilitation, the uptake of heart failure patients into UK cardiac rehabilitation programmes is poor. For the period April 2007 to March 2008 only 1% of patients referred for cardiac rehabilitation in England, Wales and Northern Ireland had a diagnosis of heart failure (British Heart Foundation Care and Education Research Group 2009) with one quarter of the 341 cardiac rehabilitation centres actively excluding patients diagnosed with this cardiac condition. These figures have not improved over the past three years and therefore, as reported by the National Health Service

Institute for Innovation and Improvement in 2009, it appears there is a real inequity of access for the heart failure patient to supervised exercise training services, such as those provided in a National Health Service (NHS) cardiac rehabilitation programme. The cause of such inequity could be attributed to a recognised lack of resources for cardiac rehabilitation services. However there may also be a barrier where, whilst cardiac rehabilitation professionals recognise the strong research evidence for exercise in heart failure, they have little personal experience or knowledge of providing a service to the general heart failure population where the type of patient referred may be different to those in clinical in trials.

1.3 Does the research evidence reflect the general heart failure population?

Pina et al. (2003) suggest that more research is needed into whether the benefits seen in small studies can be applied to the larger population of heart failure patients. Lloyd-Williams, Mair and Leitner in 2002, after reviewing the evidence for exercise reported that there is a continuing problem that clinical trials include participants who are not representative of the general population of heart failure patients. Coats et al. (1992) had made the same observation 10 years earlier following a heart failure exercise trial. In particular it appears that the New York Heart Association (NYHA) I and IV classification heart failure patient, the female, the elderly and those heart failure patients with significant co-morbidity are under represented in the research studies.

1.3.1 The heart failure patient in NYHA I and IV classification

The Scottish Intercollegiate Guideline Network (2007) recommend specifically that

heart failure patients in NYHA classes II and III are enrolled into a supervised exercise training programme. This guideline, similar to others, excludes heart failure patients in NYHA classes I and IV. These service drivers that recommend which heart failure patients should be offered exercise training only reflect the research and consequently findings can only be applied to those particular categories of heart failure. For example, the early exercise trial by Coats et al. in 1992, previously mentioned, only enrolled participants in NYHA II and NYHA III classifications of heart failure. Consequently the safety and effectiveness of exercise could only be reported for those two particular heart failure classifications. This was the trend for most subsequent trials. The review of the evidence for exercise in heart failure by Rees et al. in 2004, for the Cochrane Collaboration, found that in the 29 studies, which met the agreed criteria, all the participants were in heart failure classes NYHA II and NYHA III, therefore those patients in NYHA I or IV classification were excluded.

Consequently the evidence does not accurately reflect the wider patient population because not all classifications of heart failure have been included.

The exclusion of NYHA classes I and IV from many of the recommendations and service drivers, due to the lack of evidence for these particular groups, may be because of difficulties including them in research. The NYHA I heart failure patient may already be functioning at a higher rate of activity and at a level which appears sufficient for their needs so may be less likely to seek or be offered specific exercise training. The NYHA IV heart failure patient in particular may be difficult to recruit into exercise research, because by definition, they are the most challenging group to

exercise due to their high level of symptoms. However this group are arguably the ones who may benefit the most from exercise intervention and better understanding of how exercise could be delivered to them is needed.

McKelvie's 2008 clinical recommendations for exercising heart failure patients agrees, saying that the evidence thus far only supports exercise training for NYHA II and III heart failure patients and that stable NYHA IV patients are a particularly important group to be targeted.

Information on outcome measures, safety issues and adherence to exercise programmes specifically for NYHA I and IV patients would be valuable.

This information could be obtained from an existing UK NHS cardiac rehabilitation programme which includes NYHA I and IV patients.

1.3.2 The female heart failure patient

Cowie et al. (1999) reported that the incidence of heart failure is higher in men than women and that this may be the reason why women do not seem to feature in many of the exercise studies for heart failure. A randomised controlled trial by Bellardinelli, Georgiou, Cianci and Purcaro in 1998 into the effects of exercise training in heart failure, reported that only 11% of the study population were female. Fleg in 2002 reviewed the evidence for exercise in heart failure and agreed that there is a severe under representation of women.

There have been two heart failure studies investigating the effect of exercise on women specifically. Both the study by Tyni-Lenne, Gordon, Jansson, Bermann and Sylven (1997) and that by Pu et al. (2001), were small, with only 16 patients in the exercise groups. Both studies showed improved physical and psychological

improvement with exercise. However both these studies used resistance exercise rather than aerobic exercise as the exercise modality. This is an interesting area in itself as to whether resistance training may be as beneficial, if not more beneficial, than cardiovascular exercise. However the majority of the research for exercise in heart failure has used cardiovascular and not resistance training and the issue remains that women are under represented in the research for this type of exercise in heart failure.

For the NHS Heart Failure Audit for 2008- 2009 by the NHS Centre for Health and Social Care, when gender on heart failure hospital admission was recorded, male incidence of heart failure was reported as 57% and female as 43%. Once over the age of 75 years the incidence was reversed with more women than men admitted to hospital with the diagnosis of heart failure.

It seems that the ratio of heart failure prevalence between men and women may have changed over the last 10 years, since Cowie et al. reported it in 1999, but the research evidence for the female participation in heart failure exercise training continues to be poor. The reason for their under representation may be that women are less likely to volunteer to take part in research for fear they may not be able to adhere to the strict study requirements around their family commitments.

However women may be more likely to attend the more flexible approach available when participating in a cardiac rehabilitation exercise programme.

Thus information about their recruitment, performance and adherence in an existing exercise training and cardiac rehabilitation programme would be valuable.

1.3.3. The elderly heart failure patient

The British Association for Cardiac Rehabilitation (2007) states that stable heart failure patients, irrespective of age should be offered exercise training as part of a cardiac rehabilitation programme.

However, the effectiveness of exercise training for the elderly heart failure patient is also an area where there is less evidence. Weir, McMurray, Taylor and Brady (2006) suggest that elderly heart failure patients are less likely to receive evidence based treatment, including exercise training, and they recommend that more information is needed. It appears that older heart failure patients have been excluded from many large heart failure clinical trials for research into medication, cardiac devices and also surgery so it is unsurprising that exercise trials have followed a similar trend and also excluded them.

There are some studies which have looked specifically at elderly heart failure patients and exercise. Owen and Croucher (2000) researched the effect of exercise on 22 elderly heart failure patients, found it was beneficial but suggested that more information should be gained from a larger study. Smart et al., in 2004 following a review of exercise trials concluded that the changes in outcome measures may be smaller for heart failure patients over 70 years old.

The European Heart Failure Training Group in 1998 reviewed 134 patients who had participated in UK randomised controlled trials and concluded that patients over 70 years were able to train but that the evidence suggested less effectively. However, of the 134 patients in the trials they reviewed only 10% of the participants were aged over 70 years. This equates to

information on only 13 elderly patients. This cohort may not be large enough to make the assumption that exercise training for the elderly heart failure patient is ineffective.

Gottlieb et al. (1999) studied a slightly larger number consisting of 33 elderly heart failure patients and reported that six of the 17 patients randomised to the exercise group could not tolerate the exercise, one died during the study, four were reported as too ill and one was non compliant. This level of evidence that elderly heart failure patients struggle to exercise may discourage those referring to cardiac rehabilitation programmes from considering the more elderly patients and make those providing cardiac rehabilitation services less likely to want to accept them.

Fleg (2002) looked at elderly heart failure patients specifically and stated that there is clear evidence that exercise training improves functional capacity and quality of life in the younger heart failure patient but, as with the female heart failure patient, there is less evidence for the older heart failure patient and more study is needed to improve uptake.

Austin, Williams, Ross, Moseley and Hutchison in 2004 recognised that the elderly heart failure patient was under represented in exercise training clinical trials. They carried out a study in Wales on the effect of cardiac rehabilitation on 200 patients who were over 60 years old and in NYHA II-III classification of heart failure. The study showed greater improvements in the six minute walk test and quality of life score for the exercise group compared to a control group.

This study by Austin et al. (2004) is encouraging as it was a large study and it demonstrates clearly that the elderly heart failure patient can benefit from exercise

training as part of a cardiac rehabilitation programme.

However, it may not accurately represent the general population of elderly heart failure patients as any elderly patient with significant co-morbidity was excluded from this piece of research.

1.3.4. The heart failure patient with significant co-morbidity

Despite Austin et al. (2004) acknowledging that there is a high level of co-morbidity in elderly patients with heart failure, any patient with significant co-morbidity was excluded from their study. Initially 493 heart failure patients were selected but 52% of these were excluded due to co- morbidity which was deemed too severe for them to exercise.

Owen et al. in 2000 recommended that elderly heart failure patients be enrolled for exercise training but they had also excluded those patients with limiting musculoskeletal and pulmonary co- morbidities from their research.

Similarly Bellardinelli et al. in the 1998 heart failure exercise study excluded any participant who had orthopaedic or neurological limitations and the work by Lloyd – Williams et al. in 2002 reported that for the 31 trials included in their review, patients with co-morbidities were often excluded from the studies.

Coats et al. (1992), only included those who were limited by shortness of breath or fatigue, two of the classic symptoms of heart failure, and therefore excluding any participant who may have been limited by other factors, such as pain. The European Heart Training Group in 1998 for a review of the evidence, reported the use of the similar exclusion criteria.

More recently in 2002, the EXERT study by McKelvie et al. was a large Canadian

randomised controlled trial of 180 heart failure patients used to test exercise training against usual care. The exercise training group showed improvement in quality of life and aerobic capacity. However any patient who was unable to perform an exercise test due to co-morbidity was excluded from the study. Therefore once again heart failure patients with co-morbidity which may affect functional ability were excluded. Incidentally in the EXERT trial there was no patient over 70 years and only 20% were female.

In another study, in 1998, by Wielenga et al., 67 participants were divided into exercise or usual care and improvements in quality of life were considered. However, again as with many of the other studies, the participants for this study were male, middle aged, NYHA II-III and any participant who had an orthopaedic, peripheral vascular or neurological condition that limited their ability to exercise was excluded.

Rees et al. (2004) for the Cochrane review of exercise and heart failure reports, that of the 27 studies identified for the review, 24 used VO2 maximum testing for baseline and outcome measures. It is not clear whether the heart failure patient who had a co-morbidity that would affect their ability to undertake this type of test was included or excluded, for example musculoskeletal problems are not an absolute contraindication to exercise testing, however they can be considered a relative contraindication and therefore for a research study it is highly likely that heart failure patients with significant co-morbidity were excluded from VO2 testing and consequently the study.

Weir et al. (2006) report that older heart failure patients have an increase incidence

of co-existing medical conditions and that this has been reported to be between three and five conditions in addition to their heart failure. Weir et al. (2006) state that co-morbidity is important to consider as it contributes to rates of hospital admission and mortality. Excluding over half of the study population, as Austin et al. did in 2004 because of co-morbidity and, as other studies have also done, leaves the question as to whether significant co-morbidity in heart failure patients affects their ability to benefit from exercise training.

Cahalin, Mathier, Semigran, Dec and Disalvo in 1996 studied 45 American heart failure participants to assess whether the six minute walk was a useful test for heart failure patients. However again, as with many other studies they excluded patients who had any neurological or orthopaedic co-morbidity. Additionally the majority of this study group were men and none of the participants were over the age of 57 years.

This poses the additional question as to whether the six minute walk test is a useful outcome measure for the elderly heart failure patient who has co-existing medical problems.

It would therefore be useful to investigate the baseline characteristics and outcome measures of an established cardiac rehabilitation exercise programme such as the long established Wythenshawe Hospital cardiac rehabilitation programme in South Manchester. This programme includes NYHA I and IV patients, female heart failure patients, elderly heart failure patient and heart failure patients with significant co-morbidity.

This information may confirm previous evidence but create better understanding

of the type of patients who have been traditionally excluded from the heart failure research.

1.4 Heart failure patient adherence to exercise programmes

There is little documented regarding adherence to exercise for heart failure patients (Barbour and Miller, 2008) and in particular adherence for the more elderly heart failure patient. Martin and Sinden in 2001 reviewed randomized controlled trials for exercise course adherence of the older general adult patient and concluded that their attendance may be better than for the younger adult. However this study focused on the age of 55 years as the older adult which is at the younger end range for the heart failure population.

Covera –Tindel, Doering, Gomez and Dracup in 2004, when attempting to predict who is most likely to be non complaint to exercise, suggest that heart failure patients with an increased number of co- morbidities are less likely to adhere to an exercise programme.

It would therefore also be useful to look at completion rates for heart failure patients attending an established cardiac rehabilitation programme, such as that at Wythenshawe Hospital, particularly for the elderly heart failure patient and for those with significant co-morbidity.

1.5 Safety of exercise in heart failure

McKelvie in 2008, whilst reviewing the exercise evidence in heart failure, reported that the safety of exercise training for the heart failure patient has not been studied in any large clinical trials.

Mortality rates are high in the heart failure population. Newly diagnosed heart

failure patients have a 40% risk of dying within one year of their diagnosis (The National Health Service Information Centre for Health and Social Care 2009). It is not surprising that the exercise professional is concerned when this kind of statistic is reported because it may be their natural assumption that the heart failure patient is at high risk of an exercise related death. This assumption is confirmed by The American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR, 2004) risk stratification tool, a tool used as standard practice to risk stratify patients for the exercise component of cardiac rehabilitation programmes. This defines patients with a left ventricular ejection fraction (LVEF) of 40% or less as at a high risk of having an acute event during exercise. Most heart failure patients by definition will have a LVEF of 40% or less and therefore must be regarded to be in a high risk group for exercise.

Pina et al. (2003) reports that the incidence of adverse cardiovascular events during outpatient cardiac exercise programs is estimated to be one in 60 000 participant hours. Fletcher et al. 2001 recommends exercise training for heart failure but warn that individuals with cardiac disease are at a higher risk of sudden cardiac death during ‘vigorous’ exercise compared to healthy individuals. However, cardiac rehabilitation guidelines state that vigorous exercise or high intensity exercise is not usually recommended for heart failure patients.

Interestingly, however, Nilsson, Westheim and Risberg in 2008 exercised 40 heart failure patients to high intensity, i.e. a ‘vigorous’ level of intensity and they reported no adverse events during exercise in this study. It should be noted that the patients in this trial were monitored continuously by means of a 12 lead ECG and

blood pressure readings during exercise, this high level of monitoring may reduce their risk during exercise because life threatening arrhythmia could have been picked up early. However high levels of monitoring such as this are not available in common cardiac rehabilitation practice in the UK and indeed not advisable if patient self efficacy is to be achieved.

O'Connor et al. (2009) for the large HF ACTION study of exercise in heart failure acknowledges that there is a safety concern for exercising heart failure patients. They cite that the complication rate for heart failure patients in clinical trials of exercise training as being higher than for other cardiac patients and suggests the reason to be that there is a high risk of sudden death when suddenly changing from a sedentary lifestyle to initiating exercise. This may certainly be the case for clinical trials where patients are required to perform a maximum exercise test as entry criteria to the exercise study, but it may not be the same for UK cardiac rehabilitation programmes where maximum exercise testing is not a requirement for entry into an exercise programme.

The cardiac rehabilitation exercise professional also follows recognised standards for the assessment and prescription for exercise in the heart failure patient where risk stratification will determine the appropriate intensity of exercise and where adequate warm and cool down will reduce the risk of life threatening arrhythmia (Association of Chartered Physiotherapists in Cardiac Rehabilitation, 2009). However the poor uptake of heart failure patients into cardiac rehabilitation may suggest that health professionals and service commissioners are concerned that it may not be safe for these ' high risk' patients to exercise.

An evaluation of safety for an established NHS cardiac rehabilitation programme, such as that at Wythenshawe Hospital, for the general population of heart failure patients would be beneficial to give a clearer picture of the incidence of acute events for this specific group in everyday practice.

1.6 Latest exercise evidence in heart failure

The HF ACTION study by O'Connor et al. (2009) was eagerly awaited as the biggest and most recent randomized controlled trial to test the efficacy and safety of exercise training and its effect on quality of life in the heart failure population. The study was across more than 2000 participants in the United States, Canada and France. O'Connor et al. (2009) reported that exercise training was associated with a significant although modest reduction in hospitalization and mortality. Flynn et al. (2009) also for the HF ACTION study specifically looked at psychological improvements and reported that exercise conferred modest but statistically significant improvement in self reported quality of life compared with usual care. 30% of the subjects in the HF ACTION exercise group were women, this is an improved percentage compared to other studies yet still not reflective of the known heart failure incidence in women and possibly suggests again that women may be less likely to want to attend for exercise training sessions.

NYHA II-IV classes were included. It is encouraging that 14 NYHA IV heart failure patients were included in the exercise training arm of HF ACTION but unfortunately there is no specific subset information about their outcome measures, safety record and exercise adherence.

Participants described as having major co- morbidities or limitations that could

interfer with exercise training were excluded from the HF ACTION study so unfortunately the evidence from this study, as with so many before, is unreflective of a large percentage of heart failure patients in the general population. Participants in HF ACTION were required to be on optimal medication for six weeks prior to starting exercise. Whilst this is usual for clinical trials, it is not reflective of common practice in cardiac rehabilitation in the UK as some heart failure patients can take months to reach optimal medication requirements due to side effects or other issues. Waiting to start exercise for a prolonged length of time whilst medication is stabilised can only be detrimental to the heart failure patient as they become increasingly deconditioned with inactivity. Consequently patients routinely start rehabilitation programmes whilst medication continues to be uptitrated. The assumption from this may be that patients are more likely to suffer adverse effects from exercise if they are not on optimum medication. This may in turn affect their adherence to the exercise programme. By looking at the evidence from an established heart failure cardiac rehabilitation programme, such as that at Wythenshawe Hospital where patients are not required to be on optimal medication, the picture may become clearer.

1.7 Cardiac Rehabilitation for heart failure patients at Wythenshawe Hospital

Wythenshawe Hospital is managed by the University Hospital of South Manchester NHS Foundation Trust. The cardiac rehabilitation programme at the hospital is a standard NHS service and the heart failure patients who attend the cardiac rehabilitation programme there can be regarded as representative of the wider heart failure population.

Wythenshawe Hospital heart failure clinic, from where referrals to cardiac rehabilitation are made, as a clinic in a general hospital which serves the local community and as a tertiary centre which serves a wider region, receives hospital and GP heart failure referrals from across the Greater Manchester and Cheshire area and also from across the whole of the North West region of England.

The North West region of England can be seen to represent the wider population of heart failure across the UK. The age structure of the North West population is similar to that of England as a whole (National Statistics, 2001) and the incidence and mortality rates from coronary heart disease, the recognized primary cause of heart failure, across Greater Manchester are very high (Greater Manchester and Cheshire Cardiac Network, 2007). Life expectancy for Manchester men is the second worst in the country and the fourth worst for women (National Health Service Manchester, 2009).

Consequently the patients who have been diagnosed with heart failure and who attend the cardiac rehabilitation programme at Wythenshawe Hospital should not be regarded as part of an elite group but could be regarded as representative of the general heart failure population in the UK.

1.8 Summary

As stated by Lloyd-Williams et al. in 2002 there is still a continuing problem that clinical trials include participants who are not representative of the general population of heart failure patients. This tends to mean that female, the elderly, those heart failure patients in NYHA I and IV classification and those with significant co-morbidity are under represented in the research evidence.

Additionally research criteria such as optimal heart failure medication prior to entering an exercise programme does not reflect what is happening in everyday practice within UK NHS cardiac rehabilitation programmes and raises the question as to whether this affects safety of and adherence to everyday exercise programmes. Therefore the hypothesis to be tested is whether exercise training, when undertaken as part of a standard NHS cardiac rehabilitation programme such as that at Wythenshawe Hospital in South Manchester, is safe and effective for all stable heart failure patients, especially female, elderly, NYHA I and IV class patients and for those heart failure patients with significant co-morbidity.

word count 4610

Chapter 2 Methodology

2.1 Participants

For the period March 1998 to August 2007 inclusive, the consecutive records of 1000 patients diagnosed with heart failure and routinely enrolled for cardiac rehabilitation at Wythenshawe Hospital, South Manchester, UK were identified. Following the initial diagnosis of heart failure, all patients had been referred to the specialist heart failure clinic at Wythenshawe Hospital from where they had been referred for cardiac rehabilitation. The cardiac rehabilitation service at Wythenshawe Hospital is situated within the Physiotherapy Department of the hospital.

Left ventricular systolic dysfunction with a left ventricular ejection fraction of 40% or less is a usual diagnosis for heart failure. However a significant proportion of patients who suffer symptoms of chronic heart failure have a preserved left ventricular ejection fraction of around 60%. No distinction between these two groups was made for this study as both groups had been referred to the heart failure clinic for treatment and management of their cardiac condition.

All the patients had been recruited for cardiac rehabilitation by a heart failure specialist nurse or cardiologist on their attendance at Wythenshawe Hospital heart failure clinic.

The patients had been subsequently formally enrolled onto the cardiac rehabilitation programme by the cardiac rehabilitation staff. Therefore they had previously consented to participate in the cardiac rehabilitation programme with the standard

requirement that their personal information be recorded and stored for a set time period. The cardiac rehabilitation records of the 1000 heart failure patients were selected and the relevant information needed for the purpose of the study was obtained from them and recorded onto an electronic database by the researcher All the cardiac rehabilitation records for the heart failure patients who had attended the programme between 1998 and August 2007 were kept secure in their primary location for the purpose of this study. Cardiac rehabilitation records management was followed in accordance with the NHS code of practice.

Contraindication for referral and enrolment of a heart failure patient onto the exercise component of the cardiac rehabilitation programme was adhered to as indicated by the standards set by the Association of Chartered Physiotherapists in Cardiac Rehabilitation (see appendix 6.1). Stable heart failure patients of all ages, both genders and all classifications of the New York Heart Association (see appendix 6.2) were accepted onto the programme and there was no restricted access for patients with significant co-morbidities.

Appropriate heart failure medication had been initiated, but not necessarily optimised, prior to enrolment onto the programme and patients continued to undergo uptitration and review of medication as necessary throughout the cardiac rehabilitation course. This had been agreed locally with the heart failure clinic staff. It was considered that the heart failure patients attending the cardiac rehabilitation programme at Wythenshawe Hospital were an accurate representation of the wider community of heart failure patients in the general population.

Permission was gained from the University Hospital of South Manchester

Foundation NHS Trust as represented by the Cardiac Rehabilitation Lead Cardiac Consultant, Simon Williams to carry out the data collection on the heart failure patients who had received cardiac rehabilitation in the agreed time frame (see appendix 6.3).

Formal ethical approval by South Manchester Research Ethics Committee was sought but not required as they considered that the project was an audit or service evaluation (see appendix 6.4).The Faculty of Applied and Health Sciences Research Ethics Committee at the University of Chester approved the study application (see appendix 6.5).

2.2 Study Design

The data recorded onto an electronic database from each of the 1000 heart failure patients who had been enrolled onto the cardiac rehabilitation programme was collected as listed below:

1. Age at referral to cardiac rehabilitation
2. Gender
3. Aetiology of heart failure
4. Left ventricular ejection fraction as reported following an echocardiogram
5. New York Heart Association classification of heart failure at referral to the cardiac rehabilitation programme
6. Significant co-morbidity where formal diagnosis had been made by a general practitioner or specialist doctor
7. Six minute walk test result (in feet) at recruitment or enrolment on the exercise programme and on discharge from the cardiac rehabilitation programme

8. Minnesota Living with Heart Failure Quality of Life score at recruitment or enrolment on the exercise programme and on discharge from the cardiac rehabilitation programme
9. Hospital Anxiety and Depression Score at recruitment or enrolment on the exercise programme and on discharge from the cardiac rehabilitation programme
10. Cardiac Rehabilitation Programme adherence – if the patient had attended 50% or more of the course this was scored as completed. This was due to the belief that beneficial changes occur if 50% or more of the course has been attended. The University of York National Audit of Cardiac Rehabilitation (2002) supports follow up outcomes for patients who have attended over 50% of a cardiac rehabilitation programme for this reason.
11. Details of any recorded acute adverse events during attendance at the cardiac rehabilitation programme which had required immediate review by a hospital doctor

The data was recorded onto a Microsoft Excel software programme and later transferred to the Statistical Package for Social Sciences (SPSS) version 16 for analysis. Data that was missing from the cardiac rehabilitation record was noted. It was not possible to retrieve missing information from any other source.

2.3 Procedures

All the heart failure patients who were recruited and enrolled onto the cardiac rehabilitation programme at Wythenshawe Hospital between March 1998 and August 2007 received a standardised protocol of care. This comprised of a comprehensive 1:1 subjective and objective assessment by a cardiac rehabilitation

physiotherapist where symptom control was ascertained, baseline functional capacity was determined and the specific activity goals were identified for the individual patient. The patient was subsequently enrolled into a weekly supervised group or class exercise session to carry out an individual exercise prescription appropriate for their cardiac status and any relevant co-morbidity.

Exercise intensity was prescribed as low to moderate and was monitored by use of a target heart rate, rate of perceived exertion using the Borg CR10 scale (Borg, 1998) and by observation of the patient by the cardiac rehabilitation staff. The target heart rate for each patient was calculated using the heart rate reserve method at 40-50% of their predicted total aerobic capacity.

Blood pressure response was also noted to inform on the response to exercise and thus whether the exercise prescription was correct, however once patients were deemed competent to self monitor using rate of perceived exertion then heart rate and blood pressure monitoring was weaned as appropriate for the individual patient. Blood sugar levels were checked pre and post exercise for those patients who were diabetic, this monitoring was also weaned if the response was satisfactory dependent on the individual.

Each exercise session consisted of initial individual screening for suitability to exercise, 10 minutes of warm up exercise followed by a personalised exercise circuit (conditioning phase) for each patient and then 10 minutes of active cool down exercise and 15 minutes rest under supervision. The length of the conditioning phase for the exercise prescription was progressed relevant to the individual over the eight week exercise up to a maximum of 30 minutes. All

exercise for the conditioning phase of the exercise prescription was cardiovascular using aerobic exercise and an interval approach as necessary where muscular strength and endurance work was interspersed with cardiovascular work at a ratio individual for the patient. Modification to the specific exercises was made in accordance with altered ability due to co-morbidity. Resistance training was included for any heart failure patient where this had been identified as a specific objective for them at assessment and was incorporated into the exercise prescription during the cool down period.

Details of each exercise session were recorded onto the patient's individual clinical record sheet at each visit. Patients were also strongly advised to carry out appropriate home exercise in between the exercise sessions and were also encouraged to attend the education talks associated with the exercise programme. Some patients did not attend the education talks and attended the exercise sessions only, it was not possible to identify these particular patients for the purpose of the study. Most of the exercise sessions were in a class or group setting but some patients did receive 1:1 exercise sessions either because they required high supervision or they were unable to attend the group or class sessions. These particular patients have also not been identified for the purpose of the study.

The class sessions were mostly staffed on a ratio of 1:3, staff: patient but the ratios did alter at times dependent on the level of supervision required for each individual patient within the class, that is, at times this ratio may have been higher or lower. The class staff consisted of cardiac rehabilitation specialist physiotherapists assisted by support staff. The heart failure specialist nurses were on the hospital site and

accessible by telephone contact for advice on the heart failure management of individual patients as required. All exercise and education sessions were held in the Physiotherapy Department of Wythenshawe Hospital.

A standard protocol was followed for any patient who unexpectedly did not attend an exercise session, this consisted of a phone call to the patient by the cardiac rehabilitation staff followed up by a letter if contact was not possible by telephone. Patients were discharged from the cardiac rehabilitation programme if there was no further contact from them.

2.3.1 Six minute walk test

Most research studies use cardiopulmonary testing at baseline and as an outcome measure however this level of testing is not possible for most UK cardiac rehabilitation programmes and therefore not representative of everyday practice in cardiac rehabilitation services.

The six minute walk test is a simple functional capacity test and a recognised measure of improved outcome following exercise training. Lipkin, Scriven, Crake and Poole-Wilson (1986) describe it as inexpensive and easy to perform.

O'Keefe, Lye, Donellan and Carmichael (1998) studied a large group of 60 elderly heart failure patients to ascertain the usefulness of the six minute walk test for this particular patient group and they concluded that the six minute walk test was a useful tool for heart failure patients including those who were particularly frail.

The six minute walk test was used as a measurement of functional capacity at recruitment or enrolment onto the wythenshawe cardiac rehabilitation programme

and on discharge from the course.

The test was performed to a standard protocol by the heart failure clinic specialist nurses or by the cardiac rehabilitation physiotherapy staff (see appendix 6.6).

2.3.2. Minnesota Living with Heart Failure questionnaire (MLHFQ)

The MLHFQ (see appendix 6.7) is a recognized disease specific quality of life measurement used for heart failure patients in order to determine the effect of a particular heart failure intervention (Rector and Cohn, 1992). Licence permission was gained by the researcher from the University of Minnesota to be able to use the information from the MLHFQ for the purpose of this study (see appendix 6.8).The MLHFQ was given to the patients at recruitment or enrolment onto the cardiac rehabilitation programme and prior to the discharge session from it. It was completed by the majority of patients in their own home but occasionally at attendance at the exercise session if they had forgotten to complete it or needed some help to read or understand the questions.

The questionnaire was scored using a total point score as per the standard MLHFQ protocol where the higher the score the poorer quality of life is understood to be and the lower the score the better the quality of life is deemed to be. Consequently a reduction in total score post intervention indicated an improvement in quality of life for the individual.

2.3.3 Hospital Anxiety Depression (HAD) Scale

The hospital anxiety and depression scale (see appendix 6.9) is a simple questionnaire that has been validated for use in identifying anxiety and depression disorders (Bjelland, Dahl, Haug and Nickelman, 2002) and is used as standard for

all patients attending cardiac rehabilitation programmes.

The heart failure patients attending Wythenshawe cardiac rehabilitation programme were given the questionnaire at the same time as the MLHF questionnaire, at recruitment or enrolment onto the exercise programme and prior to discharge from the course. Similarly the majority of patients completed the HAD scale at home, otherwise they were given the opportunity and support, if needed, to complete it in the hospital setting prior to starting the exercise course and during the discharge session from the course.

The anxiety and depression scores, as determined by the relevant questions in the questionnaire, are recorded separately. An individual score of eight or above for either anxiety or depression is significant of anxiety or depression with increasing levels of anxiety or depression as the individual scores increase.

2.4 Statistical analyses

A Microsoft Excel spreadsheet was created to record the data listed as 1-11 previously. Once SPSS version 16.0 was available to the researcher, the information from the Excel sheet was transferred over to the SPSS software for analysis. Descriptive statistics including frequencies and percentages was obtained for all of the 1000 patients for gender, age, NYHA classification, left ventricular ejection fraction (LVEF) and diabetes. Central tendency and range was noted for age and left ventricular ejection fraction. Additionally descriptive statistics for heart failure aetiology and co-morbidity were obtained. Correlations were undertaken to investigate the relationships between baseline six minute walk test distance, LVEF, MLHF score, age, gender and presence of co-morbidity.

Of the 1000 consecutive patients referred to cardiac rehabilitation, some had been referred for a repeat course of exercise, having previously undertaken the programme at an earlier date. In order to continue with further accurate analysis of outcome measures those patients who had repeated the course were excluded from subsequent analysis. This is standard practice, for example, Rees et al. for the Cochrane review of exercise and heart failure in 2004 excluded trials where patients had been previously offered cardiac rehabilitation.

The repeated outcome measures, i.e. six minute walk test, Minnesota Living with Heart Failure score and Hospital Anxiety and Depression score pre and post exercise training were analysed specifically for the five subsets of patients; NYHA I and IV patients, female, the elderly (70 years and above) and those heart failure patients with significant co-morbidity.

For each of the paired outcome measures for each subset group a parametric (paired t- test) or non – parametric (wilcoxon) test was chosen dependent on the level of initial data and whether normal distribution criteria was fulfilled as required. A correlation was also conducted to investigate whether there was any significant relationship between the overall mean change in six minute walk test and overall mean change in MLHF score pre and post intervention. The significance value applied for all analyses was 0.05 in line with standard practice (Cowles and Davies, 1982). Further descriptive statistics for all 1000 patients and for the subset groups was obtained for rate of adherence of the exercise course and for any adverse events which occurred for the whole cohort whilst they attended the cardiac rehabilitation programme.

word count 2489

Chapter 3 Results

3.1 Baseline Characteristics

The baseline characteristics of all study participants, including those who had repeated the cardiac rehabilitation course over the 10 year period, are shown in Table 1. As this was a retrospective study, some data was found to be missing from the patient cardiac rehabilitation records, 18 cases were missing age details, 35 cases were missing New York Heart Association (NYHA) details, 132 cases were missing left ventricular ejection fraction details and 39 cases were missing diabetes information.

Table 1. *Baseline characteristics of the total study population (including repeaters of course)*

Gender	n = 1000	
Men		740 (74%)
Women		260 (26%)
Mean age (years)	n = 982	67 ± 11.5
Age range (years)		17-90
NYHA classification	n = 965	
I		119 (12.3%)
II		495 (51.3%)
III		335 (34.7%)
IV		16 (1.7%)
Mean LVEF %	n = 868	32 ± 10.1
LVEF range %		10-60
Diabetic Status	n = 961	
Diabetic		176 (17.6%)
Non diabetic		785 (78.5%)

NYHA, New York Heart Association, LVEF, left ventricular ejection fraction

Participants of whom 74% were male, had a mean age of 67 ± 11.5 years, the youngest participant was 17 years old and the oldest participant 90 years old. NYHA class II patients were the most common at 51.3% of the total with only 16 (1.7%) patients in NYHA class IV.

Mean left ventricular ejection fraction (LVEF) was 32 ± 10.1%, the lowest LVEF was 10% and the highest LVEF was 60%. 17.6% of the total participants had been diagnosed as diabetic.

Table 2 shows a breakdown of heart failure aetiology for the total study population. There were only six patients where aetiology data was missing.

Table 2. *Aetiology of Heart Failure for the total study population*

Coronary Heart Disease	674 (67.4%)
Valvular Heart Disease	76 (7.6%)
Hypertension	35 (3.5%)
Atrial Fibrillation	32 (3.2%)
Viral heart disease	6 (0.6%)
Excess alcohol	3 (0.3%)
Congenital heart disease	7 (0.7%)
Post chemotherapy	5 (0.5%)
Other	9 (0.9%)
Unknown	147 (14.7%)

Table 3. *Significant co- morbidity for the total study population*

None	483 (48.3%)
Osteoarthritis	141 (14.1%)
Chronic Obstructive Pulmonary Disease	78 (7.8%)
Musculoskeletal problems	19 (1.9%)
Angina	40 (4.0%)
Peripheral Vascular Disease	29 (2.9%)
Cancer	11 (1.1%)
Neurological problems	28 (2.8%)
Chronic Back problems	19 (1.9%)
Other	40 (4.0%)
Multiple (two or more)	112 (11.2%)
Total number with co-morbidity	517 (51.7%)

Significant co-morbidity determined as formal diagnosis made by General Practitioner or Specialist Doctor

The majority of participants, 67.4%, had heart failure of an ischaemic origin,

valvular disease was the second biggest cause of heart failure at 7.6% but for 14.7% of patients the cause was documented as unknown.

48.3% of participants had no documented significant co-morbidity, the remaining 51.7% therefore had significant co-morbidity as described in Table 3. The most common co-morbidity recorded was osteoarthritis with 14.1% of participants documented to be diagnosed with this.

The second commonest co-morbidity was chronic obstructive airway disease at 7.8% incidence. 11.2% of participants were described as having multiple, that is, two or more significant co-morbidities.

3.1.1 Correlation of baseline six minute walk test distance with baseline left ventricular ejection fraction, quality of life score, age, gender and presence of significant co-morbidity

A significant relationship was found between baseline six minute walk test distance and left ventricular ejection fraction, Minnesota Living with Heart Failure score, age, gender and co-morbidity as shown in Table 4. All correlations were negative relationships where the higher the value of one then the lower the value of the other would be, apart from that for baseline six minute walk test and gender where the relationship was positive.

However, all correlations, whether positive or negative and although statistically significant were either low or very low, for example the relationship between age and baseline walk test where the r value was 0.29 and thus only 8.4% of factors which account for variability were common to age and six minute walk distance.

Table 4. *Correlation of baseline six minute walk test distance with baseline left ventricular ejection fraction, quality of life score, age, gender and presence of significant co- morbidity*

	No Pairs	P value	R value	Co-efficient of Determination	Correlation
LVEF	498	0.032*	- 0.09	0.8%	-ve very low
MLHF	507	0.0005*	- 0.23	5.3%	-ve low
Age	590	0.0005*	- 0.29	8.4%	-ve low
Co-morbidity	592	0.0005*	- 0.17	2.8%	-ve very low
Gender	592	0.0005*	0.23	5.3%	+ve low

*LVEF, left ventricular ejection fraction, MLHF, minnesota living with heart failure score, co-morbidity, all participants reported to have one or more significant co-morbidity, -ve, negative, +ve, positive, * significant correlation p< 0.05*

3.2. Outcome measures

3.2.1 The heart failure patient in NYHA I and IV classification

Table 5. *NYHA I and IV: outcome measures (not including repeaters of course)*

	No Pairs	Mean Pre (SD)	Mean Post (SD)	P value
6 minute walk test (feet)				
NYHA I	30	1257 (63.3)	1366 (49.1)	0.007*
NYHA IV	0	n/a	n/a	n/a
MLHF				
NYHA I	57	22 (2.3)	18 (2.2)	0.019*
NYHA IV	2	71 (6.5)	38 (9.5)	n/a
Anxiety				
NYHA I	32	5.7 (0.8)	4.5 (0.7)	0.145
NYHA IV	1	n/a	n/a	n/a
Depression				
NYHA I	30	4.2 (0.6)	3.7 (0.5)	0.277
NYHA IV	1	n/a	n/a	n/a

*NYHA, New York Heart Association, MLHF, minnesota living with heart failure score, SD, standard deviation, n/a, not applicable,*significant change p<0.05*

The outcome measures for those patients in NYHA I and IV classification were specifically analysed for any significant change as shown in Table 5.

Those patients in NYHA I classification of heart failure showed a significant improvement in walk distance with a mean increase of 109 feet and a significant improvement in quality of life as measured by MLHF questionnaire with a mean reduction in score of four points. However those in NYHA I classification of heart failure showed no significant improvement in anxiety or depression as measured by the HAD scale but the low mean score for both anxiety and depression pre and post course indicated that the NYHA I patients could not be described as being anxious or depressed using HAD scale criteria.

Of the total 16 NYHA IV patients in the study one was excluded from outcome analysis as this was a repeat course for them. Of the remaining 15, none had repeated the six minute walk test, only two had completed a MLHF questionnaire at the end of the course and only one had repeated the HAD scale, this meant that no statistical analysis was possible for this group of patients.

This was disappointing as more specific information about the outcome of exercise intervention as part of a cardiac rehabilitation programme was particularly sought for the heart failure patient in NYHA IV classification.

3.2.2 The female heart failure patient

The outcome measures for the female participants who had completed the exercise programme, excluding those who were repeating the course, were analysed for changes. The same outcome measure for all participants, i.e. including the male patients was analysed for comparison, see Table 6.

Table 6. *All participants plus women only: outcome measures (excluding repeaters of course)*

	No Pairs	Mean Pre (SD)	Mean Post (SD)	P value
Six minute walk test (feet)				
Both sexes	241	1042 (24.9)	1147 (22.7)	0.0005*
Women only	58	268 (16.9)	321 (15.1)	0.0005*
MLHF				
Both sexes	438	40 (1.1)	33 (1.0)	0.0005*
Women only	99	40 (2.2)	33 (2.2)	0.0005*
Anxiety				
Both sexes	236	7.5 (0.29)	6.8 (0.27)	0.004*
Women only	56	8.4 (0.55)	7.4 (0.57)	0.018*
Depression				
Both sexes	233	6.5 (0.24)	5.8 (0.23)	0.002*
Women only	57	6.2 (0.44)	5.5 (0.47)	0.180

MLHF, Minnesota Living with Heart Failure score, SD, standard deviation
**significant change p<0.05*

Both sexes showed a significant improvement in six minute walk test distance with a mean increase of 105 feet. Women as a group on their own also had a significant improvement to the six minute walk test result with a mean increase of 53 feet.

Analysis of quality of life as measured by the MLHF questionnaire for both sexes showed significant improvement in the score with a mean reduction of seven points. For women only MLHF score also showed significant improvement similarly with a mean reduction of seven points.

Significant reduction was seen in anxiety for both sexes as measured by the HAD scale and also significant reduction for women as a subgroup.

Significant reduction in depression as measured by the HAD scale was present for both sexes but was not seen for women as a group on their own.

However as a score of eight and above is considered representative of anxiety or depression it would appear from the mean score on entry to the exercise programme that, generally, the heart failure patients referred to cardiac rehabilitation could not be described as being anxious or depressed.

3.2.3 The elderly heart failure patient (70 years old and above)

Table 7 shows the outcome measures for those heart failure patients who were 70 years old and above and who were not repeating the exercise course.

Table 7. 70 *years and above:* o*utcome measures (excluding repeaters of course)*

	No pairs	Mean Pre (SD)	Mean Post (SD)	P value
6 minute walk test (feet)	111	281 (10.3)	310 (9.0)	0.0005*
MLHF	20	33 (1.5)	28 (1.4)	0.0005*
Anxiety	121	6.2 (0.33)	5.7 (0.33)	0.185
Depression	118	5.7 (0.31)	5.4 (0.29)	0.091

MLHF, minnesota living with heart failure score, SD, standard deviation
**significant change p<0.05*

Significant change in six minute walk distance was seen with a mean improvement of 29 feet and also significant improvement in quality of life as measured by the MLHF questionnaire with a mean reduction of five points.

However anxiety and depression levels were not significantly changed with the course but the mean score for both anxiety and depression at exercise recruitment were both below eight and therefore levels of anxiety and depression for the elderly heart failure patient could be described as normal on entry to the exercise course.

Table 8. *Under 70 years: outcome measure for anxiety and depression (excluding repeaters of course)*

	No pairs	Mean Pre (SD)	Mean Post (SD)	P value
Anxiety	115	8.8 (0.42)	7.9 (0.40)	0.005*
Depression	115	7.2 (0.35)	6.3 (0.35)	0.007*

*SD, standard deviation, *significant change p<0.05*

These findings were explored more by comparison with those heart failure patients who were under 70 years old as shown in Table 8. Analysis showed that not only did those heart failure patients who were under 70 years have raised levels of anxiety and depression, compared to those heart failure patients over 70 years, at recruitment to cardiac rehabilitation but also that the programme significantly improved both anxiety and depression levels.

3.2.4 The heart failure patient with significant co-morbidity

For those heart failure patients with a diagnosed significant co-morbidity, as seen in Table 9, a significant improvement in six minute walk test distance was observed with a mean improvement of 34 feet and an improvement in quality of life by a mean reduction of five points as measured by MLHF questionnaire. Similarly to the elderly patients, anxiety and depression levels did not significantly improve. Mean anxiety level was raised slightly but mean depression levels could be described as normal at entry to the programme. These findings were explored further by analysing anxiety and depression for those heart failure patients who had no significant co-morbidity, as shown in Table 10.

Table 9. *Significant co-morbidity: Outcome measures (excluding repeaters of course)*

	No pairs	Mean Pre (SD)	Mean Post (SD)	P value
6 minute walk test (feet)	126	287(10.2)	321(9.3)	0.0005*
MLHF	222	42 (1.5)	37 (1.5)	0.0005*
Anxiety	122	7.5 (0.41)	7.1 (0.39)	0.156
Depression	121	6.6 (0.33)	6.4 (0.32)	0.331

MLHF, minnesota living with heart failure score, SD, standard deviation
**significant change p<0.05*

Similarly to those heart failure patients with co-morbidity mean anxiety levels were raised slightly and mean levels of depression at recruitment were considered normal. However following cardiac rehabilitation both anxiety and depression significantly reduced to lower levels.

Table 10. *Without significant co-morbidity: Outcome measures for anxiety and depression (excluding repeaters of course)*

	No pairs	Mean Pre (SD)	Mean Post (SD)	P value
Anxiety	114	7.4 (0.42)	6.4 (0.37)	0.009*
Depression	112	6.3 (0.36)	5.3 (0.31)	0.001*

*SD, standard deviation,*significant change p<0.05*

3.2.5 Relationship between change in six minute walk distance and change in MLHF for all participants (excluding repeaters of course)

A correlation between the change in six minute walk test distance and change in MLHF score pre and post cardiac rehabilitation was performed for all participants excluding those who had repeated the course. For 212 pairs no significant relationship was found ($p = 0.124$) between change in six minute

test result and change in MLHF score.

3.3 Adherence to the exercise programme

Overall for all of the 1000 participants whether repeating the course or not, adherence, quantified as completing 50% or more of the course, was 74.4%.

Table 11. *Adherence to rehabilitation course (excluding repeaters of course)*

	Number	Attended at least 50% of the course	Percent
Women	237	172	72.6%
NYHA I	114	80	70.2%
NYHA IV	15	10	33.3%
70 years old and above	396	295	74.5%
Significant co-morbidity	474	357	72.5%
Multiple co-morbidity	110	78	70.9%
All study patients	1000	744	74.4%

NYHA, New York Heart Association, significant co-morbidity determined as formal diagnosis made by General Practitioner or Specialist Doctor, multiple co-morbidity defined as two or more significant co-morbidities, Completed defined as attended four weeks or more of an eight week course

Women, the more elderly patient, those with single or multiple co-morbidity all completed the course to a similar degree, as seen in Table 11. However only 33.3% of those heart failure patients in NYHA classification IV completed the course.

3.4 Safety of the exercise programme

Of the 1000 participants only four (0.004%) had documented events which required immediate medical attention during attendance at the cardiac rehabilitation programme. This is summarised in Table 12. One patient suffered a cardiac arrest, this occurred before the exercise session had begun, similarly one patient was noted to be in complete heart block during pre-screening for exercise. The other two

patients were exercising when they each suffered a collapse due to severe hypotension. Three of the four patients required immediate hospitalisation. All patients made a good recovery and were able to return to the course at a later date.

Table 12. *Acute events during cardiac rehabilitation session which required immediate medical attention*

Gender	Age	NYHA	LVEF	Aetiology	Co-morbidity	Event	Hospitalised
Male	74	II	25%	CHD	Visually impaired	Hypotensive collapse during exercise	Yes
Male	55	III	25%	Unknown	None	Complete heart block pre exercise	Yes
Male	66	I	40%	CHD	Asthma	Hypotensive collapse during exercise	No
Male	65	III	50%	VHD	None	Cardiac Arrest on arrival for exercise	Yes

NYHA, New York Heart Association, LVEF, left ventricular ejection fraction, CHD, coronary heart disease, VHD, valvular heart disease, Hospitalised, admitted to hospital

word count 2462

Chapter 4 Discussion and Conclusion

The overall findings of this study, which shall be referred to subsequently as the Wythenshawe study, support the hypothesis that exercise training, as part of a standard NHS cardiac rehabilitation programme, is safe and effective for all heart failure patients.

However the findings specifically for the NYHA IV heart failure patient, whilst supporting the hypothesis that exercise is safe as no NYHA IV patient suffered an adverse event during exercise, cannot support the hypothesis that exercise training is effective because insufficient repeat outcome measures were collected for this group for analysis to be made. This, together with the fact that NYHA IV patients did not adhere to the programme as well as the other heart failure patients suggests that more evidence should be gathered around how exercise training should be delivered to this particular group of patients.

The premise for this study was that the Wythenshawe study participants could be representative of the wider population of heart failure patients in so far as it was inclusive rather then exclusive of the female patient, of those in NYHA class I and IV, of the more elderly heart failure patient and also inclusive of those with significant co-morbidity in addition to their heart failure. Comparison of the baseline characteristics with other studies will demonstrate where the similarities and differences lie.

4.1 Baseline Characteristics

A useful comparative of baseline characteristics, to confirm where there is concordance and also contrariety with other exercise studies, would be to compare

the Wythenshawe study specifically with the exercise cohorts for the HF ACTION study by O'Connor et al. in 2009, this being the most recent and largest heart failure exercise study, and also with the 2004 study by Austin et al., a more representative study of the elderly heart failure patients in the UK.

4.1.1 The heart failure patient in NYHA I and IV classification

12.3% of patients in this study were NYHA I classification, neither HF ACTION nor Austin et al. (2004) included any patient in NYHA I classification of heart failure.

1.7% of patients in this study were NYHA IV classification whereas, for HF ACTION, 1.2% of the total cohort were described as NYHA IV. Austin et al. (2004) excluded patients in NYHA IV classification of heart failure. Thus the proportion of NYHA IV patients referred for the Wythenshawe study is consistent with the number of NYHA IV patients in HF ACTION. As seen in the results for the Wythenshawe study, NYHA IV patients disappointingly did not complete any repeat outcome measures, so comment on the effectiveness of exercise training for this sub group cannot be made.

The NYHA IV patients completed the programme at less than half the rate of the rest of the patients, this being 33.3% compared to an overall adherence of 74.4% for the whole cohort. Although they only represent 1.7 % of the study cohort, the NYHA IV patients are the most debilitated and symptom limited of all the heart failure patients and do require some form of exercise intervention in order to be able to function on an every day basis.

However the poor adherence for the Wythenshawe study suggests that the model of

delivering exercise training in a hospital based programme may not be suitable for the NYHA IV heart failure patient. More research is needed specifically for this group to evaluate alternatives ways of delivering exercise, for example in a home or community programme and with more individual supervision and support. It seems understandable that NYHA IV heart failure patients have not been included in much of the previous research due to their complexity. It is arguably also predictable that they may find it difficult to complete an exercise programmes. This may be due to the fact that they are not well enough to participate in exercise training particularly if over a long period of time where attendance must be planned around frequent hospital or GP visits as is common for the NYHA IV patient. There may also be access issues where travelling moderate distances to attend for exercise is not practical. Comprehensive study of the exercise needs for this specific group would be very valuable to drive recommendations for future service delivery.

4.1.2 The female heart failure patient

The percentage of female participants was similar for all three studies, the Wythenshawe study where 26% were female and HF ACTION and Austin et al. (2004) where 30% and 33% respectively were female. As we have seen from the National Health Service Heart Failure Audit for 2008/09 by the NHS Information Centre for Health and Social Care, heart failure incidence on hospital admission is 57% for men and 43% for women. Therefore the lower uptake of women onto research studies and cardiac rehabilitation programmes may not be because the incidence in women is less or that women are being excluded from the research or from cardiac rehabilitation programmes, but may be due to some other factor which

makes them less likely to want to participate in exercise training programmes. The under representation of women generally in cardiac rehabilitation programmes following a cardiac event is well documented (British Heart Foundation Care and Education Research Group, 2009 and Fleg, 2002) and so perhaps it is not surprising that the same trend exists for the female patient with heart failure. Some cardiac rehabilitation programmes have tackled this issue by holding female only exercise groups on the premise that some women do not wish to exercise in a group with men. This strategy could be used for the female heart failure patient together with more in depth study as to how best to engage these patients to exercise.

4.1.3 The elderly heart failure patient

For the elderly heart failure patient, age was higher for the Wythenshawe study, median age being 68 years compared to HF ACTION where the median age was 59 years. However if mean age is used, the mean age for the wythenshawe study was 67 ± 11.5 years which is slightly below that for Austin et al., 2004 where the mean age was 72 ± 6.3 years. This is not surprising as Austin et al. (2004) were specifically targeting the elderly heart failure patient and consequently had less younger patients to bring the average age down.

4.1.4 The heart failure patient with significant co-morbidity

The greatest difference in participant inclusion for the Wythenshawe study compared to others were the inclusion of heart failure patients with significant co-morbidity. Neither HF ACTION nor Austin et al. (2004) included heart failure patients with significant co-morbidity. Austin et al. (2004) had initially recruited heart failure patients with significant co-morbidity but then subsequently excluded

any patient with a co-morbidity which may affect their ability to exercise, the amount of participants to have been excluded this way reported as 52%.
This compares very well with the Wythenshawe study where 51.7% of the heart failure patients had significant co-morbidity, however differs because none of the 51.7% were excluded if their co-morbidity limited their functional capacity. To consider that over half of the heart failure population may have significant co-morbidities makes the importance of the Wythenshawe study very relevant. It proves that, despite the co-morbidity, heart failure patients can benefit from exercise training as part of a cardiac rehabilitation programme.
However, if heart failure patients with significant co-morbidity are to be included in exercise training programmes, then the cardiac rehabilitation professionals providing the exercise training must be appropriately skilled in managing the exercise requirements of the individual patient around those co-morbidities in addition to the heart failure. Therefore the skill mix and competences for staff involved in cardiac rehabilitation programmes should reflect this requirement.
Thus it can be summarised that the baseline characteristics of the participants for the Wythenshawe study conform with previous research but also differs, most markedly, with the inclusion of NYHA I patients and those heart failure patients with significant co-morbidity. Therefore the participants in this study may be more representative of the wider heart failure population.

4.1.5 Correlation of baseline six minute walk test distance with baseline left ventricular ejection fraction, quality of life score, age, gender and presence of significant co-morbidity

It can be seen by the correlations performed in chapter 3.1.1 that, as reported by previous research such as that by Litchfield et al (1982), there is a poor relationship between LVEF and exercise ability. Additionally it can be seen from these results that baseline six minute walk test distance could not be used to predict quality of life as measured by MLHF score or vice versa as correlation was low. Furthermore age, gender or co-morbidity status also did not predict six minute walk distance or vice versa as they also had a poor relationship. For service providers and cardiac rehabilitation practitioners this should strengthen the belief and understanding that assumptions cannot be made about a patient's ability to perform a six minute walk test and participate in a cardiac rehabilitation using the baseline characteristics described above.

4.2 Repeated outcome measures

4.2.1 Six minute walk test

When looked at as individual groups, the NYHA I classification patient, women, the elderly and those with significant co-morbidity all showed a statistically significant improvement in six minute walk test distance of 109 feet (8.7% improvement), 53 feet (19.7% improvement), 29 feet (10.3% improvement) and 34 feet (11.8% improvement) respectively. This compared to an increase of 105 feet (10% improvement), for the whole cohort (excluding those that had repeated the course).

The elderly group showed a smaller improvement similar to that described by Smart et al. (2004). The exercise arm for the study on elderly heart failure patients by Austin et al (2004) demonstrated an increased six minute walk test distance of 16%.

Owen et al., in 2000 reported an increase of 20% distance walked for the elderly heart failure patient.

Thus, this compares to a smaller 10.3% improvement in walk distance for the elderly in the Wythenshawe study. However, the participants for the studies by Austin et al. in 2004 and Owen et al. in 2000, although elderly did not include elderly heart failure patients with significant co-morbidities. This may explain why the percentage improvement in the Wythenshawe study was less, as elderly heart failure patients with significant co-morbidities were included, co-morbidities which may have been the main limiting factor for mobility. However we have seen earlier that there was poor correlation found between six minute walk test and presence of co-morbidity in the Wythenshawe study. Thus further investigation into the effect of different types of co-morbidity would be useful to clarify their individual effect on a patient's exercise capability and ability to improve functional capacity.

Van Tol, Huijsmans, Kroon, Swothurst and Kwakkel (2006), following a meta-analysis of the evidence for exercise training in heart failure, specifically describe an increase in six minute walk test of 43 metres (141 feet) as clinically relevant. Thus none of the improvements for the whole cohort nor the specific groups in the Wythenshawe study, using the criteria set by Van Tol et al. (2006) could be seen as clinically relevant. Similarly Rees et al. (2004) describe a smaller distance of 40.9 metres (134 feet) as a minimum significant distance for significant improvement in six minute walk test for the heart failure patient post intervention and again the Wythenshawe participants did not achieve this. However, HF ACTION only demonstrated a mean improvement of 20 metres (66 feet) in six minute walk

distance after three months of exercise. This was viewed as significant improvement and, using this premise, the six minute walk test improvement for the whole Wythenshawe cohort and the NYHA I patients can be regarded as relevant, however the subgroups of heart failure patients with significant co-morbidity, women or the elderly could not be seen as relevant. As the HF ACTION study does not give any detail regarding specific sub groups direct comparison, however is not possible. It would be particularly difficult to set a significant clinical distance improvement for patients with co-morbidity in particular as there appears to be no comparison anywhere in the research evidence.

Other studies such as that by McKelvie et al., 2002 for the EXERT trial found no difference in the improvement in six minute walk distance for the control group and the exercise group with another study by Kostis, Rosen and Cosgrove in 1994 having a similar finding that there was no significant difference between the improvement in six minute walk test between heart failure patients in a control and an exercise group.

Hence the picture is not consistent, some research shows no significant improvement to six minute walk test distance with exercise training compared to usual care and other studies describe the opposite.

The consensus for the amount of improved distance required to represent clinical significance rather than a statistical significance seems to vary with some studies measuring it as a percentage improvement rather than an overall improvement in distance. This also confuses the picture and is worthy of further investigation.

A confounding factor for the results in six minute walk testing and certainly for the

Wythenshawe study may be as to whether a practice test was performed prior to the initial six minute walk test. Some of the studies report that a practice test was done and some do not clarify whether one was carried out or not, for example, HF ACTION and Austin et al, 2004 do not state whether a practice test was performed. The Wythenshawe study did not carry out a practice six minute walk.

The American Thoracic Society (2002) suggests that, in most clinical settings, a practice test is not needed for the six minute walk test but should be considered. They report that the mean distance walked following a practice test is reported to vary between 0 and 17% and that any training effect learnt is lost after more than one month anyway.

Bittner et al. (1993) also agree that a practice test is not necessary. However Jolly, Taylor, Lip and Singh (2008) studied over 300 shuttle walk tests to explore if a practice test was necessary and concluded that familiarisation alone of the test accounted for a mean increase of 29.5 m (96.7 feet). Thus just the repetition of a walk test may account for a increase without any exercise training having taken place.

However, in mitigation, the need for a practice walk test may be less necessary for the six minute walk test as this particular test represents an everyday familiar activity, is self paced by the patient and they are allowed to stop and rest. This differs to other types of functional capacity test, such as the shuttle walk test researched by Jolly et al. in 2008, where the participant is required to walk at an ever increasing pace, that is, where the test is externally paced, and is an activity less familiar to the individual. Therefore a practice test may be more important.

The other main confounding factor which may dictate varying results to six minute walk test outcome is the length of exercise programme. The wythenshawe programme was eight weeks long, many of the studies are much longer, for example, HF ACTION was three months, Austin et al. (2004) exercised patients for 24 weeks and the study by McKelvie et al, 2002, involved participation in a 12 month exercise programme. However considering HF ACTION showed a mean six minute walk test improvement of 66 feet after three months, yet the Wythenshawe study an overall mean improvement of 105 feet after only two months and McKelvie (2002) no difference in walk test difference between control and exercise group after 12 months, the picture remains confusing and may be attributable to too many variables.

4.2.2 Minnesota Living with Heart Failure (MLHF) Score

For the NYHA I patients, women, elderly and those heart failure patients with significant co-morbidity a reduced score showing significant improvement was seen as a mean reduction by four, seven, five and five points respectively. This compared to a mean reduction of seven points for the whole cohort (excluding those who had repeated the course). There is therefore some similarity to the finding by Austin et al. in 2004 where a mean reduction of eight points was reported. Flynn et al. 2009 for HF ACTION did not use the MLHF questionnaire to measure quality of life. Nilsson et al. (2008) reported a larger mean reduction of 11 points and Van Tol et al. in 2006 describe a reduction in the MLHF score of nine points with exercise training as clinically relevant. This would make the Wythenshawe study results less clinically significant. However Rector, 2005 a strong advocate of the

MLHF questionnaire suggests that an improvement of five points can be seen as clinically significant.

In contrast Owen at al. (2000) found no improvement in MLHF score despite patients saying they felt better and McKelvie et al. (2002) for the EXERT trial found that the improvement in quality of life as measured by the MLHF was not statistically significant for the exercise group compared to the control group at three months.

Interestingly, on entry to the exercise course the mean MLHF score for those heart failure patients 70 years and over was 33 ± 1.5 points compared to the mean for the whole cohort at entry of 39.6 ± 1.0 points, the higher score indicating a poorer quality of life. Therefore the older heart failure patient in the wythenshawe study, pre exercise training, were reporting a better quality of life compared to the rest of the cohort. Petrie, Stewart and McMurray in 2000 reported that there was little information on the effect of age on quality of life in heart failure and suggested that age itself in heart failure reduces quality of life. However from the Wythenshawe study it would appear that age over 70 years did not reduce quality of life for the heart failure patient as measured by the MLHF questionnaire.

4.2.3 Relationship between change in six minute walk distance and change in MLHF score

It was interesting to observe that there was no correlation between change in six minute walk test and change in MLHF score for 212 patients pre and post cardiac rehabilitation, as reported in the results. As both tests are proven outcome measures both in this study and others for use in the heart failure population, this information

supports the continued need of both outcome measures as one cannot predict the change in the other.

4.2.4 Hospital Anxiety and Depression (HAD) Scale

Following the Wythenshawe heart failure cardiac rehabilitation programme, although there was a significant improvement in anxiety levels for the women, there were no significant changes in depression levels. For the NYHA I patients, the elderly, and for those heart failure patients with significant co-morbidity no significant changes in anxiety or depression score was seen. However it was interesting to see that, on entry to the cardiac rehabilitation programme, where a HAD score of seven or below is considered normal, mean anxiety and depression levels for the NYHA I patients and for the elderly were normal pre exercise training and remained normal. In comparison, for those heart failure patients who were under 70 years old, at recruitment, the mean anxiety and depression score was raised with significant reduction following exercise training. This would suggest that the more elderly heart failure patient is generally less anxious and depressed than their younger counterparts.

Weir et al., (2006) when looking at older heart failure patients suggest that older patients may have a lower expectation of life and therefore tend to underscore in quality of life measures. Therefore the older heart failure patient could also be underscoring anxiety and depression levels as measured by HAD, as well as for the MLHF score as mentioned previously. This is an interesting area and a potential for future study.

Whether the heart failure patient had a significant co-morbidity or not, mean

anxiety score at recruitment was slightly raised whereas depression levels could be described as normal. However the non co-morbidity group showed significant improvement in anxiety levels with exercise whereas the co-morbidity group did not. This again is an area worthy of further in depth study as to why this should be the case, especially considering that half of the heart failure population will have a significant co-morbidity as was seen in the baseline characteristics.

An interesting confounding factor for the use of the HAD scale to measure depression in heart failure patients lies in one of the questions to measure depression. This asks whether the patient feels that they are “slowed down”, this ‘feeling’ being significant, depending on degree with depression. However fatigue is one of the classic symptoms of heart failure and a patient who feels fatigued will score that they are slowed down more as a physical symptom than a sign of depression. This raises the question whether the HAD scale is the best tool to use to detect or eliminate depression in heart failure patients.

Overall it appears from the Wythenshawe study that in general heart failure patients do not have raised levels of anxiety or depression. This is in contrast to what has been reported. The National Health Service Information Centre for Health and Social Care, Heart Failure Audit, 2008-9, suggests that over one third of heart failure patients experience severe and prolonged depression. This would be an interesting area to investigate further as to why the Wythenshawe study experience of depression and heart failure was different . This may be the difference between using different measures to detect depression or be the difference between patients who are being offered intervention such as cardiac rehabilitation to those

who are not.

4.3 Adherence

Overall adherence for completion of 50% or more of the programme was 74.4%. All the subgroups adhered at a similar rate apart from the NYHA IV patients who completed at half the rate of everyone else with 33.3% adherence. Turner, Bethell, Evans, Goddard and Mullee in 2002, for a study of over 1900 patients in a UK cardiac rehabilitation programme recorded adherence as 76% However Turner et al. (2002) quantified adherence as 100% completion of the programme and included non heart failure patients so comparison with the Wythenshawe study is difficult.

Barbour et al. in 2008 report exercise adherence in the healthy population as 63%. However their review of exercise adherence for the heart failure population concluded that there is little uniform evidence to suggest what level this should be but that it is essential to develop long term exercise maintenance strategies for this population. It would be interesting to follow up the patients in the Wythenshawe study to determine whether benefits had been sustained and whether those that completed 100% of the course did better than those who had completed less of the course.

A systematic review of 15 studies for factors associated with cardiac rehabilitation non attendance by Cooper, Jackson, Weinman and Horne in 2002 concluded that non attendees were more likely to be older. Keteyian et al. (1996) in a randomised controlled study of 40 American men also commented that more elderly patients tended to drop out. This was not the experience for the

Wythenshawe study where those heart failure patients 70 years and above completed at a rate of 74.5%. However the study by Keteyian et al. in 1996 describes the overall mean age as 56+/- 11 years with the drop out mean age as 61 +/- 10 years so even though it was the older patients who dropped out in this study the whole study population was younger compared to the Wythenshawe study. The different findings between these two studies could be the difference between research participation and an NHS cardiac rehabilitation programme participation where the former is much more rigid. However the Wythenshawe experience should be reassuring for cardiac rehabilitation services that those heart failure patients over 70 years will attend as regularly as their younger counterparts. Interestingly the adherence level for women was also good. Thus the issue for discussion must be how to recruit women considering they are under represented generally in cardiac rehabilitation programmes because, from the Wythenshawe evidence, they adhere well to the course.

As has been mentioned earlier the NYHA IV classification patients, with a much poorer attendance rate pose more of a problem and more comprehensive study into the exercise needs and how to provide them for this group of patients is needed.

4.4 Safety

For the Wythenshawe study there were four (0.004%) recorded incidents in 1000 patients. Three of the four incidents in this study resulted in the patient being hospitalised. This low level compares well to the HF ACTION study where 37 patients (3.2%) in the exercise group were hospitalised due to an event which occurred during the exercise or within three hours of having completed an

exercise session. Unfortunately for the Wythenshawe study there are not accurate records of events occurring within three hours of exercise, as for HF ACTION, as this was not officially recorded. However, any acute event which had occurred post exercise would have been communicated at or before the next planned exercise session and would have therefore been recorded on the patient's cardiac rehabilitation records and thus seen by the study researcher. However it should be acknowledged that this is a study limitation. Franklin, Bonheim, Gordon and Timmins in 1998, reported five major cardiovascular events in 246, 575 hours of exercise within cardiac rehabilitation programmes, which included heart failure patients, in Canada and America over a 16 year period, this equated to one per 49,315 hours. Unfortunately it was not possible to accurately determine the total number of exercise hours for the wythenshawe study to represent the events per number of hours.

Rees et al., for the Cochrane review of exercise and heart failure in 2004, reported that of the 29 studies that were looked at, 17 stated that no adverse events had occurred during exercise. The 2004 Cochrane review by Rees et al.
defines acute adverse events as death, myocardial infarction or arrhythmia associated with exercise. Thus, using these criteria, none of the events which were recorded for the Wythenshawe study would actually meet the set criteria as two events were blood pressure related and the cardiac arrest and the arrhythmia occurred during pre screening for exercise.

However, nevertheless, the safety record for the Wythenshawe study is useful information for other cardiac rehabilitation programmes who exercise heart failure

patients. It can also be considered a very encouraging result when taking into account that heart failure patients are considered a high risk complex group of patients.

It should also be mentioned that monitoring in many of the research studies tends to be high with the use of telemetry, heart rate monitors and regular blood pressure measurements. However the Wythenshawe study used the minimum of monitoring methods and proves that that high levels of monitoring, particularly with equipment, is not necessary to ensure the safety of the patient. The results also show that optimum heart failure medication should not be a requirement for recruitment onto the exercise component of a cardiac rehabilitation programme as far as safety is concerned.

The safety record for the Wythenshawe study is also testament to the level of skill and competence of the cardiac rehabilitation staff involved in providing the exercise training and the good management of the patient's heart failure by the heart failure specialist nurses, cardiologists and general practitioners.

4.5 Study limitations

This study used the proviso that the heart failure patients referred to Wythenshawe cardiac rehabilitation programme were representative of the wider population of heart failure patients and in particular of those heart failure patients not seen in research studies. It is assumed that all heart failure patients who had been inpatients in Wythenshawe hospital and had been diagnosed with heart failure were referred to Wythenshawe heart failure clinic from where they were referred to cardiac rehabilitation. However there was not a robust enough system in place over the time

period evaluated to be fully confident that all heart failure patients were referred to the heart failure clinic particularly those patients with multiple medical problems who were on non cardiac wards. In mitigation however in favour of the Wythenshawe study findings it can be argued that, because there was no contraindication to exercise for those heart failure patients with co-morbidity, and these made up 51.7% of the cohort studied, then these patients can be seen as representative of patients who have heart failure in addition to other medical issues. This is an area that could be looked at again once the system for identifying heart failure patients becomes more robust as is planned.

There was no control group for the Wythenshawe study so comparisons cannot be made between those that received exercise training and those that did not. This is a major study limitation but it was not possible to randomise patients when it was ethically inappropriate to deny NHS patients cardiac rehabilitation at a time when they were identified as needing this service.

The package of cardiac rehabilitation at Wythenshawe may have varied for some patients during the period of the study as the cardiac rehabilitation programme evolved during the study period between 1998 and 2007. Some patients received exercise training in a small group, some in a larger group, others as a 1:1 session, some patients received education sessions, others did not.

Although standardisation for supervising six minute walk test and instructions for completion of questionnaires was strived for at all times, because this study was over a 10 year period where staff and systems change there may have been some inconsistencies. Certainly Guyatt et al. (1984) stated that standardisation is

particularly important for walking tests where simple encouragement can improve performance.

There was a high level of missing data for the study and it was not possible or practical to retrieve this. Therefore this may have had some effect on the overall results.

It could be argued that it is difficult to compare this study to other research and to draw conclusions regarding outcome measure when patients were attending the programme whilst still undergoing uptitration of medication. Most studies only enrol participants once on optimal medical therapy and it could be proposed that increases in medication or other medical interventions may have caused the improved outcome measure rather than the exercise training.

However, this retrospective study reflects the true picture of everyday cardiac rehabilitation practice where patients are referred whilst undergoing other interventions and where exercise training as part of a cardiac rehabilitation programme can be seen to enhance the benefit of these other interventions.

4.6 Conclusion

Thus the hypothesis that exercise training is safe, as part of a cardiac rehabilitation programme, for all heart failure patients can be deemed as true. Exercise training in this setting can also be said to be effective as measured by six minute walk test and quality of life measures for NYHA I patients, female, the elderly and those heart failure patients with significant co-morbidity in terms of statistical significance. Both the six minute walk test and the Minnesota Living with Heart Failure questionnaire can be said to be independent valuable tools used to assess change.

However use of the Hospital Anxiety and Depression scale for heart failure patients may require further investigation to be confident of accuracy in detecting anxiety and depression particularly as overall Wythenshawe study patients appeared less depressed than is reported for the general heart failure population. Investigation of other tools used to measure anxiety and depression in this population would be beneficial for comparison. The hypothesis that exercise training is effective for NYHA IV patients cannot be commented upon to be true or false as there was insufficient information obtained to make a judgement either way.

4.7 Implications for research

More work is needed to specifically study the NYHA IV patient and their access to exercise training and how they can benefit from it. They appear to be a sub group which differs completely from the rest of the heart failure population and a different model of approach by the cardiac rehabilitation services may be more appropriate. Additionally study into strategies that will improve the uptake of women with heart failure onto cardiac rehabilitation exercise programmes is important. Women, as with the NYHA IV patients may require a completely different approach as to how cardiac rehabilitation services are provided in order for these services to be appealing and relevant to them.

More in depth investigation into the impact of cardiac rehabilitation on patients with specific co-morbidities and heart failure both physically and psychologically would be extremely beneficial considering such a large percentage of heart failure patients have a significant co-morbidity and considering there is such little evidence in this area.

More study into anxiety and depression in heart failure and the impact of exercise training on this would be useful and in particular research into the most accurate measurement tool to detect or eliminate this in the heart failure population.
Additionally consensus via research on whether a certain distance improvement or a percentage improvement in six minute walk test distance is clinically relevant post exercise training would make it easier to ascertain whether exercise training is clinically significant as well as statistically significant.
More detailed evidence from existing UK cardiac rehabilitation programmes as collected by the University of York for the National Audit for Cardiac Rehabilitation (NACRe) over forthcoming years will be invaluable to demonstrate the safety and effectiveness of cardiac rehabilitation in heart failure.
It is difficult to draw general conclusions for the optimal delivery of exercise for the heart failure patient when the research studies have so much potential for variation regarding intensity and type of exercise, length of exercise session and length of course and where the exercise is undertaken, home, hospital or elsewhere. Cardiac rehabilitation programmes across the UK are delivered in the main in a uniform fashion around national and professional standards and with the collection of outcome data from these programmes from sources such as NACRe, this may enhance the evidence from the clinical trials and inform practice.

4.8 Implications for everyday practice for the cardiac rehabilitation professional

The Wythenshawe study is evidence to support that outside research conditions and within the everyday practice of an NHS cardiac rehabilitation programme, where

medicine optimisation is not required and monitoring is less, heart failure patients can be exercised safely and effectively. This is with the proviso that the cardiac rehabilitation staff have the competences and skills to prescribe and deliver exercise training for the individual heart failure patient (British Association for Cardiac Rehabilitation, 2007).

NYHA I heart failure patients benefit from exercise training programmes and should not be excluded on the assumption that they are already functioning at a higher level compared to most other heart failure patients. NYHA IV patients are safe to exercise appropriately but a hospital based cardiac rehabilitation programme may not be the best setting for their adherence to an exercise programme.

Female heart failure patients should be specifically targeted with strategies to improve their uptake into exercise programmes.

There should be no exclusion of patients over 70 years or for those with significant co-morbidity which may affect their ability to exercise as both groups can benefit from rehabilitation.

Assumptions cannot be made on functional capacity as measured by the six minute walk test based on baseline characteristics such as LVEF, gender, age, MLHF score and co-morbidity status.

Six minute walk test and MLHF questionnaire are both useful outcome measures to demonstrate improvement but change in one cannot predict change in the other so both measures should be used.

Overall exercise training for all heart failure patients within an NHS cardiac rehabilitation programme is safe and effective.

word count 5936

Chapter 5 List of References

American Association of Cardiovascular and Pulmonary Rehabilitation (2004): *Guidelines for Cardiac Rehabilitation and Secondary Prevention Programs,* 4th Edition. Human Kinetics, Champaign, IL.

American Thoracic Society (2002). ATS Statement: Guidelines for the Six Minute Walk Test. *American Journal of Respiratory Care and Medicine*, 166, 111-117

Association of Chartered Physiotherapists in Cardiac Rehabilitation (2009). *Standards for Physical Activity and Exercise in the Cardiac Population*. London: Author

Austin, J., Williams, R., Ross, L., Moseley, L. & Hutchison, S. (2004). Randomised controlled trial of cardiac rehabilitation in elderly patients with heart failure. *The European Journal of Heart Failure,* 7, 411-417

Barbour, K.A & Miller, N.H. (2008). Adherence to exercise training in heart failure: a review. *Heart Failure Reviews,* 13, 81-89

Bellardinelli, R., Georgiou, D., Cianci, G. & Purcaro, A. (1998). Randomised Controlled Trial of Long-Term Moderate Exercise Training in Chronic Heart Failure. Effects on Functional Capacity, Quality of Life, and Clinical Outcome. *Circulation,* 99, 1173-1182

Bittner,V., Weiner, D.H., Yusuf, S., Rogers, W.J., McIntyre, K, M., Bangdiwala, S, I. et al. (1993). Prediction of Mortality and Morbidity With a Six Minute Walk Test in Patients with Left Ventricular Dysfunction. Journal of the American Medical Association, 270, 1702-1707

Bjelland, I., Dahl, A.A., Haug, T.T. & Neckelman, D. (2002). The validity of the Hospital Anxiety and Depression Scale: An updated Literature Review. *Journal of Psychosomatic Research*, 52 (2), 69-77

Borg, G.A. (1998). *Borg's Rating of Perceived Exertion and Pain Scales*. Champaign, IL: Human Kinetics

British Association for Cardiac Rehabilitation (2007). *Standards and Core Components for Cardiac Rehabilitation.* London:Author.

British Heart Foundation Care and Education Research Group (2009). *The National Audit of Cardiac Rehabilitation. Annual Statistical Report*. University of York: Author

Cahalin.L.P., Mathier, M.A., Semigram, M.J., Dec, G.W. & DiSalvo, T.G. (1996).The Six Minute Walk Test Predicts Peak Oxygen Uptake and Survival in Patients with Advanced Heart Failure. *Chest,* 110, 325-332

Coats, A.J.S., Adamopoulos, S., Radeaelli, A., McCance, A., Meyer, T.E., Bernadi, L. et al. (1992). Controlled Trial of Physical Training in Chronic Heart Failure. *Circulation,* 85, 2119-2131

Cooper, A.F., Jackson, G., Weinman, J.& Horne, R. (2002). Factors associated with cardiac rehabilitation attendance: a systematic review of the literature. *Clinical Rehabilitation*, 16(5), 541-552.

Covera-Tindel, T., Doering, L.V., Gomex, T.& Dracup, K. (2004). Predictors of non compliance to exercise training in heart failure. *Journal of Cardiovascular Nursing*, 19, 269-277

Cowie, M. R., Wood, D. A., Coats, A.J.S., Thompson, S.G., Poole-Wilson, P.A., Suresh, V. et al. (1999). Incidence and aetiology of heart failure. A population based study. *European Heart Journal*, 20, 421-428

Cowles, M. & Davis, C. (1982). On the origins of the .05 level of statistical significance. *American Psychologist*, 37, (5), 553-558

Davies, E.J., Moxham, T., Rees., K., Singh, S., Coats, A.J.S., Ebrahim, S., Lough, F. & Taylor, R. (2010). Exercise based rehabilitation for heart failure (review). *Cochrane Database of Systematic Reviews*. Issue 4, Art. No.: CD003331. DOI: 10.1002/14651858.CD003331.pub3

Department of Health (2000). *National Service Framework for Coronary Heart Disease*. London: Author.

European Heart Failure Training Group (1998). Protocol and patient factors in effectiveness in the improvement in exercise tolerance. *European Heart Journal*, 19, 466-475

European Society of Cardiology (2008). ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *European Heart Journal*, 29, 2388-2442.

ExTraMATCH Collaborative (2004). Exercise training meta-analysis of trials in patients with chronic heart failure (ExTraMATCH). *British Medical Journal*, 328, 189-192

Fleg, J.L (2002). Can Exercise Conditioning be Effective in Older Heart Failure Patients? *Heart Failure Reviews*, 7, 99-103

Fletcher, G, F., Balady, G.J., Amsterdam, E.A., Chaitman, B., Eckel, R., Fleg, J. et al. (2001). Exercise Standards for Testing and Trianing. A Statement for Healthcare Professionals From the American Heart Association. *Circulation*, 104, 1694-1740

Flynn, K.E., Pina, I.L., Whellan, D.J., Lin, L., Blumenthal, J.A., Ellis, S.J. et al. (2009). Effects of Exercise Training on Health Status in Patients with Chronic Heart Failure, HF-ACTION Randomized Controlled Trial. *Journal of the American Medical Association*, 310(14), 1451-1459

Franklin, B.A., Bonzheim, K., Gordon, S. & Timmins, G.C. (1998). Safety of Medically Supervised Outpatient Cardiac Rehabilitation Exercise Therapy. *Chest*, 114, 902-906

Gottlieb, S.S., Fisher, M.L., Freudenberger, M.L., Robinson, S., Zietowski, G., Alves, L. et al. (1999).Effects of exercise training on peak performance and quality of life in congestive heart failure patients. *Journal of Cardiac Failure*, 3, 188-194

Greater Manchester and Cheshire Cardiac Network (2007). *Summary of the Statin Prescribing in Cardiovascular Disease Prevention Meeting.* Retrieved from http://www.gmccsn.nhs.uk/cmsupload/Statin_prescribing_meeting_report_15th_Jan_07_final.pdf

Guyatt, G.H., Pugsley, S.O., Sullivan, M.J., Thompson, P.J., Berman, L., Jones, N.L., Fallen, E.L., Taylor. D.W. (1984). Effect of encouragement on walking test performance. *Thorax, 39, 818-822*

Jolly, K., Taylor, R.S., Lip, G.Y.H. & Singh, S. on behalf of the BRUM steering group. (2008). Reproducibility and safety of the incremental shuttle walking test for cardiac rehabilitation. *International Journal of Cardiology, 125, 144-145*

Keteyian, S.J., Levine , R.B., Brawner, C.A., Kataoka, T., Rogers, F.J., Schairer, J.R. et al. (1996). Exercise Training in Patients with Heart Failure: A Randomised, Controlled Trial. *Annals of Internal Medicine,* 124, 1051-1057

Kostis, J.B., Rosen, R.C. & Cosgrove, N.M. (1994). Nonpharmacologic therapy improves functional and emotional status in congestive heart failure. *Chest*, 106,996-1001 *Circulation* 1982; 66;129-134

Lipkin, D.P., Scriven, A.J., Crake, T. & Poole-Wilson, P.A. (1986). Six minute walking test for assessing exercise capacity in chronic heart failure. *British Medical Journal*, 292, 653-655

Litchfield, R.L., Kerber, R.E.,Benge, J.W., Mark, A.L., Sopko, J.,Bhatnagar, R.K., & Marcus, M.L.(1982). Normal exercise capacity in patients with severe left ventricular dysfunction compensatory mechanisms. *Circulation,* 66, 129- 134

Lloyd-Williams, F., Mair, F.S., Leitner, M. (2002). Exercise training and heart failure: a systematic review of current evidence. *British Journal of General Practice*, 52, 47-55

McKelvie, R.S., Koon, K.T., Roberts, R., McCartney, N., Humen, D., Montague, T. et al. (2002). Effects of exercise training in patients with heart failure: The Exercise Rehabilitation Trial (EXERT). *American Heart Journal*, 144, 23-30

McKelvie, R, S. (2008). Exercise training in patients with heart failure: clinical outcomes, safety, and indications. *Heart Failure Reviews,* 13, 3-11

Martin, K.A.& Sinden, A.R. (2001). Who will stay and who will go? A review of older adults' adherence to randomized controlled trials of exercise. *Journal of Ageing and Physical Activity*, 9(2), 91-114

National Clinical Guideline Centre (2010). *Chronic Heart Failure: The Management of Adults with Chronic Heart Failure in Primary and Secondary Care. Draft for Consultation, January 2010.* London: Author

National Health Service Information Centre for Health and Social care (2009). *National Heart Failure Audit.* Leeds: Author

National Health Service Institute for Innovation and Improvement (2009). *Focus on: Heart Failure*. Coventry: Author

National Health Service Manchester (2008). *Manchester Public Health Annual Report.* Retrieved from http://www.manchester.gov.uk/site/scripts/download_info.php?fileID=11009

National Institute for Clinical Excellence (2003). Chronic heart failure. *Management of chronic heart failure in adults in primary and secondary care. Clinical Guideline 5*. London: Author

National Statistics.(2001) *Census: North West*. Retrieved from National Statistics websitehttp://www.statistics.gov.uk/census2001/profiles/commentaries/north_west.asp

Nilsson, B.B., Westheim, A., Risberg, M.A. (2008). Long-Term Effects of a Group-Based High-Intensity Aerobic Interval-Training in Patients with Chronic Heart Failure. *American Journal of Cardiology*, 102(9), 1220-1224

O'Connor, C.M., Whellan, D.J., Lee, K.L., Keteyian, S.J., Cooper, L.S., Ellis, S.J.et al. (2009). Efficacy and Safety of Exercise Training in Patients with Chronic Heart Failure, HF-ACTION Randomized Controlled Trial. *Journal of the American Medical Association*, 301(14), 1439-1450

O'Keefe, S.T., Lye, M., Donellan, C. & Carmichael, D.N. (1998). Reproducibility and responsiveness of quality of life assessment and six minute walk test in elderly heart failure patients. *Heart*, 80, 377-382

Owen, A. & Croucher, L.(2000).Effect of an exercise programme for elderly patients with heart failure. *European Journal of Heart Failure*, 2, 65-70

Petrie, M.C., Berry, C., Stewart, S. & McMurray, J.J.V. (2001). Failing ageing hearts. *European Heart Journal*, 22, 1978-1990

Pina, I, L., Apstein, C, S., Balady, G, J., Bellardinelli, R., Chaitman, B.R., Duscha, B, D. et al.(2003). Exercise and Heart Failure: A Statement from the American Heart Association Committee on Exercise, Rehabilitation, and Prevention. *Circulation*, 107, 1210-1225

Ponikowski, P. (2004). Editorial comment on effect of exercise training in patients with heart failure. *European Journal of Cardiovascular Prevention and Rehabilitation*, 11, 168-170

Pu, C.T., Johnson, M.T., Forman, D.E., Hausdroff, J.M., Roubenoff, R., Foldvari, M. et al. (2001). Randomized trial of progressive resistance training to counteract the myopathy of chronic heart failure. *Journal of Applied Physiology*, 90 (6), 2341-2350

Rector, T.S. & Cohn, J.N (1992). Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: Reliability and validity during a randomized, double blind, placebo-controlled trial of pimobendan. *American Heart Journal*, 124, 1017-1025

Rector, T.S. (2005). Overview of the Minnesota Living with Heart Failure Questionnaire. Retrieved from http://www.mlhfq.org/_dnld/mlhfq_overview.pdf

Rees, K., Taylor, R.S., Singh, S., Coats, A.J.S. & Ebrahim, S. (2004). Exercise based rehabilitation for heart failure. *Cochrane Database of Systematic Reviews* Issue 3. Art. No.: CD003331. DOI: 10.1002/14651858.CD003331.pub2.

Scottish Intercollegiate Guidelines Network (2007). *Management of Chronic heart failure. 95, A national clinical guideline*. Edinburgh: Author.

Smart, N. & Marwick, T.H. (2004). Exercise Training for Patients with Heart Failure: A Systematic Review of factors that Improve Mortality and Morbidity. *American Journal of Medicine*, 116, 693-706

Turner, S.C., Bethnell, H, J. N., Evans, J.A., Goddard, J.R., Mullee, M.A. (2002). Patient Characteristics and Outcomes of Cardiac Rehabilitation. *Journal of Cardiopulmonary Rehabilitation*, 22, 253-260

Tyni-Lenne, R., Gordon, A., Jansson, E. & Sylven, C. (1997). Skeletal muscle endurance training improves peripheral oxidative capacity, exercise tolerance, and health related quality of life in women with chronic congestive heart failure secondary to either ischemic cardiomyopathy or idiopathic dilated cardiomyopathy. *American Journal of Cardiology*, 80 (8), 1025-9

University Of York (2002) .National Audit of Cardiac Rehabilitation. Retrieved from *http://www.cardiacrehabilitation.org.uk*

Van Tol, B.A.F., Huijsmans, R.J., Kroon, D.W., Schothorst, M. & Kwakkel, G. (2006). Effects of exercise training on cardiac performance, exercise capacity and quality of life in patients with heart failure: a meta-analysis. *The European Journal of Heart Failure*, 8, 841-850

Weir, R.A.P., McMurray, J, J.V., Taylor, J. & Brady, A, J, B. (2006). Heart failure in older patients. *Clinical Cardiology Series*, 13, 257-264

Wielenga, R.P., Erdman, R.A.M., Huisveld, I.A., Bol, E., Dunselman, P. H. J. M., Baselier, M.R.P. et al. (1998). Effect of Exercise Training on Quality of Life in patients with Chronic Heart Failure. *Journal of Psychosomatic Research*, 45(5), 459-464

Chapter 6 Appendices

6.1 Absolute contra-indications to exercise component of cardiac rehabilitation

6.2 New York Heart Association Classification of Heart Failure

6.3 Written permission University Hospital South Manchester NHS Foundation Trust

6.4 NHS Regional Ethics Committee Approval

6.5 University of Chester Faculty of Applied and Health Science Research Ethics Committee

6.6 Six minute walk test protocol

6.7 Minnesota Living with Heart Failure Questionnaire

6.8 University of Minnesota Licence for use of MLHF Questionnaire

6.9 Hospital Anxiety and Depression Questionnaire

6.10 SPSS analyses

- Outcome measures NYHA I
- Outcome measures All (excluding repeaters of course)
- Outcome measures Women
- Outcome measures 70 years and above
- Under 70 years HAD outcomes
- Outcome measures co-morbidity
- No co-morbidity HAD outcomes
- Correlation baseline statistics
- Correlation change in six minute walk test and change in MLHF score
- Completion rates

Appendix 6.1

Absolute contraindications which preclude a patient from joining or continuing the exercise component of an inpatient and outpatient cardiac rehabilitation programme:

- Unstable angina
- Resting systolic blood pressure (SBP) of > 200mmHg, or diastolic BP > 110mmHg should be assessed on a case-by-case basis
- Orthostatic blood pressure (BP) drop of > a 20 mmHg with symptoms
- Critical aortic stenosis
- Acute systemic illness or fever
- Uncontrolled atrial or ventricular arrhythmias
- Acute pericarditis or myocarditis
- Uncompensated congestive heart failure (CCF)
- 3rd degree AV block (without pacemaker)
- Active pericarditis or myocarditis
- Recent embolism
- Thrombophlebitis
- Resting ST segment displacement (> 2 mm)
- Uncontrolled diabetes
- Severe orthopaedic conditions that would prohibit exercise
- Other metabolic conditions, such as acute thyroiditis, hypokalaemia or hyperkalaemia, hypovolaemia etc
- Severe rejection (cardiac transplantation recipients)

Appendix 6.2

NEW YORK HEART ASSOCIATION (NYHA) CLASSIFICATION OF HEART FAILURE

Class I: No limitation, ordinary physical activity does not cause undue fatigue, shortness of breath or palpitations

Class II: Slight limitation of physical activity, comfortable at rest but ordinary activity results in fatigue, palpitations or shortness of breath

Class III: Marked limitation of physical activity, comfortable at rest but less than ordinary activity results in symptoms

Class IV: Unable to carry out any physical activity without discomfort, symptoms of heart failure present even at rest with increased discomfort with any physical activity

Appendix 6.3

APPROVAL FROM HOSPITAL TRUST TO USE PATIENT DATA

From:
Sent: 16 June 2009 12:20
To: Laura Burgess
Subject: RE: MSc

Hi Laura

Would be delighted for this data to be used - a worthwhile project!

Best wishes

Simon

Consultant Cardiologist
University Hospital South Manchester

From: Laura Burgess
Sent: 16 June 2009 10:19
To:
Subject: MSc

Dear Simon

I am undertaking an MSc in Cardiovascular Rehabilitation at the University of Chester (partially funded by the Trust) and have finally reached dissertation point!

I plan to use the data I have collected for the Heart Failure Rehab service over the last 10 years - see attached poster. I do not need NHS ethical approval as they regard it as service evaluation but do need University ethical approval. They need written confirmation from a representative of UHSM that the data can be used for this purpose.
As the clinical lead for Cardiac Rehab and the Heart Failure Clinic I felt you were the best person to do this for me.

If you are happy for the data to be used, could you officially reply as such to this email and I can then submit that to the ethics committee.

Thanks

Laura
Laura Burgess
Clinical Specialist Physiotherapist Cardiac Rehabilitation

Appendix 6.4

APPROVAL LOCAL NHS ETHICS COMMITTEE

From:
To:
Sent: Friday, 29 May, 2009 8:58:51 AM
Subject: FW: advice re ethics approval

Dear Laura

I have now received a response from the Chair of the South Manchester REC who feels this is audit/service evaluation using routinely collected data. Ethical review is not formally required.

Good luck with your project.

Bolton, South and Stockport Research Ethics Committees
Room 181
Gateway House
Piccadilly South
Manchester
M60 7LP
Tel: 0161-237-2051
Web-site: www.nres.npsa.nhs.uk

From:
Sent: 07 May 2009 12:52
To:
Subject: advice re ethics approval

Dear

I'm hoping you can help me.

For the dissertation for my MSc I plan to do a retrospective service evaluation on patients at the hospital where I work.

My course tutor at the University of Chester suggested I forwarded the attached poster to you summarising the proposed study for advice on what sort of ethical approval I will need to apply for.

Thank you for your help

Laura Burgess

Appendix 6.5

Faculty of Applied and Health Sciences
Research Ethics Committee

Laura Ann Burgess

14 January 2010

Dear Laura

Study title: **Is exercise training safe and effective for *all* heart failure patients? A retrospective service evaluation of a hospital-based cardiac rehabilitation programme**
FREC reference: **366/09/LB/CENS**
Version number: **2**

Thank you for sending the above-named application to the Faculty of Applied and Health Sciences Research Ethics Committee for review.

The application has been considered on behalf of the Committee by Kevin Lamb as Lead Reviewer and reported to the Faculty Research Ethics Committee.

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form and supporting documentation.

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Application Form	1	July 2009
Reference list	2	December 2009
CV of lead researcher	-	July 2009
Written permission from University Hospital of S. Mancs	-	June 2009
HADS questionnaire	?	?
MLHFQ questionnaire	?	© 1986
NYHA classifications	1	July 2009
Six minute walk test protocol	1	July 2009
Correspondence from NHS LREC	-	May 2009
Response to FRECs request for further information	1	December 2009

With the Committee's best wishes for the success of this project.

Yours sincerely,

Prof. Cynthia Burek Chair, Faculty Research Ethics Committee

Appendix 6.6

SIX MINUTE WALK TEST (6mwt)

This objective test measures functional capacity in heart failure by calculating in metres or feet how far an individual can walk in six minutes.

Most heart failure patients can do this test, although they may need to stop if they become short of breath, get chest pain, or feel tired, dizzy or light-headed. Usually, the test is done in a corridor along a course of up to 30 metres (100 feet) long but shorter distances are used in practice dependent on space. The total distance covered is therefore measured accordingly. The distance the patient must walk is clearly marked out.

Prior to the start of the test patients are prescreened for their suitability and consent to perform it.

Patients walk from one end of the set distance to the other at their own pace, trying to cover as much ground as possible. A health professional will time the test, and record the patient's reported rate of perceived exertion at pre determined points. Heart rate can also be monitored throughout the test. Patients can stop and rest on the way if necessary.

After six minutes, or before if the health professional feels it is not appropriate for them to continue, they are asked to stop and heart rate and blood pressure is recorded.

The total distance walked is calculated and recorded together with the cardiovascular response and any notable symptoms.

Appendix 6.7
MINNESOTA LIVING WITH HEART FAILURE® QUESTIONNAIRE (MLHFQ)

Appendix 6.8

Minnesota LIVING WITH HEART FAILURE® Questionnaire
COPYRIGHT USER'S LICENSE

The Regents of the University of Minnesota (hereafter referred to as "UNIVERSITY"), a constitutional corporation of the State of Minnesota having an office and principal place of business at 1000 Westgate Drive, Suite 160, St. Paul, MN 55114-8658 has created a copyrighted WORK entitled the Minnesota LIVING WITH HEART FAILURE® Questionnaire intended for use by authorized health care professionals and researchers, and desires to make the WORK available for use worldwide.

Completion of this COPYRIGHT USER'S LICENSE ("LICENSE"), whereby the LICENSEE agrees to the terms specified herein, is required to use the WORK. Users must legibly complete items 1.3, 6.1, 6.2 and 7.2, if applicable. A signature and date is also required on the last page prior to submitting this document as directed in item 7.1.

ARTICLE I - DEFINITIONS

1.1 WORK means the Minnesota LIVING WITH HEART FAILURE® Questionnaire and Instructions for Data Collection and Scoring. This WORK is in the English language, and is identified as U/M Docket #94019. An electronic copy of the WORK and supplemental information including information about translations is available at www.mlhfq.org.

1.2 APPROVED COPIES means duplicates of the WORK that shall include the following statements:

> ©1986 Regents of the University of Minnesota, All rights reserved. Do not copy or reproduce without permission. LIVING WITH HEART FAILURE® is a registered trademark of the Regents of the University of Minnesota.

1.3 LICENSEE means (**complete all of the following**)

Name of person and organization: Laura Ann Burgess, University of Chester

Address:

Telephone number:

Facsimile number: -----

Electronic mail address:

ARTICLE II - LICENSE

2.1 UNIVERSITY grants to LICENSEE the right to reproduce the WORK and use APPROVED COPIES of the WORK for purposes described below in Article 6.1 upon, (i) submission of a completed LICENSE to the UNIVERSITY, (ii) payment to the UNIVERSITY of the applicable nonrefundable LICNESE FEE specified below in Article 6.2, and (iii) notification of acceptance of (i) and (ii) by the UNIVERSITY. The EFFECTIVE DATE of this LICENSE is the date of (iii).

2.2 LICENSEE is granted no other license to or rights in the WORK other than as expressly stated in Article 2.1.

2.3 UNIVERSITY retains all rights in the WORK not granted to the LICENSEE under 2.1. UNIVERSITY retains ownership of the copyright to the WORK.

2.4 UNIVERSITY does not grant to LICENSEE any right to use the name or marks of the UNIVERSITY in any manner except as may be expressly provided in this LICENSE.

2.5 LICENSEE may not assign its license rights under this LICENSE to any entity other than a wholly-owned subsidiary of the LICENSEE.

ARTICLE III - TERM AND TERMINATION

3.1 The term of this LICENSE shall be from the EFFECTIVE DATE of this LICENSE specified in Article 2.1 until the LICENSEE completes or ceases use of the WORK described below in Article 6.1, or the UNIVERSITY terminates the LICENSE as described below in Article 3.2. However, in no event shall the term of this license exceed ten (10) years.

3.2 UNIVERSITY may terminate this LICENSE upon breach of the LICENSE by LICENSEE. UNIVERSITY shall give LICENSEE written notice of the breach and notice of the intent to terminate. If LICENSEE does not cure the breach within thirty (30) days of the notice, the LICENSE shall terminate. Upon such termination, LICENSEE's right to use the WORK shall terminate.

3.3 Termination of this LICENSE shall not extinguish any of LICENSEE's obligations under this LICENSE which, by their terms, continue after the date of such termination or expiration.

ARTICLE IV - PROTECTION OF PROPRIETARY RIGHTS

4.1 LICENSEE shall take all steps reasonable to protect UNIVERSITY's ownership rights in the WORK. LICENSEE shall not distribute copies of the WORK to third parties or employees without appropriate notice, agreement, and/or instruction with respect to use, copying, modification, and copyright protection of the WORK.

4.2 LICENSEE will not remove the UNIVERSITY copyright notice and/or other proprietary notices.

ARTICLE V - WARRANTIES AND LIMITATIONS; INDEMNIFICATION

5.1 UNIVERSITY and LICENSEE warrant that they have the right to enter into this LICENSE and the ability to comply with its terms.

5.2 UNIVERSITY MAKES NO REPRESENTATIONS OR WARRANTIES, EXPRESS OR IMPLIED. BY WAY OF EXAMPLE, BUT NOT LIMITATION, UNIVERSITY MAKES NO REPRESENTATIONS OR WARRANTIES OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE OF THE WORK. UNIVERSITY SHALL NOT BE HELD LIABLE FOR ANY LIABILITY OR FOR ANY INDIRECT OR CONSEQUENTIAL DAMAGES RESULTING FROM THE USE OF THE WORK.

5.3 LICENSEE agrees to indemnify and hold UNIVERSITY harmless against any claims or damages resulting from LICENSEE's use of the WORK including all liability to third parties arising from the negligence of LICENSEE. LICENSEE assumes no responsibility for any third party claims that the WORK, unmodified by LICENSEE, infringes a copyright of the third party, or for damages arising from the willful or negligent behavior or conduct of UNIVERSITY.

ARTICLE VI – LICENSED USE OF WORK AND FEE

6.1 The LICENSEE's use of the WORK under this LICENSE is restricted to uses indicated by an "X" in a box preceding each intended use. LICENESE FEES are in U.S. dollars.

X☐ The LICENSEE is a student or teacher who will use the WORK only for a student project(s) or didactic purposes. LICENSE FEE is waived.

☐ The LICENSEE is a health care professional or health care organization who will use the WORK only in the care of patients or to evaluate in-house services. LICENSE FEE is $500.

☐ The LICENSEE is a principal investigator who will use the WORK in not-for-profit research projects. LICENSE FEE is $500 per project. Type the title(s) of each project to be covered by this LICENSE in the following space:

☐ The LICENSEE is a pharmaceutical, medical device, biotechnology, disease management or other for-profit entity who will use the WORK to evaluate a product or service that is in development or on the market. LICENSE FEE is $2,500 per protocol. Type the title and number of each protocol to be covered by this LICENSE in the following space.

6.2 Enter the total of all applicable LICENSE FEES from Article 6.1. $000

ARTICLE VII – SUBMISSION OF LICENSE & PAYMENT; NOTIFCATION OF ACCEPTANCE

7.1 The fully completed LICENSE including signature and LICENSE FEE listed above in Article 6.2 should be sent to the following address. An incomplete or illegible LICENSE will not be accepted. The UNVERSITY will not send a separate invoice. Please keep a copy of your submission for your records. Payment should be sent as a check for U.S. dollars made payable to the University of Minnesota. If you do not send the completed LICENSE and payment together, make sure your payment identifies the LICENSEE and the Minnesota LIVING WITH HEART FAILURE® Questionnaire as the reason sending the payment to the UNIVERSITY.

Send completed LICENSE and LICENSE FEE to;

Minnesota LIVING WITH HEART FAILURE® Questionnaire
Office for Technology Commercialization
University of Minnesota
1000 Westgate Drive, Suite 160
St. Paul, MN 55114-8658

7.2 An electronic notification of acceptance will be sent by the UNIVERISTY when both a completed LICENSE and LICENSE FEE are received. If this notification is to be sent to an electronic address other than the one listed above in article 1.3, type the person's name and electronic address here:
Name: Email address:

ARTICLE VIII – MISCELLANEOUS

8.1 All questions about the LICENSE or WORK should be sent to info@mlhfq.org. The UNIVERSITY is under no obligation to provide support for the WORK.

8.2 This LICENSE contains the entire agreement of the parties concerning this subject matter and supersedes all other previous understandings and statements, written or oral, concerning this matter.

8.3 This LICENSE is binding upon and shall inure to the benefit of the LICENSEE's successors and/or assigns.

8.4 This LICENSE shall be interpreted and applied in accordance with the laws of the State of Minnesota.

8.5 Headings are for convenience only and are not to be used in interpreting this LICENSE.

8.6 The terms of this LICENSE cannot be orally modified. A modification is not effective unless it is in writing and signed by the LICENSEE and the UNIVERSITY.

IN WITNESS WHEREOF, the LICENSEE agrees to the above terms by the signature below of their duly authorized representatives.

(LICENSEE)

By: _____
(authorized signature)

LAURA ANN BURGESS, MSc Student
(print name and title)

Date: 2-10-09

LIVING WITH HEART FAILURE® is a registered trademark of the Regents of the University of Minnesota.

Appendix 6.9

HOSPITAL ANXIETY DEPRESSION (HAD) SCALE (including scoring system)

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 in each section

1 I feel tense or wound up:
Most of the time ☐3
A lot of the time ☐2
Time to time, occasionally ☐1 A
Not at all ☐0

2 I still enjoy the things I used to enjoy:
Definitely as much ☐0
Not quite so much ☐1
Only a little ☐2 D
Hardly at all ☐3

3 I get a sort of frightened feeling as if something awful is about to happen:
Very definitely and quite badly ☐3
Yes, but not too badly ☐2
A little, but it doesn't worry me ☐1 A
Not at all ☐0

4 I can laugh and see the funny side of things:
As much as I always could ☐0
Not quite so much now ☐1
Definitely not so much now ☐2 D
Not at all ☐3

5 Worrying thoughts go through my mind:
A great deal of the time
A lot of the time ☐3
From time to time bur not too often ☐2
Only occasionally ☐1 A
☐0

6 I feel cheerful
Not at all
Not often ☐3
Sometimes ☐2
Most of the time ☐1 D
☐0

7 I can sit at ease and feel relaxed:
Definitely
Usually ☐0
Not often ☐1
Not at all ☐2 A
☐3

8 I feel as if I am slowed down:
Nearly all the time ☐3
Very often ☐2
Sometimes ☐1 D
Not at all ☐0

9 I get a sort of frightened feeling like "butterflies" in the stomach:
Not at all ☐0
Occasionally ☐1
Quite often ☐2 A
Very often ☐3

10 I have lost interest in my appearance:
Definitely ☐3
I don't take so much care as I should ☐2
I may not take quite as much care ☐1 D
I take just as much care as ever ☐0

11 I feel restless as if I have to be on the move:
Very much indeed ☐3
Quite a lot ☐2
Not very much ☐1 A
Not at all ☐0

12 I look forward with enjoyment to things:
As much as I ever did ☐0
Rather less than I used to ☐1
Definitely less than I used to ☐2 D
Hardly at all ☐3

13 I get sudden feelings of panic:
Very often indeed ☐3
Quite often ☐2
Not very often ☐1 A
Not at all ☐0

14 I can enjoy a good book or radio or TV programme:
Often
Sometimes ☐0
Not often ☐1
Very seldom ☐2 D
☐3

0 – 7 normal	A = Anxiety
8 – 10 mild	
11 – 14 moderate	D = Depression
15 – 21 severe	

NYHA I outcome measures (excluding course repeaters)

Six minute walk test

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.141	30	.131	.948	30	.145
6 mwt post course	.132	30	.195	.958	30	.269

a. Lilliefors Significance Correction

Assumption of normal distribution satisfied, Paired T Test conducted

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	6 mwt pre course - 6 mwt post course	-108.700	206.661	37.731	-185.869	-31.531	-2.881	29	.007

Minnesota Living with Heart Failure Score

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
minn pre course	.161	57	.001	.899	57	.000
minn post course	.182	57	.000	.851	57	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	minn post course - minn pre course
Z	-2.351[a]
Asymp. Sig. (2-tailed)	.019

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Anxiety

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD anxiety pre course	.205	32	.001	.888	32	.003
HAD anxiety post	.154	32	.051	.911	32	.012

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD anxiety post - HAD anxiety pre course
Z	-1.456[a]
Asymp. Sig. (2-tailed)	.145

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Depression

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD depression pre course	.162	30	.044	.887	30	.004
HAD depression post	.174	30	.020	.933	30	.059

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD depression post - HAD depression pre course
Z	-1.087[a]
Asymp. Sig. (2-tailed)	.277

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Outcome all (excluding repeaters of course)

Six minute walk test

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.086	241	.000	.981	241	.002
6 mwt post course	.069	241	.007	.987	241	.032

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon test conducted

Test Statistics[b]

	6 mwt post course - 6 mwt pre course
Z	-6.799[a]
Asymp. Sig. (2-tailed)	.000

a. Based on negative ranks.

b. Wilcoxon Signed Ranks Test

Minnesota Living with Heart Failure Score

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
minn pre course	.078	438	.000	.970	438	.000
minn post course	.087	438	.000	.958	438	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	minn post course - minn pre course
Z	-7.588[a]
Asymp. Sig. (2-tailed)	.000

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Anxiety

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD anxiety pre course	.103	236	.000	.966	236	.000
HAD anxiety post	.079	236	.001	.974	236	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon test conducted

Test Statistics[b]

	HAD anxiety post - HAD anxiety pre course
Z	-2.907[a]
Asymp. Sig. (2-tailed)	.004

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Depression

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD depression pre course	.093	233	.000	.970	233	.000
HAD depression post	.109	233	.000	.964	233	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon test conducted

Test Statistics[b]

	HAD depression post - HAD depression pre course
Z	-3.109[a]
Asymp. Sig. (2-tailed)	.002

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Women Outcome measures (excluding course repeaters)

Six minute walk test

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.112	58	.068	.967	58	.115
6 mwt post course	.062	58	.200*	.991	58	.938

a. Lilliefors Significance Correction

*. This is a lower bound of the true significance.

Normal distribution assumption satisfied, Paired T Test

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	6 mwt pre course - 6 mwt post course	-171.052	293.556	38.546	-248.238	-93.865	-4.438	57	.000

Minnesota Living with Heart Failure Score

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
minn pre course	.089	99	.054	.968	99	.017
minn post course	.141	99	.000	.933	99	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test

Test Statistics[b]

	minn post course - minn pre course
Z	-3.658[a]
Asymp. Sig. (2-tailed)	.000

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Anxiety

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD anxiety pre course	.108	56	.156	.970	56	.183
HAD anxiety post	.085	56	.200*	.967	56	.124

a. Lilliefors Significance Correction

*. This is a lower bound of the true significance.

Normal distribution assumption satisfied, Paired T Test conducted

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	HAD anxiety pre course - HAD anxiety post	1.054	3.244	.434	.185	1.922	2.430	55	.018

Hospital Anxiety Depression Scale: Depression

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD depression pre course	.108	57	.097	.971	57	.177
HAD depression post	.135	57	.011	.951	57	.022

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD depression post - HAD depression pre course
Z	-1.340[a]
Asymp. Sig. (2-tailed)	.180

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Elderly (70 years and above) outcome measures (excluding repeaters of course)

Six minute walk test

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.101	111	.007	.972	111	.019
6 mwt post course	.070	111	.200*	.979	111	.081

a. Lilliefors Significance Correction

*. This is a lower bound of the true significance.

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	6 mwt post course - 6 mwt pre course
Z	-4.297[a]
Asymp. Sig. (2-tailed)	.000

a. Based on negative ranks.

b. Wilcoxon Signed Ranks Test

Minnesota Living with Heart Failure Score

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
minn pre course	.093	200	.000	.965	200	.000
minn post course	.094	200	.000	.952	200	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	minn post course - minn pre course
Z	-4.181[a]
Asymp. Sig. (2-tailed)	.000

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Anxiety

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD anxiety pre course	.130	121	.000	.950	121	.000
HAD anxiety post	.111	121	.001	.963	121	.002

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD anxiety post - HAD anxiety pre course
Z	-1.326[a]
Asymp. Sig. (2-tailed)	.185

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Scale: Depression

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD depression pre course	.120	118	.000	.961	118	.002
HAD depression post	.137	118	.000	.965	118	.004

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD depression post - HAD depression pre course
Z	-1.688[a]
Asymp. Sig. (2-tailed)	.091

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Under 70 years outcomes (excluding repeaters of course)

Hospital Anxiety Depression Scale: Anxiety

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD anxiety pre course	.083	115	.047	.971	115	.013
HAD anxiety post	.063	115	.200*	.977	115	.046

a. Lilliefors Significance Correction

*. This is a lower bound of the true significance.

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD anxiety post - HAD anxiety pre course
Z	-2.788[a]
Asymp. Sig. (2-tailed)	.005

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Scale: Depression

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD depression pre course	.078	115	.081	.976	115	.038
HAD depression post	.101	115	.006	.958	115	.001

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD depression post - HAD depression pre course
Z	-2.709[a]
Asymp. Sig. (2-tailed)	.007

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Co-morbidity outcomes

Six minute walk test

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.070	126	.200*	.988	126	.339
6 mwt post course	.059	126	.200*	.994	126	.894

a. Lilliefors Significance Correction

*. This is a lower bound of the true significance.

Normal distribution assumption satisfied, Paired T Test conducted

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	6 mwt pre course - 6 mwt post course	-110.667	305.792	27.242	-164.582	-56.751	-4.062	125	.000

Minnesota Living with Heart Failure Score

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
minn pre course	.082	222	.001	.967	222	.000
minn post course	.087	222	.000	.966	222	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	minn post course - minn pre course
Z	-4.368[a]
Asymp. Sig. (2-tailed)	.000

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Anxiety

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD anxiety pre course	.083	122	.040	.970	122	.007
HAD anxiety post	.085	122	.032	.971	122	.010

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD anxiety post - HAD anxiety pre course
Z	-1.417[a]
Asymp. Sig. (2-tailed)	.156

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Depression

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD depression pre course	.098	121	.006	.970	121	.008
HAD depression post	.093	121	.012	.966	121	.004

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD depression post - HAD depression pre course
Z	-.972[a]
Asymp. Sig. (2-tailed)	.331

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

No co-morbidity HAD outcomes (excluding repeaters of course)

Hospital Anxiety Depression Scale: Anxiety

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD anxiety pre course	.129	114	.000	.960	114	.002
HAD anxiety post	.074	114	.168	.974	114	.028

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD anxiety post - HAD anxiety pre course
Z	-2.627[a]
Asymp. Sig. (2-tailed)	.009

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Hospital Anxiety Depression Scale: Depression

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HAD depression pre course	.087	112	.035	.967	112	.007
HAD depression post	.123	112	.000	.959	112	.002

a. Lilliefors Significance Correction

Failed normal distribution assumption, Wilcoxon Test conducted

Test Statistics[b]

	HAD depression post - HAD depression pre course
Z	-3.471[a]
Asymp. Sig. (2-tailed)	.001

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Baseline Characteristic Correlations

Six minute walk Test and LVEF

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Ejection fraction	.166	498	.000	.947	498	.000
6 mwt pre course	.089	498	.000	.978	498	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Spearman's rho conducted

Correlations

			Ejection fraction	6 mwt pre course
Spearman's rho	Ejection fraction	Correlation Coefficient	1.000	-.096*
		Sig. (2-tailed)	.	.032
		N	788	498
	6 mwt pre course	Correlation Coefficient	-.096*	1.000
		Sig. (2-tailed)	.032	.
		N	498	592

*. Correlation is significant at the 0.05 level (2-tailed).

Six minute walk test and Minnesota Living with Heart Failure Score

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.098	507	.000	.975	507	.000
minn pre course	.053	507	.002	.978	507	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Spearman's rho conducted

Correlations

			6 mwt pre course	minn pre course
Spearman's rho	6 mwt pre course	Correlation Coefficient	1.000	-.234**
		Sig. (2-tailed)	.	.000
		N	592	507
	minn pre course	Correlation Coefficient	-.234**	1.000
		Sig. (2-tailed)	.000	.
		N	507	739

**. Correlation is significant at the 0.01 level (2-tailed).

Six minute walk test and age

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.080	590	.000	.982	590	.000
age	.070	590	.000	.968	590	.000

a. Lilliefors Significance Correction

Normal distribution assumption failed, Spearman's rho conducted

Correlations

			6 mwt pre course	age
Spearman's rho	6 mwt pre course	Correlation Coefficient	1.000	-.291**
		Sig. (2-tailed)	.	.000
		N	592	590
	age	Correlation Coefficient	-.291**	1.000
		Sig. (2-tailed)	.000	.
		N	590	900

**. Correlation is significant at the 0.01 level (2-tailed).

Six minute walk test and co-morbidity

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
6 mwt pre course	.079	592	.000	.982	592	.000
comorbidity	.356	592	.000	.635	592	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Spearman's rho conducted

Correlations

			comorbidity	6 mwt pre course
Spearman's rho	comorbidity	Correlation Coefficient	1.000	-.169**
		Sig. (2-tailed)	.	.000
		N	906	592
	6 mwt pre course	Correlation Coefficient	-.169**	1.000
		Sig. (2-tailed)	.000	.
		N	592	592

**. Correlation is significant at the 0.01 level (2-tailed).

Six minute walk test and gender

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
sex	.463	592	.000	.547	592	.000
6 mwt pre course	.079	592	.000	.982	592	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Spearman's rho conducted

Correlations

			sex	6 mwt pre course
Spearman's rho	sex	Correlation Coefficient	1.000	.234**
		Sig. (2-tailed)	.	.000
		N	906	592
	6 mwt pre course	Correlation Coefficient	.234**	1.000
		Sig. (2-tailed)	.000	.
		N	592	592

**. Correlation is significant at the 0.01 level (2-tailed).

Correlation change in six minute walk test and Minnesota Living with Heart Failure Score

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
sixminutewalkchange	.099	212	.000	.956	212	.000
minnchange	.102	212	.000	.937	212	.000

a. Lilliefors Significance Correction

Failed normal distribution assumption, Spearman's rho conducted

Correlations

			sixminutewalk change	minnchange
Spearman's rho	sixminutewalkchange	Correlation Coefficient	1.000	-.106
		Sig. (2-tailed)	.	.124
		N	212	212
	minnchange	Correlation Coefficient	-.106	1.000
		Sig. (2-tailed)	.124	.
		N	212	212

Completion rates (excluding course repeaters)

NYHA I

completed course

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not completed	34	29.8	29.8	29.8
	completed course	80	70.2	70.2	100.0
	Total	114	100.0	100.0	

NYHA IV

completed course

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not completed	10	66.7	66.7	66.7
	completed course	5	33.3	33.3	100.0
	Total	15	100.0	100.0	

Women

completed course

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not completed	63	26.6	26.7	26.7
	completed course	172	72.6	72.9	99.6
	unknown	1	.4	.4	100.0
	Total	236	99.6	100.0	
Missing	System	1	.4		
Total		237	100.0		

70 years and over

completed course

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not completed	98	24.7	24.9	24.9
	completed course	295	74.5	74.9	99.7
	unknown	1	.3	.3	100.0
	Total	394	99.5	100.0	
Missing	System	2	.5		
Total		396	100.0		

Co-morbidity present

completed course

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not completed	116	24.4	24.5	24.5
	completed course	357	75.2	75.5	100.0
	Total	473	99.6	100.0	
Missing	System	2	.4		
Total		475	100.0		