Integrating patients with intermittent claudication into an established cardiac rehabilitation programme: a feasibility study with embedded pilot

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Year of Submission - 2022

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Acknowledgements

Firstly, I would like to thank my supervisors Professor Malcolm Granat and Dr Mariyana Schoultz for their support during my Professional Doctorate. Their mentorship over the past 7 years has allowed me to gain a deep insight into scientific inquiry and rigour, and to appreciate the importance of critical thinking. Their support and encouragement have helped me to develop from an experienced practitioner into a practitioner-researcher.

Secondly, I would like to thank the patients at both hospital sites for participating in my study and giving their time freely to the study procedures. The process of going through rehabilitation after a cardiac or vascular diagnosis can evoke a range of emotions from the elation of surviving a heart attack to the fear of losing a limb. I am grateful that I was allowed to observe and record part of this journey. Thanks also goes to the rehabilitation programmes at both hospital sites. Like the patients in this study, their time was given freely without the offer of recompense for their involvement. I am grateful that they saw the potential of this study to support the treatment options for patients with vascular disease and allowed me access to their busy rehabilitation programmes.

Thirdly, and most importantly, I would like to thank my family and friends for their support throughout my doctoral journey. Thanks to my Mum for her encouragement to keep going – I always know she is there at my shoulder gently pushing me on. To my wife, Holly, for supporting me during the tough times and reassuring me that I can do this. Also, for taking the more direct approach of telling me to get on with it – this approach has definitely been required over the past few years! To my little boy, James, whose smiles and cuddles have helped when I have felt overwhelmed by the process of writing this thesis. And to my Dad who, although no longer at my side, would be very proud of what I have achieved.

Declaration

I declare that this thesis is my own work and that it has not been submitted for any other degree or professional qualification. I can confirm that the work submitted is my own except for work that has been formed as part of jointly authored publications. My contribution and those of the co-authors has been explicitly indicated below. I can confirm that appropriate credit has been provided within this thesis where reference has been made to the work of others.

A condensed version of the methods used in this study (Chapter 3) were published in Contemporary Clinical Trials Communications in 2019. The paper was entitled 'Incorporating an exercise rehabilitation programme for people with intermittent claudication into an established cardiac rehabilitation service: A protocol for a pilot study' and was jointly written by myself and my original supervisory team: Malcolm Granat, Mariyana Schoultz, and Andrew Findlow.

Abbreviations

6MWT	Six-minute Walk Test
AAA	Abdominal Aortic Aneurysm
AACVPR	American Association of Cardiovascular and Pulmonary Rehabilitation
ABPM	Ambulatory Blood Pressure Monitor
ABPI	Ankle-brachial Pressure Index
ACPICR	Association of Chartered Physiotherapists working in Cardiac Rehabilitation
ACSM	American College of Sports Medicine
ADL	Activities of Daily Living
AF	Atrial Fibrillation
BACPR	British Association of Cardiovascular Prevention and Rehabilitation
BMI	Body Mass Index
BP	Blood Pressure
bpm	Beats Per Minute
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CHF	Chronic Heart Failure
CLTI	Critical Limb Threatening Ischemia
CI	Confidence Interval
COT	Claudication Onset Time
CR	Cardiovascular Rehabilitation
DADL	Domestic Activities of Daily Living
ECG	Electrocardiogram
Echo	Echocardiogram
GXT	Graded Exercise Test
GP	General Practitioner
GTN	Glycerine Trinitrate
HADS	Hospital Anxiety and Depression Scale
HDL	High-density Lipoprotein
HF	Heart Failure
HR	Heart Rate
HRQL	Health-related Quality of Life
IC	Intermittent Claudication
IHD	Ischaemic Heart Disease
ISWT	Incremental Shuttle Walk Test
LDL	Low-density Lipoprotein
METs	Metabolic Equivalent of Time
MFT	Manchester NHS Foundation Trust
MHR	Maximum Heart Rate
MI	Myocardial Infarction
MWD	Maximal Walking Distance
NCD	Non-communicable Disease
NHS	National Health Service
NICE	National Institute of Health and Care Excellence
PAD	Peripheral Arterial Disease
PCI	Percutaneous Coronary Intervention
PFWT	Pain-free Walking Time

PI	Principal Investigator
PMH or PMHx	Past Medical History
PPCI	Primary Percutaneous Coronary Intervention
PVD	Peripheral Vascular Disease
RCT	Randomized Controlled Trial
RPE	Rating of Perceived Exertion
SD	Standard Deviation
SEP	Supervised Exercise Programme
SIGN	Scottish Intercollegiate Guidelines Network
SOB	Short of Breath
SOBOE	Short of Breath on Exertion
SRFT	Salford Royal NHS Foundation Trust
STEMI	ST Elevation Myocardial Infarction
TASC	Transatlantic Inter-Society Consensus Working Group for the Management of PAD
TBPI	Toe-brachial Pressure Index
THR	Target Heart Rate
UK	United Kingdom
USA	United States of America
VascuQoL	King's College Vascular Quality of Life Questionnaire
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
WHO	World Health Organisation
WIQ	Walking Impairment Questionnaire

Abstract

Introduction: In the UK, it is recommended that people diagnosed with intermittent claudication (IC) receive exercise therapy as first-line treatment of their condition. The optimal delivery of this treatment is a hospital-based, supervised exercise programme (SEP). Despite this recommendation, there is a national shortage of SEPs in the UK with limited numbers of peripheral artery disease (PAD) patients receiving this preferred treatment option. Financial restrictions and lack of qualified staff available to supervise the programmes are the main limitations to service provision. Integrating patients with IC into an already established network of Cardiac Rehabilitation Programmes (CRPs) has been proposed as a solution to this service problem, however, no study has yet been conducted to investigate the feasibility of this combined rehabilitation.

Aim: The main aim of this study was to assess the feasibility of an integrated CRP for patients with IC. The study also aimed to collect pilot data to guide the methodology for a future randomised control trial (RCT).

Methods: To address the aims of this study, a parallel two-armed feasibility study was conducted across two hospital sites. One site acted as the IC control group (standard care) and the second acted as the treatment group (integrated CRP) recruiting both IC and coronary artery disease (CAD) patients. Feasibility measures included: number of eligible patients, recruitment and retention rates, number of adverse events, and acceptability of trial and treatment procedures. Acceptability of the trial and treatment procedures was investigated through both quantitative data (e.g., return rates on questionnaires and exercise diaries) and qualitatively through semi-structured focus groups and individual interviews with both patients and staff.

Pilot data was collected pre- and post-SEP including exercise capacity, free-living activity, and patient-reported outcome measures (PROMs). Maximal walking distance (MWD), taken from the exercise test of IC participants, was used for an *a priori* sample size calculation to inform a future RCT study.

Both the quantitative and qualitative data was used to evaluate the study's methodology to guide a future large-scale RCT.

Results: Eligibility rates were 85% for the IC control group, 92% for the IC treatment group, and 81% for the CAD group. A total of 19 IC patients were recruited to the control group, and 17 IC patients and 21 CAD patients were simultaneously recruited to the intervention giving consent rates of 36%, 24%, and 26%, respectively. Retention rates were 79% IC control group, 65% for the IC intervention group and 72% for the CAD group. No adverse events were reported during the study.

There were high return rates for all questionnaires and participants found the trial measures to be low burden. The qualitative assessment of treatment acceptability recruited 8 patients from the IC control group (54%), 4 patients from the IC intervention group (36%), and 6 patients from the CAD group (40%). Four themes emerged from these interviews: Staff, Shared Experience, Rehabilitation Setting, and Barriers. Ten CRP staff were recruited to assess their acceptability to the treatment. Three themes emerged from these interviews: adaptations to service, differences between patient groups, and making a difference.

The IC control group mean maximal walking distance (MWD) significantly increased by 219 metres post-SEP ($p = <0.001$), and the IC treatment group's mean MWD significantly increased by 283.7 metres post-SEP ($p = 0.007$). The improvements in walking capacity between the two IC groups were not significantly different ($p = 0.495$). The CAD groups improved their functional capacity similar to national averages for patients attending CR in the UK.

Using the pilot data for mean improvement in PWT in the IC treatment group, for a future trial to see a significant change with an 82% power at the 5% level of significance, 25 participants would be needed for each participant group.

Conclusion: An integrated CRP is feasible for patients with IC. Furthermore, combining IC and CAD patients may have the additional benefits to a single-disease rehabilitation model due to peer support and changed patient illness perception.

Although CRP staff found the implementation of the integrated programme initially difficult, they perceived it as a logical development in service provision. They enjoyed the opportunity for professional development offered by delivering rehabilitation to a different clinical group, and felt they were making a difference to PAD and CAD patients' treatment.

A fully powered RCT is required to establish the efficacy of integrated CRP for PAD patients in the UK.

List of Publications

Caldow, E., Findlow, A., Granat, M., & Schoultz, M. (2019). Incorporating an exercise rehabilitation programme for people with intermittent claudication into an established cardiac rehabilitation service: A protocol for a pilot study. *Contemporary Clinical Trials Communications*, 15, 100389. https://doi.org/10.1016/j.conctc.2019.100389

Birkett, S.T., Harwood, A.E., Caldow, E**.**, Ibeggazene, S., Ingle, L., et al. (2021) A systematic review of exercise testing in patients with intermittent claudication: A focus on test standardisation and reporting quality in randomised controlled trials of exercise interventions. *PLOS ONE* 16(5): e0249277. https://doi.org/10.1371/journal.pone.0249277

Harwood, A. E., Pymer, S., Ibeggazene, S., Ingle, L., Caldow, E., & Birkett, S. T. (2021). Provision of exercise services in patients with peripheral artery disease in the United Kingdom. *Vascular*. https://doi.org/10.1177/17085381211035259

Ibeggazene, S., Pymer, S., Birkett, S. T., Caldow, E., & Harwood, A. E. (2022). A systematic review of exercise intervention reporting quality and dose in studies of intermittent claudication. *Vascular*. https://doi.org/10.1177/17085381211070700

Harwood, A., Caldow, E., and Cucato, G. (2022) Exercise testing in peripheral artery disease. In Davison, R.C.C., Smith, P., Hopker, J., Price, M.J., Hettinga, F., Tew, G., & Bottoms, L. (Eds.), *Sport and Exercise Physiology Testing Guidelines: Volume II - Exercise and Clinical Testing. The British Association of Sport and Exercise Sciences Guide* (2nd ed., pp. 267-276). Routledge.

Whorlton-Jones, E. R., Seed, S. A., Waddell, A., Caldow, E., Harwood, A. E., & Birkett, S. T. (2022). Does the level of encouragement affect 6-minute walk test performance in patients with intermittent claudication? A protocol for a randomised multicentre controlled trial. *Journal of the Vascular Society of GB & Ireland*. (Online Ahead of Publication). http://doi.org/10.54522/jvsgbi.2022.028

Conference Presentations

Caldow, E. Developing a Supervised Exercise Programme for Patients with Peripheral Artery Disease: Rehab for the Legs – Prehab for the heart. BACPR EPG Study Day. Aston University. May 2015

Caldow, E. Developing a Supervised Exercise Programme for Patients with Peripheral Artery Disease. College of Podiatry Annual Conference 19th November 2016 – SECC Glasgow

Poster Presentations

Birkett, S., Caldow, E., Taylor, R., Casnello, S., and Cook K. Integration of Peripheral Artery Disease Patients into a Cardiac Rehabilitation Model. Accepted Poster Presentation. BACPR EPG Study Day. Aston University. May 2015

Chapter 1 Introduction and Thesis Overview

1.1 Context of the Research

Peripheral artery disease (PAD) is a progressive disease that occurs as the result of reduced blood flow in the major arteries, most commonly of the leg (Mays et al., 2013). PAD can have a negative impact on walking ability and activities of daily living (ADLs), as well as reduced quality of life (Harwood et al., 2017; Liles et al., 2006; Sagar et al., 2012). It is the third most common form of atherosclerotic disease after coronary artery disease and stroke with an estimated incidence globally of over 236 million, which has increased from approximately 200 million in 2010 (Song, Rudan, Wang, et al., 2019). A close link exists between PAD prevalence and advancing age, with approximately 3% of adults under 50 years old affected rising to approximately 20% in those over 70 years old (Song et al., 2019).

The classic manifestation of PAD is intermittent claudication (IC) which is characterised by exertional pain or discomfort in the calf, thigh or buttock that is relieved with rest (Morley, 2018). However, not all PAD patients are symptomatic, with only 20% reporting symptoms of IC, and around a third of patients reporting atypical exertion-related symptoms (Hankey et al., 2006).

Treatment options for people with IC in the UK have previously been limited to endovascular revascularisation (angioplasty), bypass surgery (e.g., femoral-popliteal), and pharmaceutical therapy (e.g., a vasodilator such as naftidrofuryl oxalate). In 2012, the National Institute for Health and Clinical Excellence (NICE) released guidance recommending that patients with IC should be offered a supervised exercise programme (SEP) as first-line treatment (NICE, 2012b) with the options of revascularisation (angioplasty and bypass) only to be considered if the SEP had not led to sufficient improvements in symptoms. This decision to place SEP as the first-line treatment for IC was based on high-quality evidence for its efficacy and cost-effectiveness in increasing walking distances and improving quality of life (Conte et al., 2015; Gerhard-Herman et al., 2017). However, the current availability of SEPs in the UK is insufficient, and many newly diagnosed IC patients cannot access this first-line, evidence-based treatment option.

In 2009, only 24% of vascular units in the UK had an available SEP to refer patients to (Shalhoub et al., 2009), with common barriers of limited resources, availability of qualified

staff, and financial limitations being reported. A follow-up review of service provision in 2020 showed that the availability of SEPs had increased to 48% of vascular units; however, this only equated to 23 rehabilitation programmes being available in the UK. Barriers to the provision of SEPs identified were limited resources, availability of qualified staff, and financial limitations (Harwood et al., 2021). These data show that little has changed since the release of the NICE guidance nearly a decade ago. IC patients are not able to access the first-line treatment option for their limiting condition. A different approach to service provision needs to be considered.

Rather than addressing this service provision issue through new IC-specific programmes, one option is for already established rehabilitation programmes to expand their service to include people with IC. One service that has been proposed is cardiac rehabilitation (Cheetham et al., 2004; Gerhard-Herman et al., 2017; Hamburg & Balady, 2011; Milani & Lavie, 2007; Shalhoub et al., 2009). Cardiac Rehabilitation (CR) has been shown to improve functional capacity and quality of life for patients with cardiovascular disease (CVD) (BACPR, 2017; BHF, 2019c; Dalal et al., 2015), and many patients with CVD share the same atherosclerotic pathophysiology as PAD patients. With 233 cardiac rehabilitation programmes (CRPs) available in the UK (BHF, 2019c) with qualified staff delivering exercise-based rehabilitation (Dalal et al., 2015), this makes an integrated CRP for IC patients an attractive option.

To date, the feasibility of an integrated CRP for IC patients has not been explored. Although the two groups share the same underlying cause of their disease, there are major differences in the presentation and limitations of their clinical conditions. For example, patients with IC have altered walking patterns compared to non-PAD populations (Chaudru et al., 2019; Clarke et al., 2013) and a functional capacity of approximately 50% of age-matched controls (Harwood, Cayton, et al., 2016; Milani & Lavie, 2007). Another key difference is that cardiac patients are referred to CRP following treatment of their heart condition, whereas SEP is the primary treatment for IC patients. The two groups are, therefore, at different stages of their treatment journeys. Differences in illness perception and perception of the treatment being offered may exist between the two groups (Alsen et al., 2008). The impact of these and other differences on an integrated CRP needs to be investigated.

The primary aim of this thesis therefore was to investigate the feasibility of integrating patients with IC into an already established CRP. The secondary aims are:

i. Investigate the acceptability of trial procedures to patients and staff.
ii. Identify the appropriate outcome measures to use to guide a definitive study of integrated CRP efficacy.

The initial objectives for the thesis were:

i. To conduct a review of the current literature around integrated models of rehabilitation.
ii. To critique the methodological approaches used in the literature to guide the design of this current feasibility study.

1.2 Structure of this Thesis

This thesis is presented in six chapters. This current chapter has introduced the context of the research and highlighted the gap in service provision that provided the original motivation for the thesis. It also presents the overall aims and initial objectives of the thesis. **Chapter Two** provides a background to PAD and IC including prevalence, diagnosis, and treatment options. It also contains a review of the current evidence within the field of integrated rehabilitation. **Chapter Three** details the protocol of this research project and data analysis plan and provides a critical appraisal and justification for the methodological approach. The early challenges and pragmatic changes made to the protocol are also discussed. **Chapter Four** presents the study's findings with trends and interesting outcomes highlighted. **Chapter Five** evaluates the feasibility of the integrated CRP by critically exploring the study findings. The strengths and weaknesses of the study are also discussed to highlight development areas for the future definitive efficacy study. **Chapter Six** provides overall conclusions, including specific recommendations on the structure and application of a large-scale study into the efficacy of incorporating IC patients into a CR programme. There is also discussion over the general recommendations for future investigation into IC rehabilitation and integrated rehabilitation gained during the completion of this thesis.

Chapter 2 Literature Review

This literature review is separated into two parts. Part one focuses on Peripheral Artery Disease (PAD) prevalence, diagnosis, and the main treatment options for patients with symptomatic PAD – intermittent claudication (IC). A review of the evidence to support supervised exercise programmes (SEPs) in the treatment of people with IC is provided, with a review of the current poor provision of SEPs in the UK. Part two focuses on current literature on integrated models of rehabilitation as opposed to single-disease rehabilitation programmes. The methods of investigation used in this literature is reviewed to support in the development of this current study's design.

2.1 Part One – Peripheral Artery Disease

Peripheral artery disease (PAD) refers to any pathological process that causes a reduction in blood flow – also known as ischaemia – in any artery outside of the coronary and cerebral system (Hankey et al., 2006). The most common cause of PAD is a narrowing of the artery lumen due to a build-up of atherosclerotic plaque, and although it can present in any major artery, it is most commonly found in the arteries of the leg (Mays et al., 2013). PAD is the third most common form of atherosclerotic disease after coronary artery disease and stroke, with an estimated incidence globally of over 236 million. This has increased from approximately 200 million in 2010 (Song, Rudan, Wang, et al., 2019). Collecting prevalence data in the UK is made difficult by differences in primary and secondary care coding of PAD. However, a study by Cea-Soriano et al. (2018) gave the figure of 1,306,192 people living with PAD in 2014. There is a close link between PAD prevalence and advancing age with approximately 3% of adults under 50 years old affected rising to approximately 20% in those over 70 years old (Song et al., 2019).

PAD can have a negative impact on walking ability and activities of daily living (ADLs), as well as reduced quality of life (Harwood et al., 2017; Liles et al., 2006; Sagar et al., 2012). The classic manifestation of PAD is intermittent claudication (IC). This is characterised by exertional pain or discomfort in the calf, thigh or buttock that is relieved with rest (Morley, 2018). These symptoms are due to an imbalance in oxygen supply and demand in the affected working muscle as a result of the localised ischaemia (Falk, 2006). The reduced availability of

oxygen causes the muscle tissue to respire anaerobically resulting in pain and discomfort (Wasserman et al., 2011). Cessation of the exercise or exertion removes the demands placed on the muscle, and the pain or discomfort eases as the oxygen supply begins to meet the demand of the respiring muscle. As the claudication symptoms are relieved by rest, it is therefore classed as 'intermittent'. It is thought the term 'claudication' gets its name from the Roman Emperor Claudius (ruled from AD 41-54) who walked with a limp. However, only around 20% of patients with PAD report these classical symptoms. Many patients report atypical exertion-related symptoms (Hankey et al., 2006) with some having no apparent symptoms at all (Tam et al., 2016). PAD has been proven to lower walking distances and reduce walking speeds in patients regardless of whether the disease is symptomatic or not (Harwood, Cayton, et al., 2016; Tam et al., 2016).

2.2 Diagnosis of PAD

PAD diagnosis is established through patient history, clinical examination of the pulses in the lower limbs, and measurement of the ankle-brachial pressure index (ABPI) using Doppler scanning (Harwood et al., 2022). ABPI is a non-invasive procedure that compares the systolic blood pressure (SBP) of the ankle and brachial arteries. There should be little to no difference between the ankle artery and brachial artery SBP, as arteries have smooth muscle present within the media which provides elastic recoil of the artery helping to maintain blood pressure systemically (Krishna et al., 2015). A fall in SBP of the artery of the lower limb signifies ischaemia. Measurements are made using a standard BP cuff (sphygmomanometer) and Doppler probe (ultrasound) to record the SBP of the brachial arteries of both arms and then in the ankle using the posterior tibial artery, dorsalis pedis artery, and peroneal arteries (Figure 2.1). The pressure index is then calculated by dividing the highest ankle pressure by the highest arm pressure (Gerhard-Herman et al., 2017).

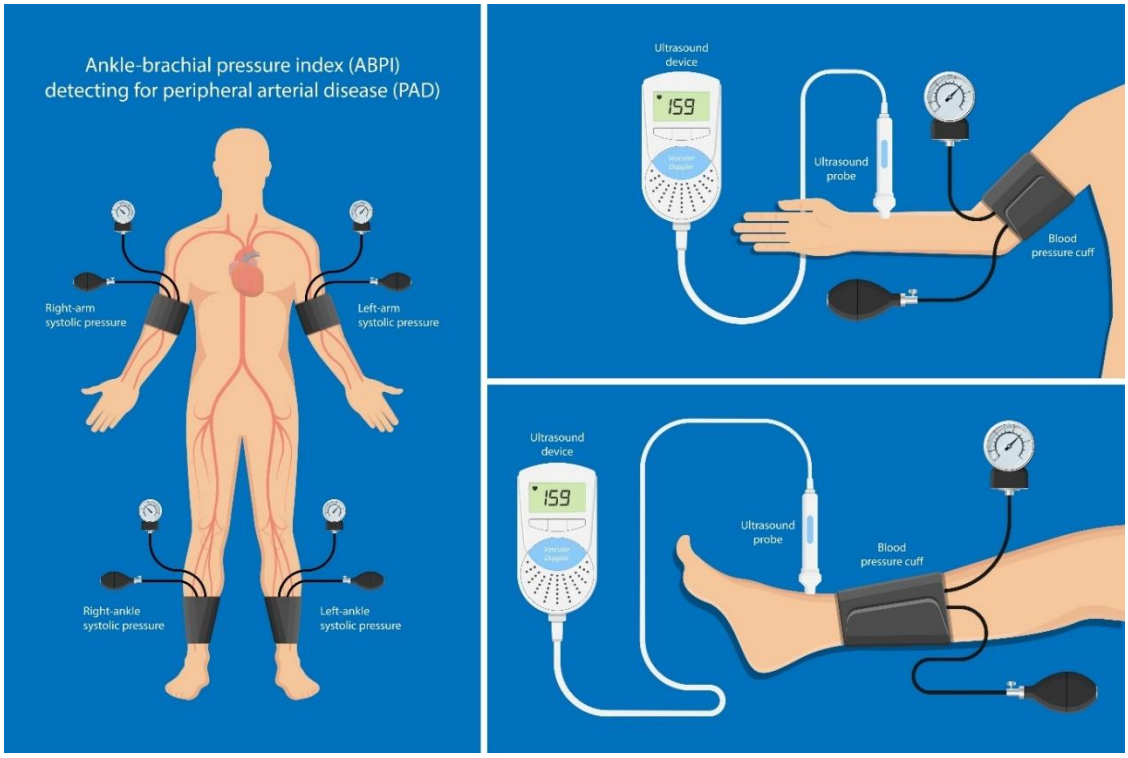


Figure 2.1 Positioning of the sphygmomanometer and Doppler (ultrasound) device for measuring ankle and brachial arteries. Image used under license from Shutterstock.com

If ABPI is between 1.00 and 1.40 the test is considered normal (Table 2.1). If the ABPI is between 0.41 and 0.90 then this shows mild to moderate PAD. Severe impairment is diagnosed when the ABPI is less than 0.40. The ABPI is highly sensitive, with a measurement of less than 0.9 being up to 95% sensitive in detecting disease that would be also identified in a more invasive angiogram (Norgren et al., 2007).

Table 2.1: Values for the ABPI used to diagnose PAD – taken from ACC/AHA Guidelines (Gerhard-Herman et al., 2017)

Interpreting the Ankle Brachial Pressure Index:	
Noncompressible	>1.4
Normal ABI	1.00 – 1.40
Borderline (equivocal)	0.91 – 0.99
Mild to Moderate Impairment	0.41 – 0.90
Severe Impairment	< 0.40

An ABPI greater than 1.4 is possible when the ankle arteries are noncompressible which indicates calcification. As described above, the atherosclerotic plaque formation reduces the diameter of the artery lumen which reduces blood flow. The atherosclerotic plaque is usually 'spongy' meaning that the artery can be fully compressed by the cuff during the BP measurement, and an accurate systolic BP can be obtained. When calcium deposits form in the plaque it becomes rigid, and the artery cannot be fully compressed during the procedure. This is common in people with a long history of diabetes and people with chronic kidney disease (Covic et al., 2010). If the artery cannot be fully occluded by the BP cuff, an ankle BP is recorded that is higher than the brachial, resulting in an ABPI of >1.4. This artificially high ABPI still suggests the presence of PAD as the lumen diameter will still be reduced by the rigid plaque, however, it requires confirmation through other methods (Gerhard-Herman et al., 2017).

2.2.1 Toe-brachial Pressure Index (TBPI)

In the case of a noncompressible artery in the ankle and artificially elevated ABPI, the use of toe pressures can be used – this is referred to as a toe-brachial pressure index (TBPI). The arteries in the toes are rarely noncompressible so they make a reliable alternative to dorsal or pedal arteries. A TBPI of ≤ 0.7 is classed as abnormal and confirms the diagnosis of PAD (Gerhard-Herman et al., 2017).

2.2.2 Post exercise ABPI to Confirm PAD

Another alternative method to assess for PAD is the assessment of ABPI following an exercise challenge. Patients are asked to walk on a treadmill until limited by claudication symptoms. The ABPI is then calculated and if the APBI then falls within the diagnostic range for PAD (≤ 0.9), then a PAD diagnosis is confirmed. If a treadmill is not available, then a pedal plantarflexion test can be administered (Gerhard-Herman et al., 2017). This involves performing standing calf raises until symptom limitation, with ABPI measurement following.

2.2.3 Other Classification Methods for PAD

Claudication symptoms and reduced ABPI highlights to the vascular specialist the severity of the PAD in terms of risk critical limb threatening ischaemia. However, the severity of the disease without ABPI can be made using one of two common systems – the Fontaine and the Rutherford classification (Table 2.2).

Table 2.2 Fontaine and Rutherford classifications for peripheral artery disease

Fontaine		Rutherford		
Stage	Clinical	Grade	Category	Clinical
I	Asymptomatic	0	0	Asymptomatic
IIA	Mild claudication	I	1	Mild Claudication
IIB	Moderate-severe claudication	I	2	Moderate claudication
		I	3	Severe claudication
III	Ischaemic rest pain	II	4	Ischaemic rest pain
IV	Ulceration or gangrene	III	5	Minor tissue loss
		III	6	Major tissue loss

2.3 Atherosclerosis and Disease Progression

Atherosclerotic plaques form on the artery wall causing a narrowing of the lumen (Falk, 2006). For plaque formation to take place, damage must occur to the endothelium – the cells lining the inside of the artery. This damage can occur as the result of shear stress (due to hypertension), chemical damage from nicotine and carbon monoxide present in cigarettes, elevated blood glucose levels (in people with diabetes or pre-diabetes), amongst other factors (Krishna et al., 2015). When the endothelial cells become damaged, low-density lipoproteins (LDLs) begin to migrate into the intima – the next layer of the artery wall (Figure 2.2). The body's natural defence mechanism is initiated, and monocytes (white blood cells) engulf the infiltrating LDL. The monocytes then become stuck in the intima and over time turn into what is called foam cells. As the atherosclerotic process progresses over time "fatty streaks" or plaques start to appear. The foam cells die, releasing the lipid (Krishna et al., 2015). The damage to the intima causes the smooth muscle present in the media (the middle layer of the artery wall) to migrate into the intima. The cells begin to divide and form a 'matrix' of proteins and collagen. Over time the plaque size develops and the lumen, and therefore the available space for blood to flow through the artery decreases (Muller et al., 2013).

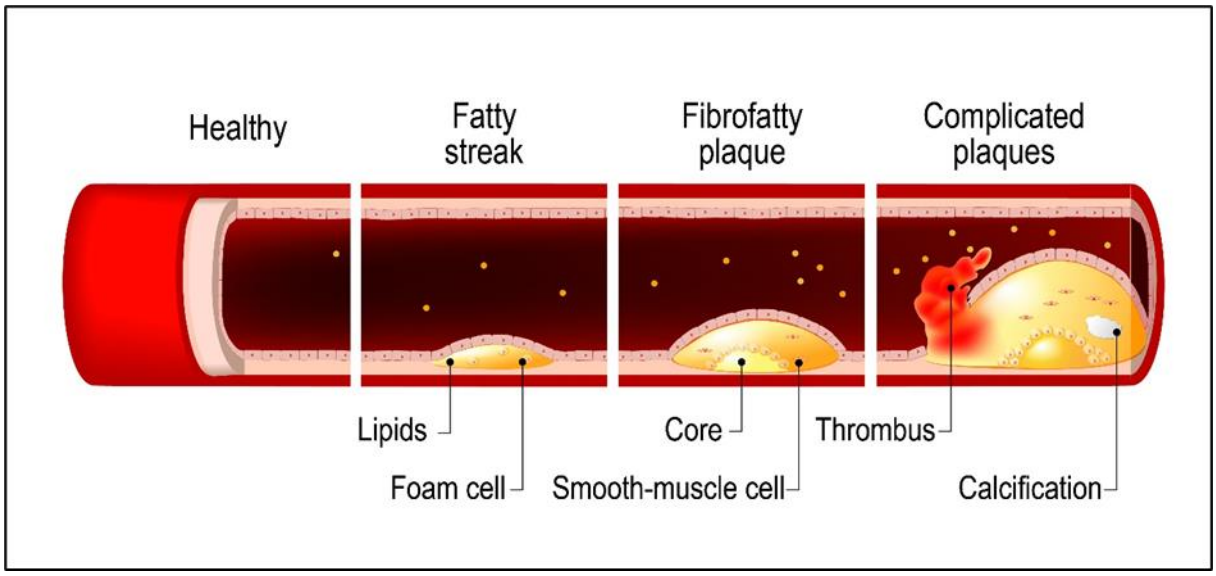


Figure 2.2: Diagram of the pathogenesis of atherosclerosis. Image used under license from Shutterstock.com

This reduction in lumen diameter causes a reduction in oxygen-rich blood delivery, known as ischaemia. When this occurs in the major arteries of the legs it can result in intermittent

claudication (IC). When there is an increased requirement for oxygen from the leg muscle, in the case of exertion or exercise, the affected artery cannot meet the demand. There is insufficient oxygen delivered to the skeletal muscle for it to work aerobically (with oxygen as the main fuel source) and the muscle begins to rely on anaerobic respiration. Anaerobic respiration results in the production of a by-product called lactic acid. Lactic acid breaks down in the skeletal muscle to form lactate and hydrogen ions. Lactate is used as a fuel source, entering the Krebs Cycle, and the hydrogen ions are buffered by bicarbonate (an alkali) to prevent acidosis. This buffering process produces water and carbon dioxide. However, if the production of lactic acid is too great, and the subsequent build-up of hydrogen ions cannot be buffeted, this results in localised acidosis as the hydrogen ions lower the pH (Wasserman et al., 2011). This acidosis leads to localised muscle fatigue, pain, and cramping. Although anaerobic respiration is a normal occurrence for healthy individuals experienced during activities of high intensity (e.g., high intensity interval training), in patients with PAD, the reduced lumen diameter results in anaerobic respiration occurring at low or even very low intensities, leading to pain and discomfort and early cessation of exercise compared to healthy individual (Milani & Lavie, 2007). These symptoms are the most common reason for individuals seeking a medical review with their general practitioner (GP) or other healthcare practitioners.

Due to the progressive nature of atherosclerosis, untreated PAD can lead to critical limb-threatening ischemia (CLTI) due to severe occlusion or full obstruction of blood flow. This is characterised by resting leg pain, ulceration, and gangrene, and can require amputation of the affected limb (Krishna et al., 2015; Peach et al., 2012). Most PAD patients do remain stable, with prevalence data on CLTI in people with PAD estimated between 10% (Conte et al., 2019) and 20% (NICE, 2013). This is similar for symptomatic PAD patients, with only 5-10% of those with IC developing CLTI within 5 years, and only 1-2% of patients requiring amputation (NICE, 2013). Although there is a relatively minimal risk of CLTI and amputation both in symptomatic and asymptomatic PAD, there is a major concern regarding the risk of PAD patients developing other atherosclerotic diseases such as cardiovascular disease (CVD) and cerebrovascular disease; both of which are linked to morbidity and premature death.

2.3.1 Risk of Other Atherosclerotic Diseases

A diagnosis of PAD is an early indicator for developing high-risk pathologies such as myocardial infarction (MI), angina and stroke (Falk, 2006; Hankey et al., 2006; Morley, 2018) due to the shared pathophysiology of atherosclerosis (Burns et al., 2003). Patients with a diagnosis of PAD have the same relative risk of cardiovascular death as those with established coronary and cerebrovascular disease (Criqui et al., 1992; Muller et al., 2013). Approximately 10- 15% of patients with IC will die prematurely due to CVD, and 20% will go on to have a non-fatal cardiac event within 5 years of diagnosis (Morley, 2018; NICE, 2013). Therefore, early diagnosis and treatment are essential due to the risk of increased cardiovascular mortality and morbidity, as well as to reduce the need for surgical invention on the affected limb or limbs.

2.4 Treatment Options for PAD

Previously in the UK, the three main treatment options for patients with intermittent claudication were:

- Endovascular revascularisation (angioplasty)
- Bypass surgery (e.g., femoral-popliteal)
- Pharmaceutical therapy (e.g., a vasodilator such as naftidrofuryl oxalate)

The aims of the above treatments are to increase the pain-free and maximal walking distances of people with PAD by restoring or increasing the blood flow to the occluded area. This in turn helps to reduce the risk of complete occlusion of the affected artery which can lead to irreversible necrosis of the surrounding tissue (CLTI) and eventual loss of limb.

2.4.1 Endovascular Revascularisation

Endovascular revascularisation, or angioplasty, is a technique used to restore blood flow to the affected artery from inside the lumen (i.e., percutaneously). For this reason, it is also known as percutaneous transluminal angioplasty (PTA). The patency or flow of blood through the affected artery is improved by flattening the atherosclerotic plaque. A catheter is inserted into the affected artery, via the femoral artery, and placed next to the blockage. A guidewire is then passed through the blockage, and a small balloon is inserted along the guidewire into the blocked area. The balloon is then inflated, which pushes the atherosclerotic plaque

spreading it out along the artery wall and thus increasing the lumen diameter. If required, a small metal structure known as a stent is placed in the blockage to support the artery. The stent is a metallic scaffold that sits around the balloon, and as the balloon inflates, the scaffold locks into place. The balloon is then deflated, and then the guidewire, catheter, and deflated balloon is withdrawn from the artery. The average cost of an elective angioplasty with stent is £3,866 (cost range £1,921 to £5,6790) (Department of Health & Social Care, 2016).

A systematic review by Fakhry et al. (2018) of three studies (125 participants) comparing PTA to usual care (advice only) showed a large increase in pain-free walking distance (PFWD) (standard mean difference (SMD) 1.29, 95% CI 0.90 to 1.68) and a moderate effect on maximum walking distance (MWD) (SMD 0.7, 95% confidence interval (CI) 0.31 to 1.08). Although this data supports the use of endovascular revascularisation versus usual care, two studies (103 participants) showed the improvements in PFWD and MWD are no longer present at 5-year follow-up: PFWD (SMD 0.69, 95% CI -0.45 to 1.82) and MWD (SMD 0.67, 95% CI -0.30 to 1.63) (Fakhry et al., 2018). One study also found there to be no long-term effect on quality of life with endovascular revascularisation.

2.4.2 Bypass Surgery

Bypass surgery is a more invasive, surgical revascularisation procedure used when endovascular revascularisation is inappropriate (Greenhalgh et al., 2008). In the case of severe or total occlusion, the guidewire and balloon used in angioplasty cannot pass through the blockage and bypass surgery may be the only option to restore blood flow. Bypass surgery may also be preferable to endovascular revascularisation if the affected artery has a high amount of calcium deposited within the atherosclerotic plaque, or vascular calcification, as this can cause procedural difficulties. As calcified plaque can be more rigid there is greater risk of incomplete stent expansion which can increase the risk of thrombosis and in-stent restenosis (Camnitz & Keeley, 2010), and increased risk of dissection or rupture of the artery (Liu et al., 2015).

During the bypass procedure a new conduit (vessel) is placed above and below the point of blockage in the artery (Muller et al., 2013). The preferred vessel is one of the patient's own blood vessels, usually the saphenous vein of the affected leg (NICE, 2012b). This is known as

an autologous or autogenous vein and has a reduced chance of infection and rejection post-bypass surgery. If there is no suitable autologous vein, then an artificial vessel made from poly-tetra-flouro-ethylene (PTFE) or a synthetic polyester material such as Dacron is used to bypass the blockage (NICE, 2012b). The average cost of bypass surgery is £10,858 (cost range £8,248 to £12,836) (Department of Health & Social Care, 2016).

2.4.3 Pharmaceutical Therapy

Following best-medical therapy guidance, when diagnosed with PAD, patients should be started on antiplatelet and cholesterol-lowering medication to reduce the risk of thromboembolic events and attenuate the atherosclerotic process (Layden et al., 2012). This usually takes the form of clopidogrel and a statin (an antiplatelet and cholesterol-lowering medication, respectively). These medications, however, are a form of secondary prevention and do not reduce claudication symptoms. Vasoactive drugs such as cilostazol, pentoxifylline, inositol nicotinate, and naftidrofuryl oxalate are used to improve symptoms, with the latter being the recommended first choice according to NICE (2012a). Naftidrofuryl oxalate (a 5HT2 receptor antagonist) is a vasodilator used to treat claudication symptoms by increasing the diameter of the artery resulting in increased lumen size and improved blood flow. Although medical therapy for IC has been shown to improve PFWD and MWD by 40%, the long-term benefits for limb preservation compared to other treatments are questionable (Mazari et al., 2013). As with endovascular revascularisation and bypass surgery, pharmaceutical therapy is not without complications and is often discontinued due to side effects of headaches, diarrhoea, and palpitations (Gerhard-Herman et al., 2017).

2.5 Evidence for Exercise Therapy for PAD

2.5.1 Exercise Therapy for PAD – A Brief History

Over the past 50 years, there has been increased support internationally for the use of exercise therapy in the treatment of PAD (Bendermacher et al., 2006; Gardner et al., 2012; Hiatt et al., 1990; Larsen & Lassen, 1966; McDermott et al., 2014; McDermott et al., 2019; Skinner & Strandness, 1967). One of the earliest studies into exercise for PAD was a small-scale trial by Skinner and Strandness (1967) which showed the benefits of repeated walking bouts on maximal walking time (MWT) in four men with IC. The authors concluded that

increased collateral circulation was the underlying cause of the increase in MWT and that this was stimulated by the initial periods of walking to claudication. Although this did show the benefits of continuing to walk once claudication pain had subsided, the research was on acute changes only, with the testing period being on four consecutive days. This research was not designed to show the benefits of long-term exercise training and further research was required to investigate this.

In 1990, Hiatt et al,. conducted a randomised control trial (RCT) investigating the effect of a programme of supervised treadmill walking. The study recruited nineteen male subjects with symptomatic PAD (ABPI 0.90 and below – although exact APBI for participants data for the group was not presented). Participants were randomised into an exercise group (60-minute session, 3 x per week, for a duration of 12 weeks) or a non-exercising control group. The exercise group significantly increased both their pain-free walking time (PWT) by 165% and MWT by 123% ($p<0.05$). The control group had a 20% increase in MWT which was significant ($p<0.05$), but there was no change in PWT. The maximal calf blood flow, measured using plethysmography, was shown to significantly increase in the exercise group by 38% from baseline ($p<0.05$). This was thought to be caused by an improvement in skeletal muscle oxidative metabolism brought about by the ischaemia-inducing exercise programme. Although the research of Hiatt et al. (1990) showed significant increases in walking ability in a group with a mean age representative of the PAD population (61 years ± 13), the subject number was small (n = 19) and there was a gender bias as all participants were male. This study also did not investigate the intervention's effect on quality of life which is known to be negatively impacted by PAD. The exercise intervention was limited to treadmill walking which, although suitable for a controlled research environment, might not be suitable to a hospital or community exercise programme with limited treadmill availability.

2.5.2 Aerobic Versus Strength Training for PAD

The first study to consider a mode of exercise outside of treadmill-based walking for people with PAD was conducted by Hiatt et al. (1994). They hypothesized that due to the presence of muscle weakness in the PAD population, a programme of strength training would be as effective as treadmill walking. Twenty-nine patients with symptomatic PAD were enrolled on a cross-over study. During the first part of the study, patients were randomised to 12 weeks

of supervised treadmill walking (3 hours per week, walking to claudication pain), a strength training group (3 hours per week, lower limb exercises), and a non-exercising control group. Post-intervention data showed that the walking group improved their PWT by 74% (± 58%) whereas the strength training group only improved by 36% (± 48%). There were no changes in the control group. In the second part of the study, the strength training group began the 12-week supervised treadmill walking programme, and the control group began a combined strength and treadmill walking programme. The improvements in both groups were similar to the initial treadmill walking group's results in the first part of the study. This study showed the strength training was less effective as supervised treadmill, but there are benefits of combined strength and treadmill exercise programmes.

Gender bias was again present as all participants of this study were male which reduces the generalisability of these research findings. Another limitation of the study was the categorisation of ABPIs in the process of diagnosis. The cut-off point for PAD diagnosis in this study was <0.94, rather than the internationally agreed <0.9. This may have resulted in inclusion of participants will borderline PAD who may not have been significantly symptom limited.

2.5.3 Supervised Versus Non-Supervised Exercise

A study by Patterson et al. (1997) was one of the first studies to look at the effectiveness of supervised versus non-supervised exercise programmes. The study randomised forty-six participants into 12 weeks of supervised exercise and education, or a 12-week home-based exercise group. There was a near 50-50 split between male and female participants in the study (52% male). Both groups had improvements in PWT and MWT, however, the supervised exercise programme showed a greater improvement than the home-based group.

A systematic review by Bendermacher et al. (2006), showed that people attending a SEP improved their walking distance by 150 meters more than people who completed an unsupervised programme. As the early research conducted in this area had small subject numbers, this systematic review provided more robust findings as it included data from 319 participants from the eight different studies it reviewed. The 319 participants had a mean age of 67 years (range 40-86) which reflects the average age of the PAD population (Song, Rudan, Wang, et al., 2019). A RCT conducted by McDermott. et al. (2014) showed that home-based

walking programmes for people with PAD are effective in increasing PWT and MWT with the benefits present at 12-month follow-up. This suggests home-based exercise programmes are a suitable alternative for PAD patients when there is no SEP available, or the patient is unwilling to attend.

2.5.4 A Comparison of SEP to Other Treatments for IC

2.5.4.1 SEP Versus Endovascular Revascularisation (Angioplasty)

A systematic review of eleven RCTs (702 participants) by Frans et al. (2012) found similar improvements in PFWD and MWD between endovascular revascularisation and SEP, with neither intervention demonstrating superiority in terms of effectiveness. Short-term improvements following endovascular revascularisation were identified, but there was no significant difference found at the one and two-year follow-up. A review of two RCTs by Fowkes and Gillespie (2008) showed at six months follow-up, patients undergoing supervised exercise had a significantly greater MWT than those undergoing angioplasty. At the six-year follow-up, the benefits of angioplasty were no longer present in one of the trials. The authors concluded that angioplasty offered only short-term benefits to the participants with symptomatic PAD. This short-term effect has also been found in a systematic review by Watson et al. (2008) where endovascular revascularisation produced greater improvements in walking distance compared to SEP, but benefits were not maintained.

In the Nottingham Health Profile (NHP) study, a comparison of SEP to angioplasty found a greater improvement in subjective health measures in the exercise group (Tisi & Shearman, 1997). There have also been high rates of restenosis reported following angioplasty which has led to further revascularisation being required (Hankey et al., 2006). Combined with the improvements in subjective health measures, this makes the more conservative approach of SEP an attractive option for the treatment of IC.

Although the benefits of angioplasty are not maintained, it does offer a ‘quick fix’ option for people with IC compared to the 12-week investment required to gain benefits from the exercise programme. This might be a key influencer for PAD patients who are not motivated to attend a 12-week SEP.

2.5.4.2 SEP Versus Bypass Surgery

There is limited comparison of exercise to bypass surgery in the literature. A systematic review by Antoniou et al. (2017) found two studies comparing bypass surgery to exercise therapy. One of the studies, by Lundgren et al. (1989), compared the walking capacity (measured using MWT) of 25 patients undergoing surgery to 25 patients completing a 6-month programme of exercise (3 x 30 minutes supervised sessions per week). Although the exercise group did not improve as much as the surgical group (150% versus 173%), the difference in walking capacity between the two groups was not significant (1.66 minutes, 95% CI, -1.25 to 4.55). The second study in the review, by Gelin et al. (2001), compared 76 patients undergoing bypass surgery to 73 patients completing a 6-month programme of exercise (using the same protocol of Lundgren et al.). In this study, the post-surgery group's mean MWD (344 ± 169 metres) was significantly higher than the exercise groups (247 ± 111 metres) following treatment (p= <0.05). This difference was maintained at 1-year follow-up.

Although there is evidence of greater improvements following bypass surgery, this option is more invasive and therefore carries a greater risk of complications compared to exercise therapy. For example, in the Lundgren et al. study comparing surgery to exercise, the recorded adverse events for the surgery group were wound haematoma (localised bleeding), thrombectomy (mechanical removal of a blood clot), and further need for reconstruction of the artery.

Due to the risk of complications, bypass surgery is usually reserved for severe levels of ischaemia (ABPI <0.4) in more proximal locations of the leg (aortoiliac or femoral-popliteal), or when there is evidence of CLTI (Peach et al., 2012). This also accounts for the limited number of studies comparing exercise to bypass surgery.

2.5.4.3 SEP Versus Pharmaceutical Therapy

A study by Kieffer et al. (2001) showed that naftidrofuryl oxalate produced a 158.7m improvement in MWD when compared to placebo (28.1m improvement, p= <0.001). This was in a relatively large study (treatment group n= 98, placebo group n=98) and the medication was taken for 24 weeks before a repeat treadmill assessment. However, the key limitation of these conclusions is the comparison of naftidrofuryl oxalate to placebo, rather than standard care. The standard care for people diagnosed with PAD is to offer a programme of supervised exercise and lifestyle modification therefore, a comparison of pharmaceutical therapy against

exercise therapy would give a better indication of clinical efficacy. In a study by McDermott and Kibbe (2017), no significant improvement in exercise capacity was shown in a vasodilator group when compared to an exercise therapy group.

2.6 Cost Effectiveness of Supervised Exercise Programmes:

Supervised exercise programmes (SEPs) improve both pain-free walking and maximal walking distances comparable to those achieved through bypass surgery, and greater than that of angioplasty (Fowkes & Gillespie, 2008; Gardner & Afaq, 2008; Murphy et al., 2008; Wind & Koelemay, 2007). SEP for PAD has also been found to be a cost-effective intervention (Bermingham et al., 2013). When the treatment cost is considered, SEPs are less expensive than the “classical” treatment options for PAD. For example, in the UK a 12-week SEP for one PAD patient would cost approximately £273 (

Table 2.3), while angioplasty with a stent would cost £3,866 (cost range £1,921 to £5,6790) and bypass surgery £10,858 (cost range £8,248 to £12,836) (Department of Health & Social Care, 2016). Combined with the fact that exercise therapy is non-invasive, this makes SEP an attractive treatment option.

Another important consideration related to cost-effectiveness is the impact of the new intervention on quality adjusted life years (QALYs). Evidence has shown that SEPs for IC patients cost between £711 to £1,608 per QALY gained (with 75-79% of models showing agreement) (NICE, 2012a).

Table 2.3: Cost of a 3-month SEP. Taken from the NICE (2012) Costing Report for Clinical Guidance 147

Resource	Estimated cost for a 1-hour session (£)	Estimated cost for 2 hours a week for 3 months (£)
2 community physiotherapists[a]	68	1,768
1 physiotherapist technician[b]	22	572
Room hire and rental equipment[c]	15	390
Total cost for 10 people	105	2,730
Cost per person	11	273

[a] From personal social services research unit – unit costs of health and social care 2011 (Curtis, 2011). Includes qualification costs.
[b]. Taken from the health economics section for supervised exercise in the full guideline.
[c] Based on expert opinion of members of the GDG.

2.7 Service Provision in the UK

With the wealth of evidence supporting its effectiveness in improving both physiological and psychological outcomes, NICE has placed SEPs at the top of their 2012 Pathway for the Management of Symptomatic PAD (Figure 2.3). This pathway states that newly diagnosed IC patients should be offered a SEP as first-line treatment, prior to consideration of surgical intervention (revascularisation). The aim of SEP is to reduce the impact of PAD on individual patients and therefore reduce the need for invasive measures that have similar benefits to SEP with increased risks of complications.

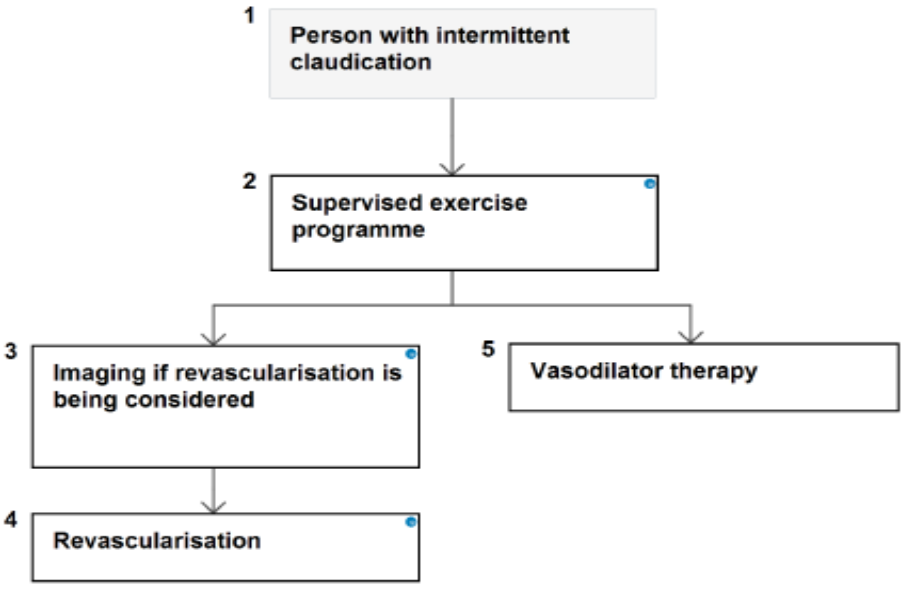


Figure 2.3 NICE Pathway for the management of IC - from Clinical Guidance CG147 (NICE 2012)

Despite this wealth of support in the literature, there is a shortage of dedicated rehabilitation programmes available in the UK. Prior to the publication of NICE Clinical Guidance 147 in 2012, only 24% of vascular units had an available exercise programme to enrol their patients on (Shalhoub et al., 2009). Since the NICE guidance on SEPs as first-line treatment for patients with IC, there has been an improvement in service provision. The review of SEP availability by Shalhoub et al., in 2009 was repeated seven years later by Harwood, Smith, et al. (2016). Their report showed an improvement in provision with 39% of vascular units now with access to a SEP. A subsequent review of provision in 2020 showed further improvement with 48% of vascular units having a SEP available (Harwood et al., 2021). This trend of increased provision

initially looks positive, but when looking at the actual number of programmes and the locations, there has been little impact of the NICE guidance on service provision. According to the 2020 survey results, there are only 23 rehabilitation programmes currently available in the UK which is a small increase from the 20 available in 2016. With 1,306,192 people living with PAD in the UK (Cea-Soriano et al., 2018), the available number of SEPs is insufficient.

When considering the geographical location of these 23 programmes, 20 programmes are based in England and the remaining three are in Wales. Northern Ireland and Scotland do not have any SEP present for PAD patients (Figure 2.4).

A limitation of this survey is that only 48 of the 93 vascular units on the National Vascular Registry (NVR) completed the survey, representing a response rate of 52% (Harwood et al., 2021). Therefore, the data does not represent all surgical units in the UK and therefore national SEP provision, however, it is unlikely the remaining 55 surgical units who did not complete the survey all have a rehabilitation programme. Even when using a conservative estimate of 50% of the 'non-responding' units having access to a programme, this would only increase the number of SEPs in the UK to 51.

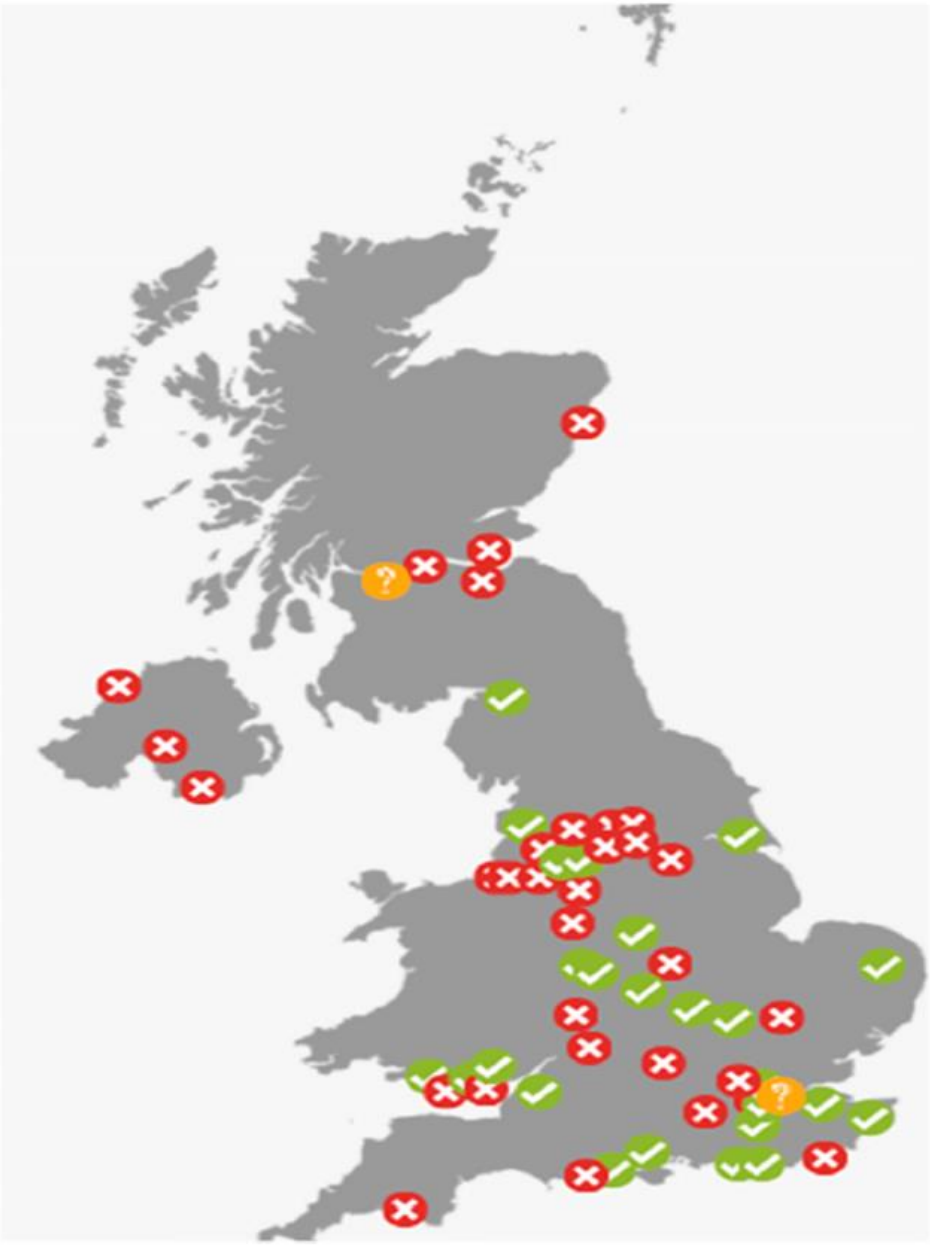


Figure 2.4 Overview of access to supervised exercise programmes (tick = access; cross = no access and question mark = don't know). Reproduced with permission from Harwood et al., (2021).

2.8 Barriers to SEP Provision

2.8.1 Resources

The main barriers to SEP provision identified are lack of available resources particularly qualified staff (Shalhoub Hamish and Davies, 2009; Bermingham et al., 2013; Popplewell & Bradbury, 2014, Harwood et al., 2021). The cost of providing a twice a week SEP for 12 weeks has been estimated at £273 per person (range £232 to £345) when delivered as a class with ten patients (Bermingham et al., 2013; NICE, 2012a). The majority of the cost (86.5%) is

staffing, with two physiotherapists and one physiotherapy technician being required. Room hire and equipment cost represent only 13.5% of the cost of providing the session. When compared to the cost of the revascularisation interventions of angioplasty and bypass surgery £3,866 and £10,858, respectively), increasing the number of SEPs within the UK could reduce costs to the NHS, and prevent the need for invasive surgery that carries risks for patients.

2.8.2 Solutions to the Barriers

The poor provision of SEP in the UK means few patients currently have access to appropriate services. With the barriers of limited resources and staff not being addressed over the last decade it is clear other solutions to service provision need to be considered. One area that has been proposed in the literature is that already established rehabilitation services, such as cardiac rehabilitation (CR), can plug the gap (Cheetham et al., 2004; Gerhard-Herman et al., 2017; Hamburg & Balady, 2011; Milani & Lavie, 2007; Shalhoub et al., 2009). Before discussing the rationale behind choosing CR for IC patients, an overview of the service will be presented.

2.9 Cardiac Rehabilitation

The British Association for Cardiovascular Prevention and Rehabilitation (BACPR) define Cardiac Rehabilitation (CR) as:

> *The coordinated sum of activities required to influence favourably the underlying cause of cardiovascular disease, as well as to provide the best physical, mental, and social conditions, so that the patients may, by their own efforts, preserve or resume optimal functioning in their community and through improved health behaviour, slow or reverse progression of disease.*
>
> *BACPR (2017)*

CR in the UK is separated into 7 stages which separate the patient journey from initial diagnosis and referral (Stage 0) all the way through to discharge and transition on to a long-term plan of ongoing support (Stage 6) (Figure 2.5).

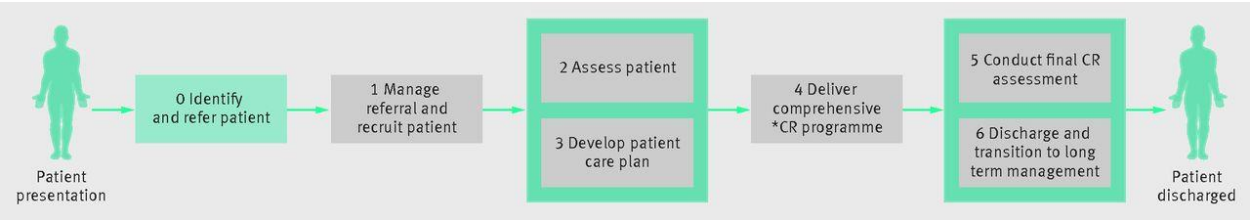


Figure 2.5 Overview of the stages of Cardiac Rehabilitation (Reproduced from Dalal et al., 2015 Cardiac Rehabilitation, BMJ. 2015;351:h5000 doi: 10.1136/bmj.h5000. CC BY-SA 4.0 license.

Although the initial stages of a Cardiac Rehabilitation Programme (CRP) can take place in a hospital or at the patient's place of residence, Stage 4 (delivery of the comprehensive CR programme) is usually provided in hospital or community settings with approximately 90% run as face-to-face as group sessions (BHF, 2019c). The average length of programmes is 8 weeks (BHF, 2019c) and consists of group-based exercise and education sessions lasting 2 hours. Approximately 10% of CRPs are offered as home-based or remote programmes (BHF, 2019c) - **N.B.** this data is pre-CV19 where service provision changed dramatically due to national lockdowns, redeployment of CR staff and repurposing of facilities, and local Trust Infection and Prevention and Control (IPC) policies.

Currently in the UK there are 233 cardiac rehabilitation programmes (CRPs) available for the 2.3 million people living with coronary artery disease (CAD) in the UK (Dalal et al., 2015).

2.9.1 Evidence for Cardiac Rehabilitation

There is a wealth of evidence showing the efficacy of CRP. A Cochrane Review of 63 trials, including 14,486 patients with CHD, showed that patients who complete a CRP following an MI or CABG reduce their absolute risk for cardiovascular mortality from 10.4% to 7.6% (Anderson et al., 2016). This review also found that attending a CRP can lead to a significant reduction in acute hospital admissions, from 30.7% to 26.1% in these two patient groups. This has a major reduction on the financial burden on the NHS as well as decreasing the overall burden of disease on the patient and their family. National audit data from CRPs in the UK have shown that they increase functional capacity above clinically meaningful levels, improve quality of life, and promote long-term self-management for cardiac patients (BHF, 2019c).

As PAD and CAD patients share a common atherosclerotic cause of their disease, there is reason for the integration of these two clinical groups to seem logical. The shared cause of disease also means that the two groups share the same risk factors. The required lifestyle

changes to address these CVD risk factors are also similar e.g., smoking cessation, lipid-lowering, and increased physical activity and exercise.

Another reason for CRP being an attractive option for improved SEP delivery for IC patients is that the BACPR promotes the expansion of its service to this group, specifically (Table 2.4).

Table 2.4: BACPR Standard 2 - Taken from the BACPR Standards and Core Components (2017)

BACPR Standard 2: Prompt identification, referral, and recruitment of eligible patient populations
Programmes should also aim to offer this service to other patient groups known to benefit (CRP): • stable angina, peripheral arterial disease, post-cerebrovascular event • post-implantation of cardiac defibrillators and resynchronisation devices • post-heart valve repair/replacement • post-heart transplantation and ventricular assist devices • Adult Congenital Heart Disease (ACHD)

However, it cannot be taken for granted that shared pathogenesis and risk factors for disease make it possible to successfully integrated PAD into rehabilitation programmes for CAD patients. There are differences between PAD and CAD in both the presenting symptoms and the limitations associated with the disease.

2.9.2 Differences in Presentation and Treatment of Disease

Both PAD patients and CAD patients share the same cardiovascular risk factors and underlying disease process, however, the treatment options are different. To illustrate this point, the comparison of the cardiac patients with stable angina pectoris (a priority group for CRP) and PAD patients with IC is offered. Both stable angina and IC are caused by the same oxygen supply and demand issues, and present with ischaemic related pain or discomfort, however, the treatment guidance differs. Patients with stable angina pectoris due to reduced blood flow to the cardiac muscle are advised to stop any exertion as soon as symptoms begin (ACPICR, 2015). These symptoms are the trigger for immediate referral for investigations e.g., cardiac catheterisation (angiography) or stress echocardiography, to assess the need for revascularisation e.g., percutaneous coronary intervention (PCI) or coronary artery bypass surgery. Patients with IC, however, are encouraged to continue to exercise through any initial

pain or discomfort and only stop at the point of near or maximal pain (NICE, 2012b). Indeed, repeated bouts of pain-inducing walking are recommended as first-line treatment for IC as part of a programme of rehabilitation. Revascularisation for IC patients is only to be considered if the exercise intervention has been unsuccessful in improving symptom management. In the case of stable angina, exercise is not considered as a first-line treatment option and is only utilised post-revascularisation intervention. This difference in treatment options is apparent in the baseline exercise capacity of PAD and CAD patients prior to starting their disease-specific, exercise-based rehabilitation.

2.9.3 Limitations of Cardiac Rehabilitation

Although there is a wealth of data supporting the use of CR, a recent study has questioned the efficacy of CR. In a multi-centred RCT of rehabilitation for patients following a MI, the RAMIT study, there was no impact on mortality, risk factors, and health-related quality of life following CR (903 participants) when compared to a non-CR control group (910 patients) (West et al., 2012). An observational cohort study of 60 cardiac patients attending one CRP found there were no changes in physical activity behaviour (measured using accelerometers) or CVD risk factor profiles following completion of a 6-week CRP (Ibeggazene et al., 2020). These recent investigations question the possibility of a CRP impacting on patients with a different condition if it cannot successfully support those patients for which it was originally designed.

There is a known association between PAD and CAD, so it is unsurprising that many patients diagnosed with a cardiac disorder also have PAD. In a review of 23,215 patients referred to Canadian CRPs following a cardiac event, a total of 1366 patients (5.9%) had a comorbidity of PAD (Devrome et al., 2019). This prevalence of PAD has also been found in patients attending CRPs in the UK (BHF, 2016) and shows the patients with PAD are already accessing CRP, albeit with a secondary diagnosis and not a primary diagnosis of IC. The study by Devrome et al. (2019) did find that patients with PAD benefitted from completing a CRP, however, on the whole they were less likely to start the programme compared to those cardiac patients without PAD. Those PAD patients that did start a CRP were also less likely to complete the programme, with limitations caused by the particular disease thought to be the casual factor of them withdrawing. This further highlights the issue that a rehabilitation programme

designed for cardiac patients might not be suitable for IC patients, unless adapted. Further investigation is required to assess the feasibility of this integrated rehabilitation. Prior to this feasibility study, the current literature on integrated models of rehabilitation needs to be reviewed.

2.10 Part Two – Literature Review

The second part of this chapter discusses the current literature on integrated rehabilitation programmes. The aim of this literature review was to establish the current knowledge-base and to identify gaps in knowledge around integrated rehabilitation. The review also aimed to critique the methodological approaches used in the literature and to guide the design of this current feasibility study. The search strategy and review of the relevant literature is presented in this next section.

2.10.1 Search Strategy

To achieve the aim of establishing the current research into integrated models of rehabilitation, a systematic search was conducted using the following databases: PubMed Central, OVID Online Database (including MEDLINE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Cochrane Library. To ensure that relevant literature was identified for this review, a robust search strategy was constructed using the Patient, Intervention, Comparison, and Outcome (PICO) structure (Table 2.5). A detailed search strategy was constructed using keywords and MeSH terms for the 'Patient' and 'Intervention' groups to ensure that all relevant literature was identified. The full details of the search strategy can be found in Appendix 1 – Literature review – Search Strategy. Records were limited to English language only including studies with adult subjects only. Due to the recent focus on integrated rehabilitation, the search was limited to articles published over the past 10 years. An initial search was conducted in June 2018 with an additional search performed in June 2021 to identify new publications.

Table 2.5: Summary of PICO structure for search strategy

Patient (or population)	Adult patients undergoing rehabilitation
Intervention	Integrated or combined rehabilitation
Comparison	Standard care (single-disease rehabilitation) or control
Outcome	Feasibility and effectiveness

The results of the database searches were exported to the Endnote citation management software and duplicate records were removed. The remaining articles were screened by reviewing the titles and abstracts to ensure their relevance prior to accessing full texts. During the screening process, the 'Comparison' elements of standard care or control and the 'Outcomes' elements of feasibility and effectiveness were used to identify relevant articles. Reference lists were hand-searched for additional relevant studies not returned in the original search. All identified articles were reviewed by the lead author for suitability to be included in the literature review. Relevant articles from grey literature were also identified during the above process and have been included in the literature review.

2.10.2 Evidence of Integrated Models of Rehabilitation

The literature review identified previous investigations into the feasibility and efficacy of integrated models of rehabilitation for patients with stroke, diabetes, chronic obstructive pulmonary disorder (COPD), and cancer. The rationale for these investigations was that there was a lack of current single-disease service provision, and integrated rehabilitation was hypothesised as a potential solution. The common programme that was utilised was cardiac rehabilitation. The results of these studies are discussed highlighting key outcomes in feasibility and potential efficacy of these integrated models. The potential efficacy of the programmes is discussed as the literature review established that there has been a limited number of RCTs conducted in this area.

2.10.2.1 Stroke Patients in CR

There is evidence supporting the efficacy of exercise-based interventions for patients following a cerebrovascular accident (CVA), or stroke, and specific rehabilitation programmes are commonly found in healthcare settings across the globe (Jeffares et al., 2021; Regan et

al., 2019; Stone et al., 2020). Despite this provision, the integration of stroke patients into CRPs has had rising interest. Stroke Rehabilitation (SR) primarily takes the form of intensive physical therapy, usually as an inpatient, that focuses on returning neurological function lost due to the stroke (Kirk et al., 2014). This initial period of post-stroke therapy is referred to as acute SR. Although acute SR is offered to all post-stroke patients (if services are available), the intervention is not designed to focus on improving aerobic-based functional capacity (cardiorespiratory fitness) and long-term CVD risk reduction. This is a real limitation for patient prognosis as the risk for future cardiovascular events such as myocardial infarction (heart attack) and recurrent strokes is high in this population. This is due to the shared disease process of atherosclerosis which is progressive. Stroke patients often leave acute SR with high levels of CVD risk factors including many modifiable ones such as physical inactivity, hypertension, dyslipidaemia, and obesity (Prior et al., 2011). This has made the CR model of exercise, education, and risk factor modification an attractive option for facilitating the medium to long-term rehabilitation for stroke patients completing the acute rehabilitation phase.

A study by Tang et al. (2010) investigated the feasibility of a 6-month once-a-week adapted CRP (with additional home-based exercise) for patients after stroke in a Canadian Healthcare Centre. Viability was assessed through uptake and retention rates from a prospective cohort of stroke patients referred to the adapted CPR after completing acute stroke rehabilitation. Out of the 41 patients starting the programme, 38 completed, giving a 93% completion rate. Participant attendance was 83.5% (± 11.5), with 31 (82%) participants attending ≥75% of classes. No adverse events were recorded during the study, and patient satisfaction with the exercise and education sessions was rated as 5 on a 1 to 5 rating scale (1 = Poor, 5 = Excellent). Changes in aerobic capacity pre- and post-CRP were assessed through mean VO_2peak and 6-minute walk test (6MWT) distance and change in risk factor profile from baseline to post-CR (6-month duration). There were improvements in VO_2peak from baseline to post-CR follow-up (14.8 ±4.8 to 16.2 ±5.1 ml/kg/min^{-1}, p= 0.046), however, there was no significant change in mean 6MWT distance of 24.6 metres (286.4 ±140 to 311 ±152.1 metres, p = 0.382). As the 6MWT is a relevant outcome measure for patients as it reflects ‘real world’ exercise tolerance (Nordanstig et al., 2014), this lack of significant change might prove important. Furthermore, there were no significant changes in stroke patients' risk factor profiles, which, considering this is a primary reason for integrating stroke patients into CRP as acute stroke rehabilitation

does not influence CVD risk factors, is an important finding. Despite these findings, the authors of this study concluded that the CR model was feasible for post-stroke patients, and CRPs should offer rehabilitation for stroke patients to improve their aerobic capacity, however, limitations in the methodology.

The Tang et al. (2010)had the stroke cohort exercise as a single-disease group and not in combination with standard CRP service users (i.e., cardiac patients). As patients from the two different groups did not mix in any way (during exercise or education sessions), the acceptability of integration into a CR programme has not been fully investigated with either patient group. Furthermore, the staff facilitating the rehabilitation programme in this study were not exposed to any possible issues of supervising stroke and cardiac patients simultaneously, so the acceptability of the treatment to staff has not been investigated. The study was therefore limited to testing the feasibility of the CRP model only, so conclusions about the feasibility of a fully integrated CRP are not supported. Considering the authors of the study stated that the main adaptation required to the CR model was the exercise session itself, this is a major weakness. In the study, the exercise sessions were adapted to suit the individual needs of each stroke patient. Although this is common practice in CRP, due to the neurological deficits present in the stroke cohort, a greater staffing level was required. Ratios of 1 staff member to 5 stroke patients were used in this study compared to 1 staff member to 12 cardiac patients reported as usual practice in the authors' standard CRP. Class sizes were required to be limited to 20 stroke patients rather than the 80-100 cardiac patients in their standard CRP. This is a significant change in staffing levels that would have financial and infrastructure issues for any rehabilitation programme incorporating stroke patients and present a potential barrier to adoption.

2.10.2.2 Integrated CRP for Patients at Risk of Stroke

Following the initial work by Tang et al. (2010) there was continual support for integrating stroke patients into CRP in healthcare settings in Canada and USA. The attraction of potential CVD risk reduction offered by the CRP model was also extended to patients with an increased likelihood of stroke patients following a transient ischaemic attack (TIA). Marzolini et al. (2016) investigated the feasibility and effectiveness of CRP for this patient group using secondary data collection of TIA patients in CRP (n= 39) and prospectively recruited TIA

patients (n = 20). The CRP utilised the same 6-month hospital-based CRP used in Tang et al.'s (2011) study: 90-minute sessions, once per week for 24 weeks, with additional home-based exercise. There was a similar convenience sampling technique and lack of control group comparison but, unlike Tang et al.'s study, TIA patients were enrolled on the CRP simultaneously with cardiac patients and were integrated during their rehabilitation programme. Overall, participant adherence to the programme was high, with a completion rate of 62% and an attendance rate of 73% for the weekly hospital-based sessions. There was a 9.3% improvement in VO_{2peak} in the retrospective group, measured using cardiopulmonary exercise testing, and a 14.3% improvement in VO_{2peak} in the prospective group with both improvements reaching statistical significance (p= 0.001 and p= 0.01, respectively). There was an improvement in mean 6MWD in the prospective TIA group (61.0 ± 73.5 metres, p= 0.06), showing a similar lack of translation to 'real world' measures of functional capacity as Tang et al. (2011). The retrospective group did not complete a 6MWT. The study did report a reduction in CVD-related risk factors; however, this was not consistent across both groups. The retrospective group had a significant reduction in mean BMI (p= 0.03) and reduced waist circumference (p= 0.001); however, these changes were not seen in the prospective group. The prospective group only showed a significant reduction in depression, measured using the Centre for Epidemiologic Studies Depression Scale (CED-D), (p= 0.007), and systolic blood pressure (p= 0.01), with neither change occurring in the retrospective group. Interestingly, the change in systolic BP was an increase, not a decrease in pressure. Although the change was from 123.6 mmHg to 131.4 mmHg, which is still classed as normotensive in the UK (JBS3, 2014). Although the changes in risk factors were not consistent across the two groups, this study does show a positive impact on participants' cerebrovascular and cardiovascular risk profiles that are not present in (Tang et al., 2010). Unfortunately, this study did not contain a qualitative arm to assess the views of patients and staff of the integrated rehabilitation programme, so an important element is missing from this current study required in future, similar studies.

To date, the evidence base for integrating stroke patients seems to be based on pilot and feasibility data, with no initial study being followed up by a larger RCT. However, CR programmes in the USA and Canada have been offering their programmes to patients for medium to long-term stroke recovery (post-acute stroke) since the initial study by Tang et al., (2011). A web-based survey conducted a review of integrated service provision by Canadian

CRPs by (Toma et al., 2020). The authors found that there was poor uptake of CRP by stroke patients. When patients did enrol, they placed similar demands on staff as found in previous feasibility studies, with 1:1 staff to patient ratios required, particularly at the start of the programme, due to the neurological deficits of stroke patients. Staff also reported a lack of resources and training to support them in facilitating rehabilitation for complex stroke patients as being a barrier to service provision. This highlighted the need for a full assessment of the feasibility of novel ways of integrating patients, particularly around the acceptability of patients and staff to the treatment and processes. This study again highlights the required adaptations to CRP and that it is not a case of opening the doors to a new patient group (Stone et al., 2020).

2.10.2.3 Stroke Patients in UK CRPs

Although Canadian and USA CRPs have integrated stroke patients for over ten years, this is not the case currently in the UK. CRPs in the NHS do not routinely take on cerebrovascular patients. However, due to the shared pathophysiology of the disease, approximately 5% of cardiac patients referred to CR have a comorbidity of stroke. In an observational study, using data from the UK's National Audit of Cardiac Rehabilitation (NACR), uptake rates to CRP in cardiac patients with a comorbidity of stroke comorbidity were investigated (Harrison et al., 2020). The authors found that programmes that were well-resourced with higher staffing levels had a greater attendance of stroke patients. Although this study was on patients with a comorbidity of stroke, it does support the findings of Tang et al. (2010) on the need for greater levels of staff required to adequately facilitate exercise sessions for patients with stroke.

2.10.2.4 Cost-effectiveness of Integrated CRP for Stroke Patients

One common finding in the studies conducted in USA and Canada is the requirement of the initial SR required in the acute stroke period (Jeffares et al., 2021; Marzolini et al., 2016; Prior et al., 2011; Regan et al., 2019). Unlike post-TIA patients, stroke patients have specific limitations in physical function following their event which means the majority of stroke patients could not enrol on a CR programme without initially completing the acute SR. If future RCTs prove the efficacy of an integrated CRP for stroke patients, the cost-effectiveness of the treatment will be limited by the requirement for most patients undergoing intensive

acute-stroke physical therapy prior to starting CRP. CRP will remain an option for medium to long-term care only.

2.10.2.5 Diabetes Patients and CRP

There is a wealth of evidence for the role of exercise and lifestyle modification for patients diagnosed with type 2 diabetes mellitus (T2DM), however, the availability of dedicated rehabilitation programmes in the UK is limited. Like with stroke patients, the suggestion of bridging the gap in service provision by expanding the offer of CRP to T2DM patients has been made. Both cardiac and diabetes patients have shared risk factors of hypertension, poor diet, obesity, and physical inactivity; they also have similar cardiac mortality rates. Although complications associated with diabetes are often non-cardiac in nature (e.g., neuropathy, retinopathy, and nephropathy), coronary artery disease (CAD) is the leading cause of premature death among people with diabetes (Banzer et al., 2004; Mourot et al., 2010). Although the suggestion of integrated CRP for T2DM has been made there has been no studies in the UK conducted to investigate the feasibility or efficacy of this type of service. Evidence can be synthesised from standard CRP research that suggested that, as is the case with stroke patients, expanding service delivery to patients with diabetes might not be an 'easy fit'.

In 2004, a prospective cohort study conducted by Verges et al. (2004) compared the benefits of a 12-week CRP for coronary artery disease (CAD) patients with diabetes (n=59) compared to age-matched non-diabetic CAD patients (n= 36). Although there was no difference in exercise capacity between groups at baseline, measured through VO_2peak, there was a significantly lower improvement in exercise capacity following CRP in the CAD patients with diabetes compared to the non-diabetes group (13% vs 30%, p= 0.002). The authors suggested that this reduced response to the CR exercise intervention was influenced by diabetic control, as they found an inverse relationship between fasting blood glucose and VO_2peak in the diabetic group (r= -0.40, p= 0.002). This further highlighted a key difference between the two sub-sets of cardiac patients: blood glucose levels. A similar study by Banzer et al. (2004) compared the change in exercise capacity following a 10-week CRP between diabetic CAD patients (n= 205) and non-diabetic cardiac patients (n=702) retrospectively and found the opposite to Verges et al. (2004). Diabetic patients with CAD had a significantly lower exercise

capacity at baseline, measured in peak METs, than their non-diabetic counterparts (5.7 ±2.3 vs 7.0 ±2.6 METs, respectively; p=<0.001), however, both groups significantly increased their exercise capacity by a similar amount (26% vs 27%, respectively, p<0.001). There were, however, significant differences in the risk factor profile of the diabetic CAD patients both at baseline and completion of the CRP, with a higher prevalence of obesity, hypertension, and presence of peripheral artery disease (PAD). Both the Verges et al. and Banzer et al. studies concluded that the current CRP design was not suitable for CAD patients with diabetes and an adapted programme with a more aggressive risk factor management reduction than their non-diabetic counterparts. A study conducted by Mourot et al. (2010) further assessed the difference in CVD risk factor profile and exercise capacity of cardiac patients with and without T2DM pre- and post-CR (n= 413 with diabetes and n= 614 without diabetes). The authors found differences in baseline characteristics upon starting the CR programme. Patients with T2DM had a higher prevalence of CVD risk factors and lower VO_2peak than their non-diabetic counterparts (14.3 ± 4.4 vs 16.6± 5.4 ml.kg.min^{-1}; p = <0.001). This lower aerobic capacity was matched with a significantly shorter 6MWT distance compared to non-diabetic cardiac patients (404 ± 117m vs 445 ± 116 metres; p= <0.001). Following a 6-week CRP, both groups had similar improvements in aerobic capacity and strength, however, the programme was intensive, with 13-hours of exercise per week including water-based exercise. This does not reflect the current delivery of hospital-based CRP delivery in the UK.

Although previous studies have not investigated the integration of diabetic patients without CAD into CRP, synthesising the evidence above suggests that patients with diabetes may have a more limited exercise capacity than non-diabetic patients. The differences between these clinical populations highlight the need for adaptation and service redesign to adequately support the new patient group. Like stroke patients, it is not just a case of opening the doors to new service users who do not have access to disease-specific services elsewhere.

2.10.2.6 Cancer Patients in CR

Similar to stroke, diabetes, and PAD, there is a wealth of literature showing the effectiveness of rehabilitation programmes for patients diagnosed with cancer. Evidence has shown that exercise-based interventions can reduce cancer-related fatigue, improve quality of life, and improve recovery times for patients before, during, and after treatment for many types of cancer (Dolan et al., 2018). As is the case with stroke, diabetes, and PAD, comprehensive

rehabilitation programmes of exercise and education have not yet become standard care for cancer patients in the UK (Hubbard, O'Carroll, et al., 2016; Munro et al., 2014). As with other rehabilitation programmes, resource limitations exist that present barriers to implementing cancer rehabilitation programmes within the NHS. Following the trend in stroke, diabetes, and PAD, the suggestion of CRPs expanding their provision to include cancer patients has been made. Although cancer patients and cardiac patients do not share the same disease process, cancer patients have a high prevalence of CVD risk factors such as physical inactivity, hypertension, and obesity (Munro et al., 2014). They also have reduced aerobic capacity and post-treatment fatigue that is common to cardiac patients, and the modality of exercise therapy is similar: aerobic-based circuit training with supplementary resistance training, further supporting the possibility of successful integrated rehabilitation. There is also a commonality between cancer and cardiac patients that is not present with diabetes and PAD patients – that they are post-treatment. Cancer patients, similar to cardiac patients, are recovering after a major event that has most likely involved intensive treatment, whether that be radio or chemotherapy, or major surgery (e.g., mastectomy for breast cancer, or bowel resection for colon cancer). The viability of integrating cancer patients into CRPs has recently been investigated within UK healthcare setting.

The Cardiac Rehabilitation in Bowel Cancer (CRIB) trial was a pilot RCT assessing the feasibility of patient integration into CR following a surgical intervention (Hubbard, Adams, et al., 2016; Hubbard, O'Carroll, et al., 2016). The trial was conducted across three NHS CRPs already established in Scotland. The standard exercise model for CR was used (60–90-minute sessions, 1-2 sessions per week, consisting of exercise followed by patient education sessions) enhancing the study's external validity and generalisability to the wider NHS CRPs. Both cancer and cardiac patients exercised together with no major adaptations to the CR exercise circuit. Feasibility was assessed through eligibility and consent rates, retention and adherence rates, and the number of adverse events recorded. A total of 74 out of 133 eligible bowel cancer patients (56%) expressed interest in the study, with 41 (31%) consenting to participate in the CRP. Following exclusion and withdrawal, 21 participants started the CRP, with 13 participants (62%) completing the required 10 out of 12 weeks.

Although the efficacy of integrating cancer patients into CR is yet to be established through a large scale RCT, the initial feasibility results from the CRIB study are positive. Both staff and patients found the combined rehabilitation acceptable, with an additional benefit of shared

experience being identified between the patient groups. The inclusion of both clinical populations in the assessment of treatment acceptability is a strength of the study. The use of a standard CR exercise circuit ensures the results of an RCT will be generalisable across the NHS.

Although there are several studies investigating the suitability of CRPs to fill the gap in service provision for non-cardiac populations, there have been other rehabilitation programmes that have assessed their suitability for plugging the gap. Interestingly, one rehabilitation programme has assessed its suitability for providing rehabilitation for a priority cardiac group that has difficulty in accessing CR.

2.10.2.7 Chronic Obstructive Pulmonary Disease and Chronic Heart Failure

An RCT by Evans et al. (2010) investigated the efficacy of an integrated rehabilitation for patients with chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) based on shared symptoms and shared disability, rather than a shared disease process. Both COPD and CHF patients report the early onset of shortness of breath and fatigue during exercise, which has similar functional capacity limitations and reductions in quality of life. Pulmonary rehabilitation for COPD is well established (Singh, 2014), however, CHF rehabilitation is not, with only 13% CRPs in the UK accepting CHF patients (BHF, 2019a) despite them being a priority group (BACPR, 2017). Although CHF comes under the CRP remit, it requires a different modality of exercise than other cardiac conditions such as post-myocardial infarction and post-revascularisation. Many patients with CHF are unable to adhere to the standard CR exercise prescription and adaptations are required. Evans et al. (2010) hypothesised that pulmonary rehabilitation clinicians who have experience in dealing with COPD patients limited by poor exercise tolerance and exertional dyspnoea would be well placed to extend their rehabilitation offer to CHF patients. After a 7-week, twice-weekly programme of integrated exercise and education, CHF patients showed significant improvement in functional capacity with a mean ISWT distance of 45 (95% CI, 23-66) metres ($p=<0.001$). The CHF control group did not show any improvement in functional capacity, with a mean ISWT distance of -5 (95% CI, -9 to 19) metres ($p= 0.46$). However, this result is unsurprising as the control group received only their usual care, and despite no detail being provided as to what constituted this ‘usual care’, the lack of improvement in ISWT distance suggests the control group were not encouraged to perform the structured exercise as part

of usual care (i.e., attend a disease-specific rehabilitation programme). A more appropriate comparison would be to a control group that was undergoing structured rehabilitation (single-disease only group), especially if the current guidance indicates this treatment option as standard or usual care.

The Evans et al. study did find that the improvement in mean ISWT distance of 60 metres (95% CI, 50-85) in the COPD patients was similar to that of the CHF patients in the same group (p=0.69). This is noteworthy, as it shows that both patient groups not only improve following a programme of rehabilitation but improve by a similar amount. The improvements of the COPD patients were also comparable to those expected in a standard pulmonary rehabilitation programme, evidencing the feasibility of simultaneous rehabilitation without negative interactions between the groups, and without the usual clinical population (in this study COPD patients) not realising the potential due to a different clinical group being present.

A limitation of this study, however, was the lack of qualitative investigation into the perceptions of staff and service users regarding this integrated rehabilitation to access acceptability.

2.10.2.8 Evidence for PAD in CR

To date, there has only been one study identified that has investigated the feasibility of integrating patients with a primary diagnosis of PAD into a CR programme. This study by Sami et al. (2021) evaluated the safety and feasibility of CR for patients who had undergone bypass surgery or endovascular revascularisation. This prospective pilot study had 100% retention to the programme, with all patients in the intervention group (n= 10) completing all sessions (36 out of 36). They also showed statistically significant improvement in mean 6MWT distance post-CR (63.8m) compared to the control group (n = 10) who only improved by 10.6 metres (p=0.043). Interestingly, no significant improvements in quality of life were found (measured using the VascuQoL-6 and SF-36) when compared to control. Although this study provides some promising findings, there are several limitations.

The study's sample size of twenty is comparable to other pilots, however, patients were not randomised to the CRP or control group. Instead, patients who could attend the programme were enrolled in the treatment group. Those unable to attend the CRP due to logistical barriers such as transportation issues or travel distance issues were assigned to the control

group. No detail was provided as to whether logistical issues were patient-reported, or formally assessed by researchers or clinicians. This may have added selection bias to the study as patients not sufficiently motivated to attend the intervention, or who perceived themselves to be too unfit to attend, could be more likely to report a barrier to attendance and assigned to the control group. Those patients who were motivated and therefore more likely to attend and complete the CRP, were assigned to the treatment group. This negatively impacts the external validity of the study.

A further limitation of the study was the lack of data for the number of patients that needed to be screened to achieve these 20 eligible patients. This information is vital for any large-scale study that follows on from the initial pilot to inform recruitment periods and overall study duration. Furthermore, for programmes interested in integrating different patient groups (e.g., CRP expanding their offer to PAD patients), staff responsible for the management and coordination of referrals require this data to forecast the likely demand placed on the service by the new patient group. Similar to previous studies in the area, there is a reliance on quantitative measurement of feasibility only, with no assessment of the acceptability of the intervention to patients and staff. Patients in the intervention group (CRP) may have been motivated to attend and complete the CR programme, and therefore reported treatment acceptability, however, staff may have been over-burdened by facilitating the service. For example, one of the quality of life measures used in the study, the VascuQoL-6 is a disease-specific measure for PAD patients, so it would unlikely that CR staff had used this before. There was also no consideration for the cardiac patients who form the usual group of patients attending the CRP. The impact on current service users (cardiac patients) needs to be assessed to ensure expanded provision does not reduce care for cardiac patients, a potential impact found in the integrated stroke patient studies. Conversely, the inclusion of a patient group could improve the service offered to the 'usual' service users, such as the benefits of cognitive impairment education to CHF patients found by (Jeffares et al., 2021). Without measurement of treatment acceptability, the potential impact can only be hypothesized.

Although this study by Sami et al. (2021) is the first to compare a novel way of offering rehabilitation to PAD patients post-revascularisation (an integrated CRP), the comparison group was a non-exercise control which is a weakness of the study. The researchers justified this non-exercise control as the current standard care in their medical centre was education

only, with no rehabilitation programme available. However, international guidance states that exercise rehabilitation should be offered to patients post-PAD diagnosis. Therefore, it would be useful for future studies to compare a novel combined rehabilitation programme to a single disease programme involving exercise. Improvements in walking distance in the novel group could then be compared more appropriately to the single-disease group. The improvements in 6MWT distance in the CRP group in this study are significantly higher than control, but this is not surprising to the nature of the control group (non-exercise). The 63.6 metre improvements post-CR programme may not be high as expected for a PAD-only group, considering studies have found improvements in walking distance of over 200% (Frans et al., 2012; Gardner et al., 2001; Gardner & Poehlman, 1995; Watson et al., 2008; Wind & Koelemay, 2007).

As this study took place in a USA medical centre, the CRP followed their specific guidance and consisted of three 90-minute sessions per week for 12 weeks. Although this duration is less than other studies involving CRP in the USA and Canada (commonly a 6-month duration), it was more intensive than CRP provision in the hospital-based programmes in the UK which is usually 60-minute sessions, 1-2 times per week for 8 weeks (ACPICR, 2015; BACPR, 2017), making it unlikely that the Sami et al. protocol could be sustainably provided in the UK.

2.10.3 Implementing Integrated Rehabilitation Programmes – Lessons From the Literature

What we know about integrated rehabilitation is largely based on evidence from feasibility studies that have yet to be followed up by RCTs. Effectiveness and efficacy of integrated rehabilitation has yet to be rigorously established in single sites, and across multiple healthcare settings. However, through reviewing the methodologies of these preliminary studies, several important areas have been identified that can guide future studies in this area. Areas such as the pre-and post-rehabilitation assessment, exercise modality, education and lifestyle modifications (risk factor reduction), psychological health, and medical management.

2.10.4 Programme Evaluation - What Outcome Measures to Use?

2.10.4.1 Current Measures Used by the Rehabilitation Programme

Measurement of intervention/rehabilitation success is an important part of any medical or health intervention. For the individual, and their families, having an objective measure of pre and post-intervention differences in physical measures such as blood pressure, body mass index (BMI) and exercise capacity, and qualitative measures such as quality of life are essential. They can support the patient's own assessment of the intervention's success or challenge their subjective assessment of lack of improvement. They can also help to quantify the level of change post-intervention from the results of the outcome measure. Not only is this important to the patient and their family, but it is also a requirement of the service to assess the impact of their programme across all patients enrolled in their service. This requirement for audit and evaluation will need to be considered as the requirement to complete additional outcome measures may impact the integration of the new patient group.

In the UK, audit and evaluation is essential for NHS services, and is usually conducted across a specific period (e.g., 12-months, or length of a pilot programme) to ensure continued funding and prevent services from becoming decommissioned. Audit and evaluation are not just a local requirement but might be required at a regional or national level. An example of this requirement is that of the BACPR who have audit and evaluation as one of their core components of cardiovascular disease prevention and rehabilitation (Figure 2.6).

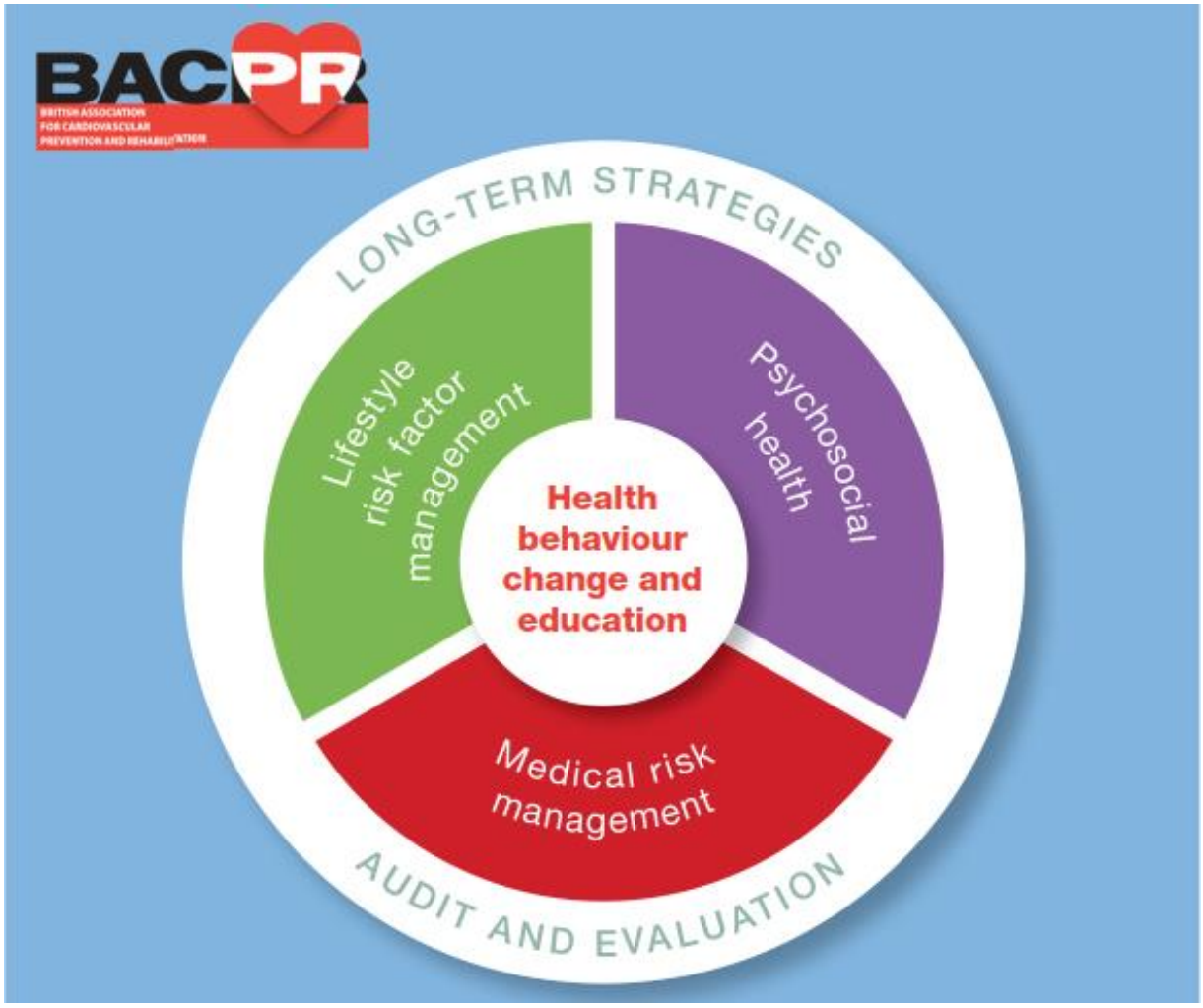


Figure 2.6 The six core components for cardiovascular disease prevention and rehabilitation. Taken from BACPR Standards and Core Components (2017).

Furthermore, CRPs in the UK are required to feed their local level data into a National Audit of Cardiovascular Rehabilitation (NACR). The NACR specifies which outcome measures to record (e.g., functional capacity and quality of life), and stipulates the specific measuring tools to be used to record these outcomes (e.g., 6-minute walk test [6MWT] or incremental shuttle walk test [ISWT] for exercise capacity, and the Hospital Anxiety and Depression Scale [HADS] for quality of life). When integrating a new clinical population group into an existing CRP, issues may arise as to which disease-specific outcome measures can be utilised in addition to the standard/required measures for the original rehabilitation programme (i.e., BACPR-required).

With differences in disease-specific limitations comes differences in assessment tools used to measure impairment, and response to treatment. For example, the PAD-specific Walking Impairment Questionnaire (WIQ) specifically asks for patient-reported limitations on walking

distance, speed and stair climbing. There is no similar cardiac-specific related questionnaire apart from patient-reported physical activity (PA) and exercise levels using generic the Total Activity Measure 2 (TAMS2) questionnaire (BHF, 2019c). When integrating PAD patients into a CRP, clinicians must consider the utilisation of these disease-specific assessment tools, otherwise, they risk adaptations to treatment being missed due to generic, or cardiac-specific measurement tools that are not sensitive to the PAD-related changes.

2.10.4.2 Exercise Assessment

In the literature on integrated rehabilitation, a range of exercise modes and protocols have been used to assess the baseline and post-SEP functional capacity of participants. Functional capacity has been measured through VO_2 peak (cycle-based), incremental shuttle walk test (ISWT), and 6MWT. Assessment using VO_2 peak is appropriate in PAD patients, however, this establishes cardiorespiratory fitness and not limitations caused by IC (Wasserman et al., 2011). Although the 6MWT has been shown to be an appropriate protocol for assessing patients with IC (McDermott et al., 2014; Montgomery & Gardner, 1998; Nordanstig et al., 2014), research into the efficacy of exercise therapy for IC has commonly used treadmill-based protocols (Gerhard-Herman et al., 2017; Hiatt et al., 2014; McDermott et al., 2020).

There are two types of protocols used in PAD-related research, constant-load (single-stage) protocols and progressive or graded protocols (Nicolaï, Viechtbauer, et al., 2009). One benefit of using a constant-load protocol is that they often employ a low starting pace (e.g., 2 km/hr) and no gradient, making it accessible to a wider number of patients within the PAD population, especially those with severely limiting PAD. For patients with mild PAD, however, the time taken to reach initial claudication pain and maximal walking pain can be prolonged (Hiatt et al., 2014) thus making it unsuitable for inclusion in a hospital-based clinical assessment where limitations on time-availability might be present. Most constant-load protocols have a starting gradient of 10-12% which can quickly limit patients with severe PAD and therefore reduce the amount of useful data collected for exercise prescription purposes. Another weakness of the constant-load protocols is that they have a low reliability for PWD and MWD, with coefficients of variation of 30% to 45%, respectively (Hiatt et al., 2014). Constant-load protocols are also affected by familiarisation to the protocol leading to improvements seen independent of exercise intervention. In contrast, graded treadmill tests

present higher reliability compared to continuous protocols with a coefficient of variation for PFWD in 15% to 25% and 12% to 13% for MWD. Also, graded treadmill tests increase progressively the workload, so each patient can have an individual PAD-limited walking performance and even patients with more PAD severity may reach a peak walking performance. In addition, the graded treadmill test has been less affected by the placebo effect with response change to 9% to 12% at 3 months and 13% to 23% at 6 months of follow-up (Brass et al., 2007). Thus, despite both treadmill exercise protocols being considered useful, the graded test better reflects the mechanism of the walking impairment in PAD, presenting the greatest reliability and allowing testing in a wide range of functional disease severity in PAD.

2.10.4.3 Quality of Life Assessment

There is consensus across the guidance that all treatment programmes for patients with PAD should assess quality of life measure (Conte et al., 2015; Gerhard-Herman et al., 2017; NICE, 2012b; Norgren et al., 2007). However, there is a variation in the chosen quality of life measures with both generic and disease-specific questionnaires being used. A study by Mehta et al. (2006) reviewed the quality of life measurement tools available for research into IC. They identified a range of generic measures such as the Short-Form 36 Health Survey Questionnaire (SF-36) and Hospital Anxiety and Depression Scale (HADS). Generic measures are usually validated, reliable, and sensitive to change in health conditions (Ware, 2000). The disadvantage of a generic tool is that it lacks sensitivity or responsiveness to change in a disease population. For example, when the SF-36 questionnaire was used in a cohort of patients with increasing worsening ischaemia it failed to show significant changes in the dimensions of emotional role, mental health, and social functioning (Mehta et al., 2006). Also, there was no significant difference between the different degrees of limitation. The use of disease-specific measurement tools offers this sensitivity and responsiveness to change in symptom control. Therefore, they can be used as an alternative or adjunct to generic QoL tools. However, currently the most appropriate method for disease specific QoL analysis is disputed.

One measure of disease-specific quality of life in PAD is the King's College Vascular Quality of Life measure (VascuQoL). This is a 25-item disease-specific questionnaire that has 5 domains

(pain, symptoms, activities, social and emotional) and has been widely used in PAD and IC research (Morgan et al., 2001; Vries et al., 2005' Mehta et al., 2006). Disease-specific quality of life measures are recommended by TASC (2007) as they are more sensitive to change in disease-specific symptoms than generic questionnaires.

The Walking Impairment Questionnaire (WIQ) has been widely used in research and is the best-known disease-specific questionnaire in claudication (Nicolaï, Kruidenier, et al., 2009). However, the WIQ does not specifically address the effect of claudication on quality of life. Mehta et al. (2006) therefore recommend that it is not used for this purpose. The WIQ is however, useful for assessing the perceived impact of claudication symptoms on the individual being measured. There are problems with this measurement technique, however. The measurement of walking distance ranges from home-based to longer distances and are given in blocks, not metres. This is a distance measure very specific to the USA. For this measure to be used in clinical practice in the UK, the measurements will have to be given as 50 metres (the distance of one block). However, the validity of this adaptation is questionable. An American citizen maybe able to picture a 'block' easily as this is a familiar quantity. Although the 50-metre distance can be given to the UK patient, they may not be able to accurately picture this distance. There is no 'block' equivalent measure in the UK that would aid measurement.

2.10.4.4 Mode of Exercise

An editorial by Stone et al. (2020) stated that commonalities in disease between stroke and cardiac patients made them appear closely related, siblings, and differences in functional impairments made them more like strangers. There is clear heterogeneity in presentation and functional limitation between all the of the conditions discussed in this literature review. Even with a shared aetiology and pathophysiology of atherosclerotic disease, PAD and CAD patients present differently, symptomatically, due to the location of their disease, anatomically. Not only is there a difference in location, but there is also a difference in severity, with a wealth of evidence showing that PAD patients are more limited than CAD patients in terms of functional capacity and ADLs (Clarke et al., 2013; Nguyen et al., 2021). In a retrospective review by Devrome et al. (2019), PAD patients were found to have lower baseline fitness and did not respond to rehabilitation as well when compared to cardiac counterparts. There was also a greater prevalence of CVD risk factors in the PAD population

and greater dropout rates, resulting in the authors concluding cardiac and PAD patients could not just be treated the same (more strangers than siblings). This has been supported in other studies into cardiac patients with PAD (Reiner et al., 2021).

2.10.4.5 Delivery of Education and Life-style Advice

One area of integrated rehabilitation that needs to be considered is the delivery of education and lifestyle advice. Previous studies into integrated rehabilitation have used different approaches to this problem. In the combined COPD and CHF programme by Evans et al (2010) the group education sessions kept the original pulmonary rehabilitation content, with no CHF-specific topics covered. The authors of the study linked this to the lack of improvement in health-related quality of life (HRQL) in the CHF group, suggesting it as the causal factor. They suggested an adapted education programme in future interventions to cater for the disease-specific needs of the CHF patients. This was also found in the studies into T2DM patients in CRP. The need to tailor the patient education sessions to ensure focus on disease-specific elements was recommended as the current CRP format was not able to reduce CVD risk factors for the diabetic group (Banzer et al., 2004; Verges et al., 2004).

This also raises the question about who would deliver the sessions, and in what format. In the CRIB study by Hubbard et al. (2016), the education sessions for cancer patients were delivered by a cancer specialist, not the CR staff. These were delivered separately, either through cancer-only patient groups or over the telephone. This poses an additional demand for staff to facilitate separate patient education sessions and could present resource and financial barriers to implementation. An important element of this study was that before implementing the combined rehabilitation, CRP staff attended a cancer rehabilitation training course. This training was received well by CRP staff and was found to support the successful implementation of the integrated programme. This highlighted the potential requirement for 'upskilling' staff before new service delivery, and the need for continual educational updates and professional development once the programme has started.

2.10.5 Acceptance of the Integration to Patient and Staff

There has been limited appraisal of the acceptability of integrated models of rehabilitation to both patients and staff involved in the programme, with initial research focusing on

quantitative measurement (Banzer et al., 2004; Evans et al., 2010; Kowal et al., 2015; Marzolini et al., 2016; Marzolini et al., 2014; Mourot et al., 2010; Prior et al., 2011; Tang et al., 2010; Verges et al., 2004). More recent studies have begun to include a qualitative analysis of acceptability which is a vital element of the investigation of feasibility.

The CRIB trial (Hubbard, Munro, et al., 2016) was one of the first to investigate the acceptability of the treatment to both patient and staff through the use of focus groups. A high level of acceptability of the integrated rehabilitation was found in both groups. Patients reported the benefits of the shared rehabilitation experience, despite having different health conditions. There was a perception of peer support between cancer and cardiac patients that enhanced their view of the programme. This challenged the view at the time that shared experience was related to having a shared disease and not the shared experience of the rehabilitation itself (Hubbard et al., 2016). The bowel cancer clinicians and CR clinicians interviewed also found the combined treatment acceptable. Cancer clinicians viewed the offering of CRPs to cancer patients as essential to enhancing recovery. CRP clinicians found the integration of cancer patients into their programmes appropriate, however, there were adaptations required to the programme infrastructure. For example, the referral procedure required amending as it was burdensome. There was also concern from CRP staff around the specialist nature of cancer care, and some staff felt unconfident when approached by patients for advice related to their cancer diagnosis.

A service review by Cowie et al (2018), investigated the perceptions of staff and patients to a 10-week multimorbidity rehabilitation programme set up in a Scottish Hospital Trust. The participants in this qualitative review represented a wide range of clinical conditions: cardiac, pulmonary, cancer, stroke, and diabetes (primary diagnosis). Service users reported improved confidence and self-management following completion of the combined programme which was similar to the single-disease programmes previously offered in the area (Cowie et al, 2018). They also found the integration with patients with difference health conditions to be acceptable. Cowie et al (2018) also found that by merging staff and facilities, the service was able to offer rehabilitation for patient groups that had previously had no provision in that area (atrial fibrillation and stable angina) due to resource limitations. Further qualitative investigation found that 3-years on, staff delivering the programme found the switch from a single-disease programme to a multi-morbidity programme to be still acceptable. Staff felt

the programme offered them opportunity for personal development in knowledge and the confidence in treating different patient groups (Cowie et al., 2021).

A qualitative review of cardiac and stroke rehabilitation professionals was conducted to investigate the acceptability of integrated CRP for stroke patients to staff members who would be providing the service (Jeffares et al., 2021). The sample included clinicians currently delivering an integrated service in a Swiss healthcare setting (n= 7) and clinicians who were considering implementing an integrated service in their healthcare setting in Ireland (n= 7). Overall, clinicians agreed that current stroke rehabilitation provision is poor, and an integrated CRP could be a possible solution to fill the gap in service. Commonalities in disease aetiology and shared risk factors between stroke and cardiac patients made the integration seem logical. The expected benefits of integrated rehabilitation were not perceived to be solely for the integrated stroke patient group. Clinicians hypothesised that cardiac patients might benefit from stroke-specific elements such as the focus on cognitive impairment as patients following cardiac arrest and those with heart failure can often present with similar deficits as stroke patients. However, clinicians reported that the amalgamation of the two patient groups might not be an "easy-fit". Stroke-specific limitations of fatigue and physical disability mean that patients often require a greater focus of resources during exercise session compared to cardiac patients, even patients following a mild to moderate stroke and not necessarily severe. Adaptations to CRPs would be required to ensure stroke patients could be incorporated successfully, and service providers would have to assess these demands on their current systems. Over-subscription of current cardiac patients and lack of stroke-specific expertise within the CRP were presented as barriers to expansion of CRP to stroke patients.

2.11 Summary of Literature Review

The current knowledge base for integrated rehabilitation shows that it is feasible for services to extend their offer to patient groups that have poor accessibility to exercise and education. Studies have shown that integrated rehabilitation can lead to improved functional capacity and quality of life for the new patient group, although this is currently based on feasibility and pilot studies, so the efficacy of the treatment has not been established.

The merging of resources and staff allows for increased service provision without imposing large financial burdens on healthcare providers. There is also the benefit of using clinicians who have knowledge and experience of supervising exercise and providing education to support those less experienced staff. Despite these benefits, there are gaps in the current knowledgebase that need to be addressed.

Most of the studies into integrated models using CRP have been conducted in healthcare settings outside of the UK and have different modes of delivery. Programmes delivered in the USA and Canadian healthcare for example, have more intensive models of delivery with high frequency per week (3 x per week) for longer durations (6 months), compared to the delivery in the NHS (1-2 x per week for 3 months). The feasibility of a programme with reduced delivery, as used in the UK, needs investigation.

To fully establish the feasibility of an integrated model of rehabilitation, the views of both the service users and staff involved in the programme need to be investigated. Without this, the acceptability of the novel treatment cannot be fully established. This includes gaining the views of the current patient group, the cardiac patients (in the case of CRP integration).

For successful integration of one patient group into an established rehabilitation programme, the needs and requirements of both groups need to be addressed. There must not be a compromise or preference to one of the two groups. Both groups need to receive optimal care as per the guidance. For example, the educational sessions should not be focus solely on areas relevant to one of the two diseases as this would lead to exclusion, to the detriment of one of the patients. This would therefore make the idea of an integrated service less preferential to the standard care or single-disease rehabilitation programme. The required adaptations to the existing programme to ensure this successful integration needs to be fully investigated. The mode of exercise is also a key consideration as guidelines changes from patient group to patient group. This might involve the need for further training again, as well as additional staff to meet extra supervision needs. The decision on how to monitor and evaluate the treatment effect using disease-specific outcome measures, without overburdening rehabilitation staff is essential. Ultimately, rehabilitation services have priority groups that require a consistent and equitable service that cannot be compromised by additional demands outside of the scope of the service.

2.11.1 Refined Aims and Objectives

The primary aim of this thesis was to investigate the feasibility of integrating patients with IC into an already established CRP. The secondary aims were:

i. Investigate the acceptability of trial procedures to patients and staff;
ii. Identify the appropriate outcome measures to use to guide a definitive study of integrated CRP efficacy.

The objectives for next stage of the thesis were:

i. To design a study to investigate the feasibility of an integrated CRP for patients with IC

Chapter 3 Methods

3.1 Study Design

This study was designed to assess the feasibility an integrated Cardiac Rehabilitation Programme (CRP) for patients with intermittent claudication (IC). The feasibility study had an embedded pilot study which was designed to collect clinical outcome data to guide the methodology for a definitive efficacy trial, including an *a priori* sample size calculation for the larger scale study. To ensure the scientific rigour, the study design followed recommendations for good practice in pilot studies by Lancaster, Dodd & Williamson (2004).

This feasibility study had two arms: an intervention arm in which IC and CAD patients were integrated into a Cardiac Rehabilitation Programme (CRP), and a stand-alone IC group which acted as the control arm.

In line with Medical Research Council (MRC) guidance on the development of complex interventions (Craig et al., 2008), the feasibility study was designed to investigate the suitability of the trial procedures and the acceptability of the treatment itself for both patients and rehabilitation staff. Measures of the feasibility of the treatment included quantitative data such as the eligibility rate of patients, recruitment and retention rates, and the acceptability of the trial procedures (e.g., questionnaires return, missing data, the performance of activity monitors). Qualitative data was collected using focus groups and individual interviews with participants and clinicians, to assess the perceptions of the trial procedures. The suitability of the treatment (integrated rehabilitation) was also assessed during the focus groups and interviews stage.

The study used a mixed methods approach to assess the feasibility of an integrated CRP (Figure 3.1). A mixed methods approach provides strengths that offset the weaknesses of qualitative and quantitative methods when used in isolation (Creswell, Plano-Clarke, 2007). A purely quantitative approach would provide the descriptive statistics of eligibility and recruitment rates; however, it would not show the perceptions of the service users and clinicians. It is also important to establish the thoughts and experiences of service users to assess whether future patients will engage with the treatment (Thomas, Nelson & Silverman, 2011). As the programme of combined IC and CAD exercise rehabilitation is novel, it is vital to establish the viewpoints of the service users regarding the trial and treatment, as this will

influence the protocol design of any future, large-scale study to aid recruitment rates and to help guide future service provision (Risom, Zwisler, Rasmussen et al., 2013, Barker et al., 2018).

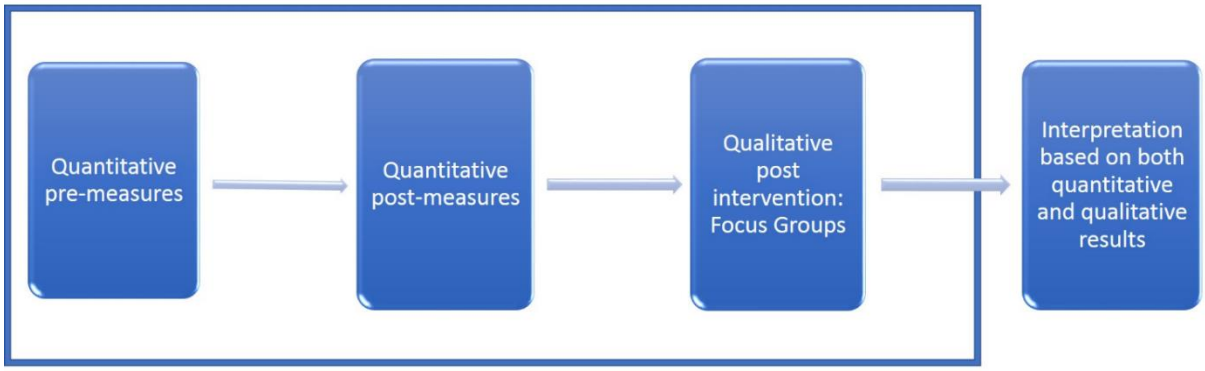


Figure 3.1 This diagram shows the overall flow of the mixed-methods study design. The initial quantitative study was followed by the qualitative study looking at the participant perceptions of the programme

3.1.1 Rationale for a Feasibility Study with Embedded Pilot

There has been increased importance placed on the use of preliminary work before undertaking publicly funded clinical trials (Craig et al., 2008; Whitehead et al., 2014). Clinical trials, particularly randomised control trials (RCTs), are robust methods of scientific enquiry (Mantzoukas, 2008) that often require large-scale recruitment of participants from several independent sites (i.e., hospitals or clinics). Therefore, they are often costly to undertake (Lancaster et al., 2004). To ensure such expensive full-scale studies run smoothly, small scale studies or 'pre-studies' are encouraged before the main trial (Thabane et al., 2010). Pre-studies, also referred to as pilot or feasibility studies are used to test out parameters such as eligibility, recruitment, and retention rates. Acceptability of the study protocol and intervention can be investigated, as well as identification of methodological issues can help guide the design of the final study (Craig et al., 2008). Where no previous data is available, preliminary outcome data can be recorded and used to perform sample size calculations to guide recruitment for the future, larger-scale trial (Lancaster et al., 2004). Although the rationale behind conducting preliminary work has been evidenced, and funding bodies are supporting this work more regularly (Whitehead et al., 2014), there remains debate over what classifies as a feasibility or pilot study, and indeed, if there is any difference between the two.

A review of the literature shows that there is no clear, internationally agreed definition of feasibility and pilot work. An audit of the UK Clinical Research Network's database Billingham et al. (2013) highlighted that out of seventy-nine studies returned from a search of 'pilot' or 'feasibility' search terms, fourteen (17%) described themselves as being both pilot and feasibility trials. The Medical Research Council's (MRC) 2008 guidance includes feasibility and pilot work as a key element of their framework for developing and evaluating complex interventions (Craig et al., 2008), however, they do not provide separate definitions of the two terms and treat them synonymously. The UK's National Institute for Health Research (NIHR) Evaluation, Trials and Studies Coordination Centre defines feasibilities studies as research with the primary aim of identifying 'Can this study be done?' and pilot studies are 'miniature' versions of the main study to test if all components can work together (NIHR, 2016). Eldridge et al. (2016) consider pilot studies to be a subset of feasibility studies, with 'feasibility' being the overarching term for all preliminary work. Similarly, Leon et al. (2011) consider pilot studies to be a special type of feasibility study. The common difference found across the literature is that pilot studies differ from feasibility studies in that they resemble the intended main study, by including a control group or randomisation into the study protocol (Whitehead et al., 2014). Also, there is an intention for future work with a pilot study, whereas a feasibility study aims to assess the viability and ethical appropriateness of a future study, so future work is not guaranteed. In fact, the feasibility study is designed to prevent future studies going ahead as this would be an unethical waste of patients' time and other resources (Craig et al., 2008; NIHR, 2016).

As this current study is designed to assess the practicality of running a future study across two hospital sites, it certainly falls under the category of preliminary work. The important feasibility outcomes of eligibility, consent and retention rates are assessed, as well as the acceptability of trial procedures and intervention (for both patients and clinicians), so it falls under the definitions given in the current literature for 'feasibility'. However, the research also meets the criteria for a pilot study, as stated by Leon et al., (2011), of having a stricter methodology that reflects the future, or main study, specifically in the use of a control group. The decision to embed a pilot study was due to the lack of previous studies in the area of integrated CRP for patients with IC. This study offered the opportunity to record preliminary outcome data further guide a large-scale, future study. As no previous investigation of incorporating IC patients into CR has been conducted, no data on effect sizes is available to

power a large-scale control trial. Therefore, the embedded pilot study offers outcome data that can be used for an *a priori* sample size calculation. Although it is noted that any calculation will be interpreted with caution due to possible recruitment bias associated with underpowered, non-randomised trials (Thabane et al., 2010) and participant uptake rates for a larger, multi-centre study may be smaller when methods such as randomisation are introduced (Craig et al., 2008).

After consideration of the above debate around feasibility and pilot work, this current study has been positioned as a feasibility study with embedded pilot study.

3.2 Study Setting

This study was conducted in two separate rehabilitation departments in two different NHS Trusts: Manchester Foundation Trust (MFT) and Salford Royal NHS Foundation Trust (SRFT). The programme at MFT is a 12-week IC-specific programme, offering exercise and education. This site was selected to recruit patients for the control group (referred to as IC Control group), as supervised exercise is currently the recommended standard treatment for PAD patients (NICE 2012a).

The programme at SRFT is a 12-week Cardiovascular Rehabilitation programme (CRP) of exercise and education. This site recruited both IC and CAD patients for the intervention group (referred to as IC treatment and CAD group, respectively). This site was selected as it had integrated IC patients into their CRP since 2015. This offered the opportunity to investigate the experiences of CR staff providing the service over a longer period, alongside the experiences and perceptions of the IC and CAD patients newly enrolled on the integrated programme.

Both the MFT and SRFT programme has been running for over 15 years and followed the recommended guidelines for SEP delivery for IC patients (NICE 2012b) and CAD patients (ACPICR, 2015 and BACPR, 2017). As the intervention and control arm were recruited from two separate hospitals, the feasibility of trial procedures for individual sites was analysed and presented separately as per Consolidated Standards of Reporting Trials (CONSORT) guidance (Eldridge et al., 2016).

3.3 Sample Size:

As this was a feasibility study, and due to the unique nature of this investigation, there was no previous effect size data available to perform an *a priori* sample size calculation. The aim of the embedded pilot study, therefore, was to generate an effect size from the preliminary outcome data for sample size calculation for a large-scale clinical trial. As recommended by MRC guidance on designing feasibility and pilot studies (Craig et al., 2008), the sample size of this investigation was guided by protocols of previous studies conducted in the area of combined rehabilitation, notably a study by Evans et al., (2010).

In this study, Evans et al., (2010) investigated the suitability of integrating chronic heart failure (CHF) patients into a chronic obstructive pulmonary disease (COPD) rehabilitation was investigated. Like this study, functional capacity and disease-specific quality of life outcome measures were used. Evans et al., (2010) found that seventeen participants were required in each of their three groups (COPD control, COPD integrated, and CHF integrated) for their outcome measures to reach significance level. As the study showed statistically significant improvements in both outcome measures for both disease groups, their sample size has been used as guidance to improve the likelihood of sufficient data being collected in this study for accurate sample size calculations that would then be used to power a full control trial. To achieve these seventeen participants, the recruitment aim of thirty-four patients for each of the three groups was set. This double recruitment was deemed necessary due to an expectation of potential high patient dropout rates from the SEPs. Research and audit have shown that there are high dropout rates for both IC and CAD patients are seen within UK-based programmes (Shalhoub Hamish and Davies, 2009, Harwood et al 2016, Harwood et al 2021; NACR, 2019). For example, the 2019 NACR showed the average completion rate for patients starting a CR programme was 50%. As thirty-four patients were required to be recruited in order to have seventeen completers in a group (IC treatment, IC control and CAD Group), this required a total of 102 participants needing to be recruited (Figure 3.2).

3.3.1 Sampling Technique

A purposive sampling technique was used, as participants came from those patients who had been referred to and agreed to enrol on the SEP that was being studied.

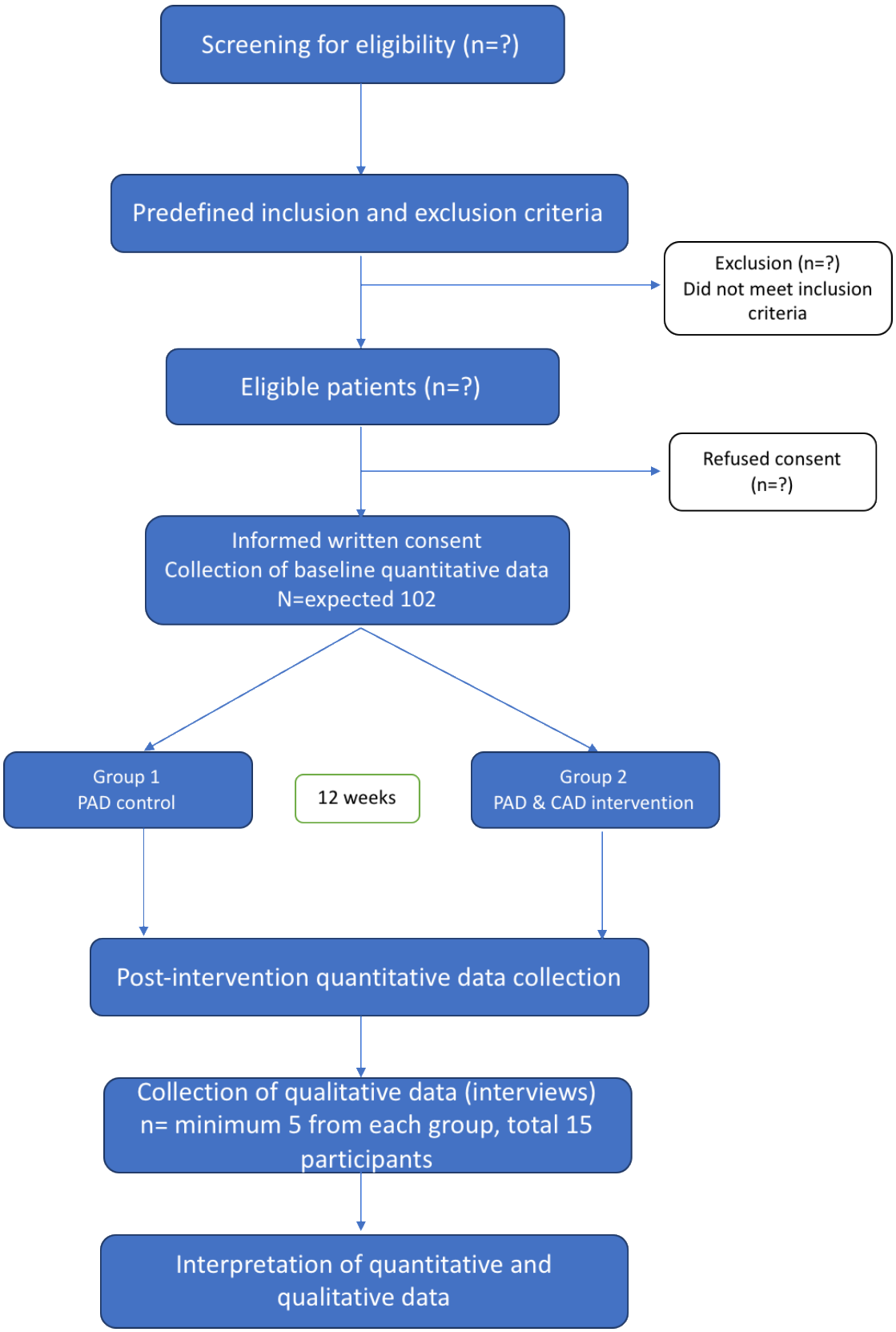


Figure 3.2 Flowchart of study. This shows the outline of the 12-week study with the 2 arms

3.4 Participant Recruitment

An overview of the participant's journey through the research process is provided in Figure 3.3.

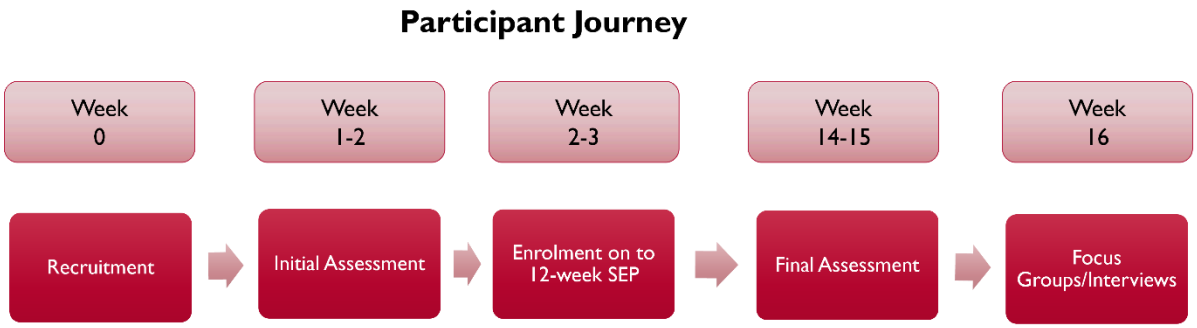


Figure 3.3 Overall timeline of the patient journey through the study process.

3.4.1 IC Control Group (Standard Care):

Patients for the IC control group were recruited from an already established IC-only SEP at a separate hospital (MFT). Due to delays in acceptance by the R&D Team at the hospital, recruitment period was reduced to 8 months (February to September 2019) which was less than the treatment groups recruitment period of 13 months August 2018 to September 2019). Symptomatic PAD patients referred to this SEP were screened by the Vascular Specialist Nurse and Specialist Physiotherapist against the inclusion criteria, with uncertainty clarified by the Principal Investigator (PI).

Patients were deemed suitable if they met the following inclusion criteria:

1. they were above 18 years old
2. they had a recent diagnosis (within the last 12 months) of symptomatic PAD (IC) made by either a vascular surgeon, vascular specialist nurse, or specialist podiatrist*
3. they had the ability to perform the initial stage of the Gardner Skinner graded exercise test (GXT) (3.2km/hr or 2mph)
4. they were able to engage in the majority of exercises prescribed in the programme (see Supervised Exercise Programme outline below)
5. they had the capacity to give informed consent.

*Diagnosis for symptomatic PAD was made if one of the following criteria was met:

- Resting ABPI <0.9
- TBPI <0.70 (if ABPI ≥ 1.4)
- Reduction in ankle systolic BP of ≥20 mmHg post exercise challenge (plantar flexion) if ABPI normal (1.0 – 1.4)

Patients were deemed unsuitable if they met any of the following exclusion:

1. had a previous intervention for PAD e.g., balloon angioplasty with or without a stent, femoral-popliteal bypass, vasodilating medication (e.g., naftidrofuryl oxalate), or who had previously completed an SEP
2. were currently on vasodilatory medication or commenced such medication during their SEP 3) had a recent diagnosis of CAD (within past 12 months) or had ongoing symptoms of CAD or
3. had a primary diagnosis of heart failure (HF)
4. had an existing skin condition such as psoriasis or eczema that would be affected by the application of a medical dressing to secure the accelerometer were excluded from the study.

The use of an IC-only SEP has been chosen as the control group as this is the first-line treatment for patients who are diagnosed with symptom-limiting PAD, according to national guidance (NICE 2012a). Although most eligible patients in the UK are unable to access an SEP due to poor service provision (Shalhoub et al, 2009, Harwood et al, 2016, Harwood et al, 2021), and it could be argued that the 'standard care' for IC patients is more likely to be exercise and lifestyle advice only, it was deemed an unrealistic comparison to have a 'non-SEP' control group. So, in effect, this study compares a new treatment option to the current 'optimal care' for newly diagnosed, symptom-limited PAD patients, rather than the 'standard' care for most IC patients.

The option to have a non-SEP control group at the SRFT site was initially considered during the design process. This would have allowed for homogeneity in the trial and treatment processes as well as testing of a randomisation process. Research into PAD-specific rehabilitation has used this approach with patients being randomized to either an SEP group or an "exercise advice only" control group (Cheetham et al., 2004). However, this was not

deemed ethical in the current study as it has been previously established that supervised exercise improves patient outcomes to a greater extent than exercise advice only (Bendermacher et al., 2006). Also, there was an integrated SEP available for patients to attend at this location. After discussion with the rehabilitation team, it was therefore considered unethical for some patients who had been referred to SRFT to be denied the recommended first-line treatment of SEP due to the study design. A future, large-scale study may require an internal pilot stage where the feasibility of the randomisation process can be assessed.

3.4.2 IC Intervention Group

Between August 2018 and September 2019, the medical records of IC patients referred to the CR programme at SRFT were screened for study eligibility by the services' Cardiovascular Specialist nurses against the inclusion criteria. Review of eligibility was made by the PI if clarification on eligibility was required. The inclusion and exclusion criteria for the IC control group were the same as the IC treatment group to ensure reliability and validity of any between-group comparisons made in the analysis of results.

Eligible patients were then invited to participate in the study during their initial telephone consultation which was conducted by the Specialist Nurses as part of the standard CR assessment process. Patients then had time between this telephone consultation and their pre-SEP to consider voluntary enrolment into the research study.

3.4.2.1 Rationale for IC Treatment Group Exclusion Criteria:

Patients who had previous interventions for PAD were excluded from the study due to the possibility of previous interventions having an impact on patient perceptions of the SEP.

Participants who were on vasodilatory medication for symptomatic PAD (e.g., naftidrofuryl oxalate) were excluded from the study as this can improve symptom management and increase functional capacity. For this same reason, participants who started vasodilatory medication during the study were also withdrawn from the study as this may artificially improve post-SEP functional capacity and perceived claudication symptoms (Peach et al., 2012).

Any PAD patient who also had a recent diagnosis of CAD or ongoing symptoms of CAD (e.g., angina pectoris) was withdrawn from the study, as the investigation was investigating specific changes in PAD-related symptom management, rather than CAD.

As part of this study, participants were required to wear an activity monitor, the activPAL3 (PAL Technologies Ltd, Glasgow, UK), on the first week and last week of the 12-week study. The activity monitor was kept in place by a medical dressing (e.g., Tegederm®, PAL Stickie®). People with an existing skin condition such as psoriasis or eczema that would be affected by the application of a medical dressing were therefore excluded from the study.

3.4.3 Cardiac Intervention Group Recruitment

At the same time as recruitment to the IC treatment group (August 2018 to September 2019), CAD patients were recruited to the study to form the CAD group. These patients exercised alongside the IC treatment patients. This was to assess the feasibility of integrating IC patients into the CRP on the CAD patients who are the usual patient group for this service. Previous studies have not taken this approach or have included a 'usual care' group in the intervention but have not investigated the impact on this group. As with the IC treatment group, participants were screened by the Cardiovascular Specialist Nurses at SRFT upon referral to the CR programme, with the PI being consulted if clarification on eligibility was required.

Patients were deemed suitable if they met the following inclusion criteria:

1. ≥ 18 years old
2. they had a recent diagnosis (within 12 months) of angina pectoris, myocardial infarction (MI), or coronary artery bypass graft (CABG)
3. they had the ability to complete the first stage of the Incremental Shuttle Walk Test (ISWT) which started at a 1.8 km/hr (1.1 mph)
4. they had the functional capacity to undertake the majority of exercises in the CR circuit class (detailed in a later section).

Patients were deemed unsuitable if they met any of the following exclusion:

1. they had an unstable cardiovascular condition (e.g., unstable angina pectoris)
2. they had a previous diagnosis of PAD

3. they had an existing skin condition such as psoriasis or eczema that would be affected by the application of a medical dressing to secure the accelerometer and were excluded from the study.

Eligible patients were then invited to participate in the study during their initial telephone consultation which was conducted by the Specialist Nurses as part of the standard CR assessment process. Patients then had time between this telephone consultation and their pre-SEP to consider voluntary enrolment on to the research study.

Due to the service provision of the two NHS programmes, and the availability of the PI, it was not possible to provide a control group for the CAD patients (i.e., a CAD-only SEP). To provide a comparison group for the CAD participants who were integrated with the IC group, the physical fitness and quality of life outcome data was compared to the National Audit of Cardiac Rehabilitation (NACR). The NACR compiles outcome data that allows for comparison to a national average for these two outcome measures. The most recent year's audit was used for this comparison. Physical fitness was measured using the incremental shuttle walk test (ISWT) and quality of life using the Hospital Anxiety and Depression scale (HADS) and Dartmouth COOP quality of life tool (as detailed in the secondary outcome measures section).

3.4.3.1 Rational for Exclusion Criteria for Cardiac Treatment Group

Patients with a primary diagnosis of heart failure (HF) were excluded from this study as the focus is comparing CAD with PAD. A diagnosis of HF generates a referral to CR as this is one of the target clinical populations for CR services (BACPR, 2017). This meant that patients identified with HF during initial screening were excluded due to ineligibility for study participation.

Any CAD patient with a previous diagnosis of PAD was excluded from the study, as their exercise could be limited by PAD symptoms (i.e., intermittent claudication) rather than the cardiac condition. Any improvement in exercise capacity may therefore be confounded by improvements in PAD-related symptoms (Tam et al., 2016).

Any participant with unstable CAD (e.g., unstable angina pectoris) was excluded from the study as this is a contraindication to partaking in a structured exercise programme (BACPR, 2017, ACPICR, 2015).

3.4.4 General Exclusion Criteria – Medication Change

All participants enrolling on the study required a stable prescription of medication. Initiation of a new drug, or a dosage change on a current drug during a patient's 12-week SEP that would impact the functional outcome data resulted in that patient being withdrawn from the study. Examples of these drugs are beta-blockers and vasodilators. Beta-blockers (β-blockers) such as bisoprolol and atenolol are parasympathetic mimetic drugs that lower the heart rate response to exercise and can increase functional capacity (ACPICR, 2015, ACSM 2018). This could impact the validity of the study due to participant functional capacity improving due to this medication optimisation rather than being due to physiological benefits of the SEP – likelihood of committing a Type 1 error. Vasodilators such as naftidrofuryl oxalate are used in the treatment of intermittent claudication (IC) and can reduce the onset and intensity of exertional symptoms (NICE, 2012a; Peach et al., 2012). A patient being started on this drug may increase functional capacity due to the drug mechanism of action, rather than physiological improvements in response to the exercise programme. This risk to the validity of the study resulted in participants being excluded if any medication changes were reported.

3.4.5 Pragmatic Changes in the Exclusion Criteria

It was initially planned that patients with IC who had a previous diagnosis of CAD within any timescale would be excluded from the study. This was to ensure a clean comparison of PAD and CAD. However, during the initial screening process, it became clear that a large amount of IC patients referred to both hospitals SEPs also had a previous diagnosis of CAD. Therefore, it was apparent that there would be an issue with recruitment if the exclusion criterion of any previous CAD diagnosis was kept. The sample characteristics would unlikely be a true representative of the PAD population who have a high prevalence of CAD (Cea-Soriano et al., 2018; Shammas, 2007; Song, Rudan, Zhu, et al., 2019). The protocol was pragmatically altered so that PAD patients with a previous diagnosis of CAD were included. To maintain interval validity, this inclusion of PAD patients with a history of CAD was restricted to those without a recent diagnosis of CAD (not within the previous 12 months) and no recent symptoms (e.g., angina). During the discussion with specialists within the rehabilitation departments, and evidence from functional capacity data (Clarke et al., 2012), it was agreed that the symptoms

of PAD (intermittent claudication) would be more limiting than any symptoms related to their CAD.

The amount of symptomatic PAD patients with a past medical history of CAD is not surprising, as a systematic review by Peach et al., (2012) found around 65% of people diagnosed with PAD also had clinically relevant cerebrovascular or cardiovascular disease.

Another pragmatic change was the exclusion of patients who could not be assessed by the PI within a 3-week period from their initial telephone consultation (SRFT) or clinic assessment (MFT). Once the recruitment process started, it became clear that the PI's availability for pre-SEP assessments, where patients would be consented, was not sufficient, and patients would have a greater than usual wait to be assessed. The CR service had an aim to start patients on their programme within 3 weeks of them verbally agreeing to participate during their initial telephone assessment. Any delay greater than this was deemed unethical as the link between long waiting times for CR programmes and poor patient uptake has been established (ACPICR, 2015, Piepoli et al., 2015, BACPR, 2017). After discussion with the CR Team, it was decided that if an assessment date with the PI was not available within a 3-week timeframe from the initial assessment, the patients were offered an assessment with a member of the rehabilitation team and enrolled on the SEP without being offered enrolment to the research study. This was discussed and agreed to be part of the protocol for the IC control group at MFT.

3.4.6 Informed Consent

In order to gain informed consent from patients recruited to the IC treatment and CAD groups (SRFT), the content and layout of the study were verbally explained to the participants during their initial telephone consultation (Figure 3.3). They were invited to consider involvement in the study by the Specialist Nurse, and if willing, the study would be discussed in more detail during the patient's pre-SEP assessment with the PI. At the pre-SEP assessment, an easy-to-read Participant Information Sheet (PIS) with a full description of the study (Appendix 4) was provided to the patient. Patients were given time to consider enrolment in the study, and if willing to participate in the study, consent took place on their first SEP session (Appendix 5). This session occurred a minimum of three days after the pre-SEP assessment but was usually

seven days afterwards, giving between three to seven days for each patient to consider enrolling on the study.

For patients recruited to the IC control group, informed consent was gained by a slightly different process. The Vascular Specialist Nurse and Specialist Physiotherapist conducted the initial assessment face to face in the Vascular Clinic. During this assessment, patients were given a verbal overview of the study and provided with the PIS. Patients who were willing to consider enrolment on the study were offered the next available start date for the SEP. The PI was informed of the date and arranged to meet the patient during their first SEP. During this first SEP session, the Vascular Physiotherapist conducted a short assessment, including the graded exercise test (GXT), which is discussed later. Following this, the PI met with the patient to discuss the programme further and to enrol onto the programme using the consent form (Appendix 5).

To avoid any risk of coercion, it was explicitly stated to all patients that they had the right to withdraw from the study at any point and that no present or future treatment would be affected by enrolling or not enrolling on the study as per Good Clinical Practice guidance (Clinical Research Network, 2016). All PIS documents were made available in large print upon request.

3.5 Pre-SEP Assessment

3.5.1 IC Control Group

All participants had an initial clinic visit with the Vascular Specialist Nurse and Physiotherapist before starting their 12-week SEP. During this session, verbal information on the study was provided and the PI was available in a separate room for patients who were willing to discuss the research programme further. At this point, the baseline measures of resting BP and RHR, height, weight, and waist circumference were recorded, and BMI was calculated. The VascuQoL questionnaire and HADS questionnaire were given to the patient to take home, complete, and return on their first SEP session if they decided to enrol on the study. If patients did not wish to enrol, all records of clinical measures were destroyed.

3.5.2 IC Treatment Group

All participants were assessed before starting their 12-week SEP. This assessment was a standard part of Stage 4 CR process and involved recording a range of standard clinical measures (e.g., resting BP, height, weight, and waist circumference) as well as a graded exercise test (GXT). The VascuQoL and HADS questionnaires were given to patients to complete and return on their next visit.

3.5.3 CAD Group

The cardiac group followed the same process as the IC treatment group, as detailed above.

3.5.4 Exercise Interventions

Before commencing their SEP, all patients were assessed by the Rehabilitation Team for suitability to undergo a graded exercise test (GXT) and partake in rehabilitation. The American College of Sports Medicine's Contraindications for Outpatient Cardiac Rehabilitation (Table 3.1) was used for this screening process (ACSM. 2014). Any patients with current contraindications were referred to their General Practitioner (GP), Cardiologist or Vascular Specialist for immediate follow-up.

Table 3.1 Contraindications for Outpatient Cardiac Rehabilitation - American College of Sports Medicine

Contraindications for Outpatient Cardiac Rehabilitation

- Unstable Angina
- Uncontrolled hypertension
  - Resting SBP > 180 mmHg and/or resting DBP >110 mmHg
- Drop in BP >20 mmHg on standing (orthostatic)
- Uncompensated heart failure
- Uncontrolled sinus tachycardia (>120 bpm)
- Significant aortic stenosis
- Uncontrolled arrhythmias (atrial or ventricular)
- Severe orthopaedic conditions that would prohibit exercise
- Acute systemic illness or fever
- Third-degree AV block without pacemaker
- Active pericarditis or myocarditis
- Recent embolism
- Acute thrombophlebitis
- Uncontrolled diabetes
- Other metabolic conditions (e.g. hypokalaemia, hyperkalaemia, hypovolemia) – until adequately treated

An overview of each programme has been provided in Table 3.2 for easy comparison of the differences at each location using the Template for Description and Replication (TIDieR) Checklist. Detailed descriptions are then provided in the sections following.

Table 3.2 Comparison of the two rehabilitation sites and their programmes using the TIDieR (Template for Description and Replication) Checklist

Intervention Component	Site 1 (IC Control)	Site 2 (IC Intervention)	Site 2 (Cardiac Intervention)
WHAT – Materials	Home exercise booklet VS and CF patient information leaflets Education IC and lifestyle modifications given during clinic visit Ad hoc education to patients during SEP	Home exercise booklet BHF booklets VS and CF patient information leaflets Weekly education sessions covering: • CVD – diagnosis and treatments • Risk Factors for CVD • PA and Exercise • Stress Management • Weight Management • Medications	CR Home Resource Booklet Home exercise booklet BHF booklets Weekly education sessions covering: • CVD – diagnosis and treatments • Risk Factors for CVD • PA and Exercise • Stress Management • Weight Management • Medications •

WHAT – Procedures	***Assessment***: 2:1 initial assessment with GXT ***Class****:* Group warm up (5 minutes), 7 x stations (3 minutes on each), Individual cool down – stretching (approx. 5 minutes) ***Discharge Assessment***: 1:1 assessment with GXT	***Assessment***: Initial telephone consultation with Specialist nurse followed by 1:1 pre-SEP assessment with GXT ***Class***: Individual warm up on static exercise bike (5-10 minutes), 20-30 minutes of CV stations (3-4 minutes on each), Individual cool down – static exercise bike and stretching (approx. 10 minutes) Education session – 20 to 40 minutes long (see above for topics) ***Discharge Assessment***: 1:1 assessment with GXT	***Assessment***: Initial telephone consultation with Specialist nurse followed by 1:1 pre-SEP assessment with GXT ***Class***: Group warm up (15 minutes), 20-30 minutes of CV stations (each followed by 1 minute AR station), Group cool down (10 minutes) Education session – 20 to 40 minutes long (see above for topics) ***Discharge Assessment***: 1:1 assessment with GXT
WHO	Vascular Specialist Nurse, Vascular Specialist Physiotherapist, and Physiotherapy Assistant	CR Specialist Nurses, CR Physiotherapist, CR Exercise Physiologists, CR Exercise Specialists, CR Exercise Assistants	CR Specialist Nurses, CR Physiotherapist, CR Exercise Physiologists, CR Exercise Specialists, CR Exercise Assistants
HOW	Face to face group classes 10-15 per class	Face to face group classes 20-25 per class	Face to face group classes 20-25 per class
WHERE	Hospital Gym	Hospital Gym	Hospital Gym

WHEN and HOW MUCH	***Frequency***: Once a week for 12 weeks ***Duration***: 45-60 minutes total. Time on each station was monitored and recorded by patient using exercise record sheet. ***Intensity***: Encouraged to exercise to point of maximal claudication pain on each station (4 out of 4 on 0 – 4 IC AACVPR IC Pain Scale). ***Type***: Treadmill, static exercise bike, sit to stand, calf raises, stair climbing, shuttle-walking, tip-toe walking.	***Frequency***: Once a week for 12 weeks ***Duration***: 45-60 minutes total. Time on each station was monitored and recorded by patient using exercise record sheet. ***Intensity***: Encouraged to exercise to point of maximal claudication pain on each station (4 out of 4 on 0 – 4 IC Pain Scale). ***Type***: Treadmill, static exercise bike, sit to stand, calf raises, step ups, shuttle-walking, tip-toe walking, trampette	***Frequency***: Once a week for 12 weeks ***Duration***: 60 minutes total. Time on each station was allocated at the start of each session (using ACPICR 'Levels' approach). ***Intensity***: 40-70% HRR, RPE 11-15 (on Borg's 6-20 scale). ***Type***: CV stations - treadmill, static exercise bike, sit to stand, rowing machine, step ups, trampette. AR stations – biceps curl, side-arm raises, calf raises, resistance band chest press, weighted ball (core) exercise

TAILORING – If the intervention was planned to be personalised, titrated, or adapted, then describe what, why, when, and how.	Initial exercise prescribed using the initial assessment GXT. When 3 minutes achieved on a station, the exercise was intensified i.e., treadmill speed/gradient increased, or ankle weights worn when shuttle-walking. Exercise record sheet reviewed by Rehab Team each week.	Initial exercise prescribed using the initial assessment GXT. When 3 minutes achieved on a station, the exercise was intensified i.e., treadmill speed/gradient increased, or ankle weights worn when shuttle-walking. Exercise record sheet reviewed by Rehab Team each week. Including pedometer use.	Initial exercise prescribed from result of the initial assessment GXT and results of AACVPR risk stratification. Patient monitored using HRM and RPE at two or more points during the CV exercise stations – recorded in patient notes and reviewed each week. When patient is comfortably exercising within or below target HRR and RPE, the time on each station is increased (following ACPICR 'Levels' approach)

Abbreviations:

AACVPR – American Association of Cardiovascular Prevention and Rehabilitation, AR – active recovery, BACPR – British Association of Cardiovascular Prevention and Rehabilitation, CF – Circulation Foundation, CR – cardiovascular rehabilitation, CV – cardiovascular, CVD – cardiovascular disease, GXT – graded exercise test, HRM – heart rate monitor, HRR – Heart Rate Reserve, IC – Intermittent Claudication, PA – Physical Activity, RPE – Rating of Perceived Exertion, VS – Vascular Society

3.5.4.1 IC Control Group Exercise

Patients were encouraged to exercise to the point of maximal pain and then stop and rest as per NICE Guidance CG147 (2012a). The ACCVPR Intermittent Claudication Scale was used to monitor and report claudication pain (Table 3.3). Patients recorded the duration of each exercise, and the pain level, and exercise intensity was progressed when the three-minute pain-free target was reached. Progression was made by the Specialist Physiotherapist.

There were some differences in the control group circuit compared to the IC treatment group. Patients completed a group-based warmup period of five using body movement exercises (not equipment-based). There were seven exercise stations as no trampette exercise base was available at this location (Table 3.2). The step-up exercise station was also different from the other location. Instead of an adjustable step block (as used in the IC treatment group), this circuit had a Rehabilitation Corner Steps unit. Patients initially used the bottom step (choice of two heights) and then progressed to stair climbing (four small steps, or three larger steps) when appropriate. Another difference at this site was the use of additional ankle weights. When patients could complete the shuttle walk comfortably for the three minutes, ankle weights were worn by the patient during their next exercise session to progress the intensity (0.5 to 1kg weights used depending on ability).

The session was completed by a five-minute period of lower limb stretches that were performed individually by each patient.

Table 3.3 This shows the Intermittent Claudication Rating Scale that was used by patients to grade the amount of claudication pain they experience during the GXT and SEP. Taken from ACCPVR Guidelines for CR and Secondary Prevention Programmes

Intermittent Claudication Rating Scale	
0	No claudication pain
1	Initial, minimal pain
2	Moderate, bothersome pain
3	Intense pain
4	Maximal pain, cannot continue

3.5.4.2 IC Treatment Group Exercise

The IC treatment group patients completed a 10-minute warmup either on a static bike or, if able, they joined the group warmup with the cardiac patients. Some patients had a split warmup, completing some of the group warmup and then moving to the static bike if initial claudication pain was experienced. Patients then completed a circuit of eight exercises (Table 3.2). Patients were encouraged to exercise to the point of maximal pain and then stop and rest as per NICE guidance (NICE, 2012b). The ACCVPR Intermittent Claudication Scale was used to monitor and report claudication pain (Table 3.3). Rest periods were usually seated, with chairs being available as close to the exercise stations as possible. Patients were informed not to begin the next exercise until their claudication pain had fully subsided. During this rest period, patients recorded the time spent performing the exercise until having to stop. When patients were able to complete three minutes of an exercise without being limited by claudication pain, the exercise was progressed by a member of the CR staff, either a Physiotherapist or Exercise Specialist.

All patients were then required to complete a cool-down period. This lasted for a minimum of 5 minutes and was either performed on the static exercise bike, group-based stretches, or a combination of both (as in warmup).

As participants attend each exercise programme only once a week, the rehabilitation team provided guidance and encouragement for patients to keep active outside of the sessions.

3.5.4.3 CAD Group

The cardiac patients recruited to the study followed the recommendations for circuit-based CR exercise from the BACPR (2017) and ACPICR (2015).

All patients completed a group warmup that lasted for fifteen minutes consisting of mobilisation exercises, pulse-raising movements, and stretches. The main circuit of exercise used the same eight exercise stations as the IC treatment patients, with the additional option of the rowing machine. Cardiac patients did not perform the same 'exercise to pain and rest' protocol as the IC patients, however. The interval-based exercise was used with a suitable ratio of cardiovascular (CV) exercise to active recovery (AR) – not complete rest - following the 'Levels' approach (ACPICR, 2015). AR involved completing a low-intensity resistance exercise (details in Table 3.2). The initial exercise session intensity was set between 40% to 70% heart rate reserve (HRR) for the cardiovascular exercise stations, depending on the results of the pre-SEP GXT and AACVPR Risk Stratification (AACVPR, 2013) and was individually prescribed by the PI. Patients were told to stop exercising if they felt any unusual responses to exercise (chest pain or discomfort, light-headedness, joint pain). Patients were monitored using a Polar® FT2 heart rate monitor (HRM) and rating of perceived exertion (RPE) scale at two or more points during the cardiovascular exercise stations by the CR Exercise Team. These details were recorded in patient notes and reviewed each week by a member of the Exercise Team. When a patient could comfortably exercise within or below their target HRR and RPE at their prescribed 'Level' (e.g., 2 minutes CV to 1 minute AR), the time on each CV station was increased.

All patients then underwent a 10-minute group-based cool down of low-intensity exercise and stretches to decrease HR and BP.

3.5.5 Patient Education

3.5.5.1 IC Control Group Education and Advice

There were no group education classes provided as part of the IC control SEP. Patient education was provided during the initial clinic appointment with the Vascular Specialist Nurse and Physiotherapist, and ad hoc during the exercise classes as and when patients required.

3.5.5.2 IC Treatment and Cardiac Group

Following each of the 12 exercise sessions, all patients were invited to attend educational sessions lasting between 20 to 50 minutes. Attendance of education sessions was not recorded. The standard CR topics were covered are detailed below:

- CVD – Diagnosis and Treatments
- Risk Factors for CVD
- Cardiac Medication
- PA and Exercise (x2 talks)
- Stress Management (x2 talks)
- Weight Management (x2 talks)
- Basic Life Support

There was a large overlap in the areas of IC patient education identified by NICE (2012) and topics already included in the current CR programme educational talks:

- Key modifiable risk factors, such as smoking, control of diabetes, hyperlipidaemia, diet, body weight and exercise (for secondary prevention of cardiovascular disease)
- Dealing with depression and anxiety
- The causes of their symptoms and the severity of their disease (atherosclerosis)

The talks were modified to include specific detail relevant to patients with PAD and IC such as relevant treatment options (risks and benefits) for example, femoral-popliteal bypass surgery and lower limb stenting was added to the 'CVD – Diagnosis and Treatment' talk. The risks of limb loss and cardiovascular events associated with peripheral arterial disease were also covered in this educational talk.

3.5.6 Post-SEP Assessment

All clinical outcome measures (resting BP and HR, height, weight, and waist circumference) were recorded again upon completion of the SEP. The quality of life questionnaires were also given to the participants to complete. Both pre and post-SEP assessments were conducted by the PI to maintain consistency of data collection as per Good Clinical Practice (GCP) guidance (Clinical Research Network, 2016).

3.6 Primary Outcome Measures

3.6.1 Feasibility of Treatment

The primary aim of this study was to assess the feasibility of an integrated CRP for patients with IC. Feasibility was assessed using the following outcomes:

3.6.1.1 Eligibility of patients

This was defined as the number of patients who met the inclusion criteria as a percentage of the total number of patients referred to each rehabilitation programme.

3.6.1.2 Consent Rate

This was defined as the number of patients who enrolled on the study as a percentage of the total number of patients who were approached about the study.

3.6.1.3 Retention Rate

This was defined as the total number of patients who completed the SEP and follow-up assessment as a percentage of the total number of participants who were consented.

3.6.1.4 Adverse events

Adverse events such as death, cardiac arrest, development of resting leg pain or critical limb ischaemia during the study and follow-up period were recorded and reported to the NHS research ethics committee and study sponsor as per GCP and HRA guidance.

3.6.1.5 Acceptability of Treatment and Trial Processes

The acceptability of the treatment and trial processes was measured both quantitatively and qualitatively to give a valuable insight into areas of the current protocol that might not be widely accepted in a large study (Lancaster et al., 2004). Quantitative measures included return rates for questionnaires, accelerometers including activity diary completion, as well missing data from clinic outcome measures (resting BP and HR etc.). Qualitative data on the suitability of the trial processes were also collected during the focus group and individual interviews. These interviews were planned to be held at the same site as the SEP took place as close to the follow-up session (post-SEP assessment) as possible. During these interviews, patients were asked their opinions on the trial processes (e.g., burden of questionnaires used, acceptability of thigh-worn accelerometers). As well as patient opinion, clinicians were also invited to focus groups and interviews to enquire on their opinion on the acceptability of the study protocol.

3.6.1.6 Research Team Involved with Qualitative Investigation

Three investigators facilitated the focus groups and individual interviews with patients (AS, PG, and EC). AR and PG were experienced in collecting qualitative date. AR had over fifteen years of conducting FGs and interviews and had received training during their PhD. PG had ten years' experience and had completed two separate training courses on conducting FGs and interviews over this period. EC was the principal Investigator (PI) for this study and had received limited training on facilitating focus groups during their student candidature.

3.6.1.6.1 Transparency and Assumptions

Both AR and PG were not involved in any other part of the study and had not had any interactions with patients prior to conducting the interviews. They also had no previous experience of working in a CRP or IC-specific rehabilitation programme. EC was previously employed by the CRP providing the integrated rehabilitation and was involved in its original design and implementation. EC has left the employment at the CRP when the study began but did have an honorary contract throughout the study period. EC was known to the patients as the clinical researcher responsible for the study and had completed the pre- and

post-SEP assessments with all participants that were involved in the qualitative interviews. EC was not involved in the day-to-day patient care.

3.6.2 Participant Selection

Purposive sampling was used to select patients and staff for the qualitative arm of the study to ensure representation from each of the group of participants. All patients completing their SEP were invited to attend either a focus group or individual interview which was conducted at the hospital site where their rehabilitation took place. Patients were invited to an FG or interview as close to their completion of the SEP to increase likelihood of attendance. CRP staff were invited to three separate focus groups which took place within the rehabilitation department to reduce burden on staff. Due to work demand, one focus group had only one CRP staff member attend, so resulted in it being an individual interview.

3.6.3 Data Collection

Patients focus groups were made up only of participants from the distinct groups (i.e., patient from the IC intervention and CAD groups were interviewed separately) so there was no interaction during the interview process. This was to promote open and honest discussion which may not have been possible with members of the other patient group present. The CRP staff focus groups were also conducted separately to the patient focus groups. This was also to keep honest and open discussion around the treatment process as staff might not want to discuss difficulties looking after patients if patients were present.

AR and PG collected most of the qualitative data for the patients as they were not involved with any other part of the study. The plan for the study was for AR and PG to conduct all interviews, due to their impartiality, however, this was not possible. One focus group involving IC control group patients was conducted by EC due to the other investigators not being available. Due to restrictions imposed by COVID-19, some interviews patients had to be conducted over the phone as no face-to-face appointments were allowed at the hospital. Due to patient confidentiality and GDPR regulations, the contact details for these participants could not be passed on to AR and PG, so EC only could conduct these telephone interviews due to his honorary contract with that hospital.

Dates were arranged when at least five participants had completed the SEP from the same group (i.e., IC control, IC treatment, or CAD group). CRP staff were invited for focus groups after the completion of all patient data collection. Semi-structured interviews were used for all qualitative data collection to ensure free flow of conversation with topics used only to guide the flow of discussion if required. The interviews were kept as open-ended as possible with the topic guides used to ensure specific areas of acceptability to trial and treatment procedures were addressed.

A list of topic areas was provided to guide the interviewer to ensure all relevant areas were covered (Table 3.4 for patient and Table 3.5 for staff); however, this was not followed in a specific order. The participants still had free flow over the conversation and were not limited in any way.

Table 3.4 List of topic guides for the post-intervention patient interviews

List of topic guides for interviews
What were your experiences of the exercise sessions?
What were your experiences of any education or advice given about your heart/leg condition?
How did you find the setting of the programme?
Where there any factors that influenced your attendance of the programme?
Where there any elements of the programme that may provide barriers to people attending in the future?
PAD group: How did you feel about exercising alongside people with heart disease (such as heart attacks, bypass surgery?) **CAD group**: How did you feel about exercising alongside people with peripheral artery disease?
Did the combined programme have any effect (both positive or negative) on your attendance and compliance with the programme (e.g., motivation)
How did you find the questionnaires you had to complete?
How did you find wearing the accelerometer?

Table 3.5: List of topic guides for the post-intervention staff interviews

List of topic guides for patient interviews
What were your experiences of the integrating PAD into CRP?
What were your experiences of the referral process?
What were your experiences of the assessment?
What were your experiences of the exercise sessions?
What were your experiences of the education sessions?
How did the integration with CAD patients go?
What were the similarities or differences between PAD and CAD patients?
Where there any other factors that influenced attendance of the programme?
Where there any elements of the programme that may provide barriers to people attending in the future?

3.6.4 Rationale for Semi-structured Focus Groups and Interviews

All qualitative data were collected using a semi-structured interview format, either focus group or individual interview, rather than through a closed question format or questionnaire. Semi-structured interviews allow a free flow of consciousness (Robson, 2011; Taylor and Francis 2013). Taylor and Francis (2013) state that "the underlying epistemological assumption in seeking participants' lived accounts from semi-structured interviews is that the information gathered constitutes valid and valuable knowledge, relative to participants' unique context of time, place and personal experiences." The use of unstructured interviews has also been shown to provide in-depth insights into the participant's experiential knowledge, which is paramount to any relativistic epistemological viewpoint, however, the wealth of data that can be produced in unstructured interviews would be too much for the scope of this study. As this study aimed to show the views of patients on a specific area – perceptions of combined rehabilitation programmes – semi-structured interviews were deemed a suitable format. In this format, prompts can be used by the facilitator to focus the patient's attention to a specific area. The facilitator can probe relevant areas for more detail or seek clarification and expansion as required.

One benefit of using focus groups in this study is the reduced frequency and duration of both data collection and construction. Bringing together groups of patients for discussion is more time-efficient that collecting individual accounts of the shared experience of the SEP. However, the individual perceptions of SEPs may not be wholly shared by all participants, so sufficient time was allowed to collect all participants' experiences fully. Also, there was a greater chance of strong personalities “over-shadowing” some members of the group, and their input being missed, making focus groups harder to facilitate. However, the establishing of clear ‘ground rules’ by the interviewer at the start of the focus group was made to help reduce the chance of this occurring.

The use of telephone interviews has been well documented in qualitative research however, one of the major weaknesses of this form of interview is the difficulty of developing a rapport with the participant. This can lead to data on sensitive issues not being covered. Furthermore, during telephone interviews, it is hard to record the non-verbal cues of participants such as body language and facial expressions and to fully assess the significance of any pauses in conversation and what they might mean (Robinson 2006). The aim of this study is to gain insight into the participants experience therefore, telephone interviews were not initially offered (although they had been included in the original ethics application). If a participant was unable or unwilling to attend a focus group, and individual interview was arranged at a suitable location for the participant. This is to ensure that no views are excluded purely down to being uncomfortable expressing opinions in a group format.

3.6.5 Pragmatic Changes to the Interview Stage

Due to the reduced availability of suitable rooms at the hospital site where the treatment arm took place, it became difficult to arrange suitable dates and times for patients. There were interview rooms with the R&D Department, however, the use of these had to be arranged with the original research agreement with the Trust and were not available for use (due to use in other research projects). Several patients were lost due to this reason. After continued difficulty to arrange suitable interview rooms, it was decided that telephone interviews would be utilised. Due to the lack of availability of independent interviewers, and the issue around data protection (sharing of patient telephone numbers to non-clinical staff), the PI of the

study, who had an honorary contract with the Trust, conducted the individual telephone interviews. This introduced bias to the interviews as the PI had been involved with the study conception and delivery itself and the patients were aware of the PI's connection to the CR department (honorary contract). Participants were also aware that the study is led by the PI was their own research being conducted as part of their studentship (from PIS detail and verbal discussion with PI). This again introduced bias, as participants may have wanted to give what they thought to be more favourable responses to the interview, and not want to come across as too critical. This risk of bias was weighed up against the reduced amount of qualitative data for the study, and the decision was made for the PI to go ahead with the telephone interviews.

3.7 Secondary Outcome Measures*:*

This feasibility study had an embedded pilot study which was designed to collect preliminary data to guide future RCT. Outcome measures were also used to perform an *a priori* sample size calculation for a larger scale study. The following measures were used:

- Functional capacity
    - Pain-free walking distance (PFWD) and maximal walking distance (MWD) – IC patients only
    - Metabolic Equivalents of Task [METS] (all groups)
- Quality of life – both generic and disease-specific (all groups)
- Free-living activity – physical activity and sedentary time outside of treatment sessions (all groups)

Table 3.6 This table provides a summary of quantitative outcome measures and the time-point at which they were recorded

Quantities subjected to post hoc analysis	
Quantity	Time of measure (weeks)
Clinical	
Blood Pressure (mmHg)	BL, 12 weeks
Resting Heart rate (bpm)	BL, 12 weeks
BMI ($kg.m^2$)	BL, 12 weeks
Waist circumference (cm)	BL, 12 weeks
Physical Functioning	
Gardner-Skinner Treadmill Test (IC patients only)	BL, 12 weeks
Incremental Shuttle Walk Test (CAD patients only)	BL, 12 weeks
Activity monitoring (accelerometer)	BL, 12 weeks
Questionnaires	
VascuQoL (IC patients only)	BL, 12 weeks
Hospital Anxiety and Depression Scale (HADS)	BL, 12 weeks
Walking Impairment Questionnaire (WIQ)	BL, 12 weeks
Dartmouth COOP (CAD patients only)	BL, 12 weeks
BL, Baseline; CAD, coronary artery disease IC, intermittent claudication	

The IC-specific tests have been recommended by the Transatlantic Inter-Society Consensus (TASC) Working Group for the Management of PAD (2007). The CAD-specific outcomes are standard outcomes measures recommended by the British Association of Cardiovascular Prevention and Rehabilitation (BACPR). All are detailed and rationalised in the following section.

3.7.1 Functional Capacity

3.7.1.1 IC-specific Treadmill Test Protocol

The Gardner-Skinner Protocol was used during this study to measure the pain-free and maximal walking distance in the IC participants. The Gardner-Skinner is a standardised graded exercise test (GXT) that is commonly used throughout PAD exercise rehabilitation programmes. It is a validated graded protocol that has been shown to have a greater reliability than continuous treadmill protocols when assessing maximal walking distance in symptom-limited PAD patients (Nicolai et al, 2009).

The treadmill protocol is as follows:

- Treadmill speed is held constant at 2 mph (3.2.km/hr)
- Treadmill incline begins at 0 per cent and increases 2 per cent every 2 minutes

For IC patients, the GXT was used to establish the pain-free walking distance (PFWD) and maximal walking distance (MWD). Using an IC pain scale (Table 3.3), PFWD was defined as the point at which patients verbally reported initial claudication (1 out of 4 on the pain scale) and MWD was defined as the point at which the patient could no longer walk. Patients were encouraged to walk to the point of maximal pain (4 out of 4 on the pain scale) however, they could stop before this point if necessary.

To reduce the likelihood of systematic error or bias, each participant had a practice test on the treadmill before undertaking the GXT that was used for analysis. In a report by Buckley et al. (2004) it was evidenced that increases in performance during exercise tests can be due to becoming familiar with the testing procedure (e.g., treadmill walking). They recommended a 'familiarisation test' be completed before main data collection to reduce the impact of the learning effect overestimating improvements in functional capacity measures. The familiarisation test was completed during their initial assessment (at SRFT) and repeated on their first session rehabilitation session. This second test was used for baseline data collection.

To further enhance methodological rigour, all participants were instructed not to hold the handrail of the treadmill whilst completing the test. A study by Gardner et al. (1991) showed that COT and MWT were significantly increased (both $p<0.05$) when subjects held the handrail compared to when handrail holding was not permitted. Therefore, handrail holding was only

permitted if their balance could not be maintained during the treadmill test. If a participant used the handrail in their initial test it was documented in their notes and the participant was instructed to hold the handrail during their post-SEP test to ensure consistency. The post-SEP test, or follow-up test, was conducted on their last SEP session as part of their discharge assessment. This was to reduce the burden of hospital visits.

3.7.2 CAD-specific Incremental Shuttle Walk Test

The Incremental Shuttle Walk Test (ISWT) is a progressive test that increases speed by 0.6 km/hr every minute. Originally developed and validated for use in pulmonary rehabilitation to assess exercise capacity (Singh et al., 1992), it has been validated for use in a range of clinical conditions and is a standardised exercise test used in CR settings (ACPICR, 2015). The test can be performed on a 10-metre course, with participants shuttle walking keeping to an audio pacing. The test has also been modified to be performed on a treadmill. Due to space limitations in the SEP recruiting cardiac patients, the modified treadmill version of the ISWT was used. The test is terminated when participants reach 80% of their heart rate reserve (HRR), a rating of perceived exertion of 15 or 'Hard' on the Borg 6-20 scale (Borg, 1998).

As with the IC patients, a practice or familiarisation test was administered to reduce systematic error or bias. The familiarisation test was completed during their initial assessment (at SRFT) and repeated during their first session rehabilitation session. This second test was used for baseline data collection.

All participants were instructed not to hold the handrail of the treadmill whilst completing the test unless balance could not be maintained during the treadmill test. If a participant used the handrail in their initial test it was documented in their notes and the participant was instructed to hold the handrail during their post-SEP test to ensure consistency. The post-SEP test, or follow-up test, was conducted on their last SEP session as part of their discharge assessment. This was to reduce the burden of hospital visits.

3.7.3 Quality of Life Measures

For all three groups under investigation within this study, the impact of the SEP on quality of life was recorded. These were measured by both generic and disease-specific measures. Research has shown that people living with PAD and CAD have a reduced quality of life when compared to non-disease populations due to a range of symptom limitations (Liles et al., 2006; Sagar et al., 2012)(Liles et al., 2006; Sagar et al., 2012). Rehabilitation programmes have been shown to improve symptom management and have a positive impact on quality of life. Although the quality of life measures used in this study are validated through research and recommended for use by the respective condition-specific guidelines (Gerhard-Herman, 2016; BACPR, 2017), the feasibility of collecting all outcome data simultaneously, at both time points (pre and post-SEP) needed to be assessed to ensure as part of the trial procedures. A total of four different quality of life measures were used:

- Hospital Anxiety and Depression Sore
- King's College Vascular Quality of Life Questionnaire
- Walking Impairment Questionnaire
- Dartmouth COOP Questionnaire

3.7.4 Hospital Anxiety and Depression Scale (HADS) questionnaire - Generic

This is a 14-item questionnaire with 7 questions measuring anxiety and 7 questions measuring depression. Responses to each question range from 0 to 3, with 0 being the optimal response (no anxiety or depression reported) and 3 being high levels of reported anxiety or depression. The scores for anxiety and depression are treated separately (i.e., not combined to create an overall score) so the total range for anxiety scores and depression scores is therefore from 0 to 21 with scores above 11 in either anxiety or depression being classed as abnormal (Zigmond and Snaith, 1983). This is a commonly used test for clinical settings and is a standard questionnaire used in Cardiac Rehab departments (ACPICR, 2015; BACPR, 2017) and is included in the National Audit of Cardiac Rehab. It takes on average 5 minutes to complete this questionnaire.

Participants were given this to complete at two time-points: baseline and completion of the SEP. The baseline HADS was provided at their pre-SEP assessment or first exercise session.

The second HADS questionnaire was provided on their penultimate SEP session for them to complete and return on their final session. This gave opportunity for patients to complete both HADS questionnaires at home which was deemed suitable due to the nature of the questions.

3.7.5 King's College Vascular Quality of Life (VascuQoL) Questionnaire (PAD-specific)

This is a 25-item disease-specific quality of life questionnaire that has 5 domains (pain, symptoms, activities, social and emotional) and has been widely used in PAD and IC research (Morgan et al., 2001; Vries et al., 2005' Mehta et al., 2006). Disease-specific quality of life measures are recommended by TASC (2007) as they are more sensitive to change in disease-specific symptoms than generic questionnaires. The VascuQoL takes on average 10 minutes to complete and were given at baseline and follow up assessment. As with the HADS questionnaire, participants were advised to complete it on their own, at home. As this is a disease-specific questionnaire, it was not given to CAD participants to complete.

3.7.6 Walking Impairment Questionnaire (WIQ):

This WIQ is a PAD disease-specific questionnaire assessing the perceived impact of claudication symptoms on the individual being measured. Patients give their perceived walking ability in terms of walking distance, walking speeds, and stair climbing. The scores for each of the three areas are then given as a percentage, with 100% showing no perceived impairment in that area, and 0% being unable to do due to limitations due to claudication or another limiting factor. Changes following any treatment or intervention are given in percentage points. The WIQ is a validated tool (Hiatt, Hirsch, Regensteiner, and Brass, 1995; Nichloai et al., 2009; Sagar et al., 2012) that has been commonly used in PAD research since its development by Regensteiner et al. (1995) and is recommended by TASC (2007) to assess patient-perceived symptoms. It takes on average 5 minutes to complete and was completed as part of the baseline (pre-SEP) and follow-up (post-SEP assessments). As this is a disease-specific questionnaire, it was not given to the CAD participants to complete.

3.7.7 Dartmouth COOP – Generic, Health-related Quality of Life Questionnaire

The Dartmouth COOP is a 7-item questionnaire. Each question measures a different domain of health status (physical fitness, feelings, daily activities, social activities, change in health status, current overall health perceptions, and bodily pain). Responses are scored on an ordinal scale from 1 to 5, with 1 being the optimal score. The overall score is calculated with the lower the score the better (Eaton et al., 2005). This questionnaire was given to cardiac patients at baseline and completion of the SEP. The baseline questionnaire was given during the patient's pre-SEP assessment, and the second questionnaire was given on their penultimate session to compete and return on the last SEP (discharge assessment).

Although this is a commonly used, validated questionnaire in patients with COPD (Jenkinson et al., 2002), the National Audit of Cardiac Rehabilitation (NACR) use this in their annual audit of patient outcomes and is used in most CR programmes in the UK (Jones et al., 2020).

3.7.8 Free-living Activity

Free-living activity was recorded by an activPAL™ micro accelerometer-based activity monitor to assess any changes in activity levels outside of the supervised exercise sessions (Figure 3.4). No activity data was collected during the rehabilitation exercise sessions. The activPAL™ micro weighs 15g and was attached to the front of the thigh using a medical-grade waterproof dressing (Figure 3.5).

Figure 3.4: The activPAL™ micro accelerometer that was used in the study. The figure on the front indicates the correct orientation of the device to support correct application

Data from the activPAL™ classifies activities into sedentary, standing and stride events. Consecutive stride events are combined to give walking events. The output has been validated for classification of sedentary, upright, standing and walking activities in a range of

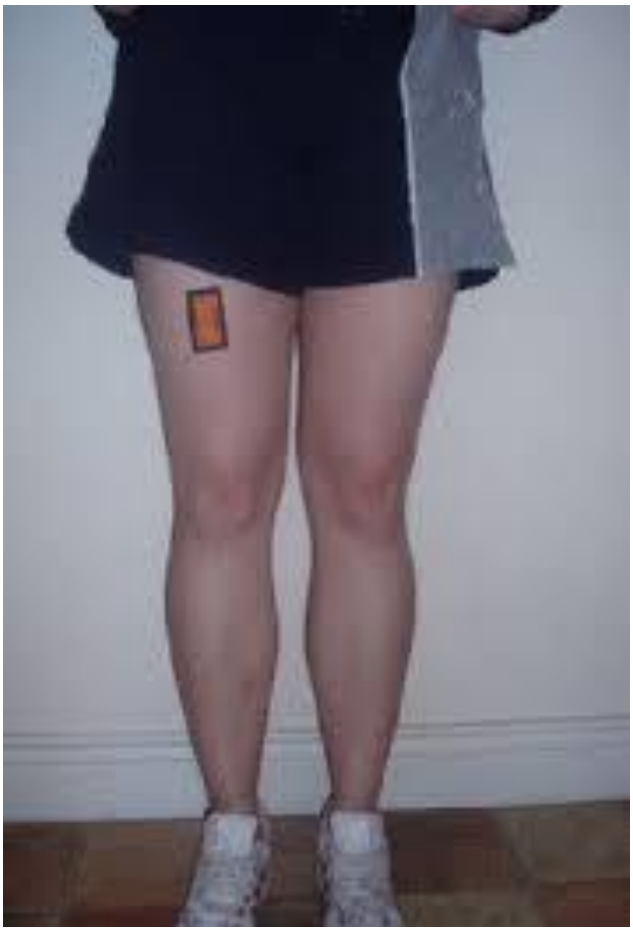


Figure 3.5 Picture of the thigh-worn accelerometer in-situ

populations including older adults and patients with IC (Bassett, 2012; Clarke et al., 2013). Baseline activity was recorded before starting the SEP, with the aim of a 7-day wear period not including a day with supervised exercise. During the week before completing their SEP, participants wore the activPAL again to record another 7-day period of activity. The outcome data recorded of interest included steps per day, sedentary time, upright time, and walking cadence. At the start of the study, the activity monitor algorithm could not distinguish the difference between seated time and lying time, due to the similarity of thigh orientation (horizontal) during these two positions.

Participants were therefore given a daily activity record sheet (Appendix 9) on which they were asked to record the time they woke up and got out of bed and the time they went to bed and fell asleep. The participants' sleep time could then be identified and removed from data and therefore not classed as sedentary time. The log also had a section to record periods that the device was not worn (e.g., pool swimming, or having a bath), or if there was any irritation from the waterproof dressing. This information was also used to assess the acceptability of this particular outcome measure. All participants were given an information sheet with details on how to place attach the monitor, if required, and how to record the information in the daily activity record sheet (Appendix 10).

3.8 Analysis

3.8.1 Primary Outcome Measures: Feasibility

3.8.1.1 Quantitative Data

Descriptive statistics were used to present the feasibility of the treatment such as the number of eligible patients, recruitment rates, and retention rates and were presented as frequencies and percentages. Adverse events were given as a frequency. Completion of trial outcome measures such as questionnaire completion and activPAL were also presented as frequency as percentage rates.

3.8.1.2 Qualitative Data

The data construction and thematic analysis were conducted by two individuals – the PI and MS. MS was the PI's supervisor and was experienced in thematic analysis. The analysis process followed Braun and Clare's (2006) six phases of thematic analysis as described in Table 3.7. Firstly, the audio recordings of each focus group and individual interview were transcribed. This involved the use of a professional transcribing service, and an online artificial intelligence transcription service (Otter.ai). The PI then spent a large amount of time checking over each transcription individually and correcting the scripts. Although transcription services were used, the quality of the transcriptions were poor with frequent errors in text, and text missing due to issues with overlapping conversation. Despite a large amount of time being required in this 're-transcribing' process (approximately two weeks), this did serve as an in-depth 'familiarisation' process for the PI.

The PI reviewed all transcripts again to generate initial codes and collected relevant text to support these codes. Codes were then reviewed and grouped together into potential themes. The second reviewer (MS) reviewed half of the transcripts, containing both patient and staff interviews, and generated initial codes and potential themes separately. Both reviewers then met to discuss the potential themes generated from this selection of transcriptions to identify those themes that matched and to discuss any separate themes identified as part of a process of triangulation. Themes were then refined, and a final list of themes was created with

appropriate definitions. The PI then presented the themes, with examples of verbatim text to support each theme.

Table 3.7 - This table outlines the steps taken in the thematic analysis of the focus group data. Taken from: Braun & Clarke, (2006) Using thematic analysis in psychology. Qualitative Research in Psychology. 3: pp77-101

Phase	Description of the process
1. Familiarizing yourself with your data:	Transcribing data (if necessary), reading and re-reading the data, noting down initial ideas.
2. Generating initial codes:	Coding interesting features of the data in a systematic fashion across the entire data set, collating data relevant to each code.
3. Searching for themes:	Collating codes into potential themes, gathering all data relevant to each potential theme.
4. Reviewing themes:	Checking if the themes work in relation to the coded extracts (Level 1) and the entire data set (Level 2), generating a thematic 'map' of the analysis.
5. Defining and naming themes:	Ongoing analysis to refine the specifics of each theme, and the overall story the analysis tells, generating clear definitions and names for each theme.
6. Producing the report:	The final opportunity for analysis. Selection of vivid, compelling extract examples, final analysis of selected extracts, relating back of the analysis to the research question and literature, producing a scholarly report of the analysis.

3.8.2 Secondary Outcome Measures: Pre and Post-SEP data:

The distribution of secondary outcome data was assessed using the Shapiro-Wilks test for normality before appropriate parametric and non-parametric tests were performed. Descriptive statistics for continuous variables were presented as means, standard deviations (SD) and confidence intervals (set at 95%). For within-group difference, the paired t-test or Wilcoxon Signed Rank test was used (for normally and non-normal distributed data, respectively). Between-group differences were analysed using an independent t-test or Mann Whitney U-test – for comparison of two groups – or an ANOVA or Kruskall-Wallis 1-way ANOVA for comparison of three groups. Comparison of nominal variables was made using the Chi-square test. All statistical tests were performed using SPSS statistical analysis software (IBM SPSS Statistics 26®).

The CAD group secondary outcome measures of functional capacity (GXT result) and quality of life (HADS and Dartmouth) were compared to the National Audit of Cardiac Rehabilitation (NACR) data to assess the impact on the CAD group performance against expected national levels.

3.8.2.1 Power Calculations

To ensure the future definitive study on treatment efficacy is adequately powered, an *a-priori* sample size calculation was performed. An *a priori* sample size calculation uses a given effect size (Cohen's d), alpha (α) level, and power from previous research to calculate out the required number of participants for an adequately power study (Faul et al., 2009). As pilot data was being collected during this study, this gave an opportunity to use data that closely reflected the design of the future study. The following section explains how sample size calculation was performed.

It was decided that both the MWD data and total VascuQoL score data from the IC treatment group would be used as improving these outcomes are the main focus of interventions for the management of IC (Ibeggazene et al., 2022). The test with the highest recommended sample would then be used to guide the future study.

Using the online G*Power Software (Version 3.1.9.7), the achieved power of each outcome was determined using the *post hoc* power calculation. This uses the known effect size, the α level of used in the study (0.05), and the measures sample size. Following this, the *a prior* sample size calculation was performed. The selected statistical test was an independent t-test (2-tailed), as the future trial will compare the means of the control and intervention groups.

3.8.3 Ethics and Code of Conduct

As this study involved participants who were NHS patients, both University of Salford and NHS ethical approval was required. Ethical approval was granted by University of Salford Research Ethics Committee on 19th December 2017 (Reference HSR1617-184 – See Appendix 2). Approval was obtained from the Northwest - Greater Manchester West Research Ethics Committee on 13th June 2018 (IRAS ID: 230391 – See Appendix 3). This study was registered with clinicaltrials.gov (NCT03564080) and conforms to the Declaration of Helsinki.

The PI for this study completed the Health Research Authority's (HRA) Good Clinical Practice (GCP) Primary Care eLearning package prior to initiating recruitment to ensure that appropriate procedures were followed during the study (e.g., confidentiality and anonymity). The PI also gained an honorary contract with one of the study centres (SRFT) which allowed access to patients' electronic and paper notes for screening purposes and the ability to contact prospective participants (when onsite at the hospital) to discuss enrolling on the study. As part of the honorary contract, mandatory training was completed to ensure safe and effective practice was conducted by the PI throughout the study. This was essential as they were actively involved in the assessment of participants both before and after the SEP intervention and in programming the level of exercise intensity for participants' initial sessions. Mandatory training was set by the local NHS Trust and involved Adult Basic Life Support (BLS), Patient Manual Handling and Adult and Children Safeguarding.

Due to differences in R&D policy at the second hospital site, an honorary contract was not a possibility, so a member of the rehabilitation team was identified to lead the recruitment process there. This identified member of staff initially approached patients about the study and identified an interest to participate prior to the PI being able to meet the patient directly. The identified member of staff was required to have up to date HRA Good Clinical Practice

Primary Care training. The PI was not allowed to view patient notes so required information for the study was recorded on a Case Report Form (Appendix 8).

3.8.3.1 Pre-screening For Programme Suitability

Prior to starting the SEP, all patients were risk stratified to assess their likelihood of adverse events during exercise using the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) Risk Stratification Tool (AACVPR, 2013). This is standard procedure in cardiac rehabilitation programmes as risk stratification determines the level of intensity that is prescribe (i.e., safe heart rate zones for exercise) and dictates the level of supervision required. This is in keeping with the guidelines of the British Association of Cardiovascular Prevention and Rehabilitation (BACPR) the national governing body of CR programmes. All safety information for physical activity was discussed with the participant prior to commencing any exercise test or the exercise programme itself.

3.8.3.2 Psychological Support

During the research project, participants can disclose information that required ongoing support or investigation. An example of this is the identification of significantly high levels of anxiety or depression (HADS score >11) because of their recent cardiovascular diagnosis. If any area of concern was raised during the study, participants were able to access appropriate support systems within their rehabilitation department. For example, both rehabilitation programmes offered psychological support via a counselling service, and these were discussed with participants and referrals made if required.

3.8.3.3 IC Participants

Due to the progressive nature of the cardiovascular condition, a patient's PAD may worsen during their time in the study. If a participant developed worsening symptoms such as resting leg pain – a sign of critical limb-threatening ischemia – they were removed from the study and referred to their vascular specialist for immediate review.

The individual exercise prescriptions were designed to be above the intensity that participants would usually perform at home, or in their occupation and therefore could unearth symptoms of other cardiovascular conditions such as angina pectoris that had not been experienced before. If participants developed such symptoms, they were referred to their GP to arrange an appropriate Cardiology referral. They were removed from the research programme.

3.8.3.4 CAD Participants

Due to the underlying cardiovascular condition, patients who are unwell (e.g., systemic infection) may not be able to exercise on the day of testing, or during their SEP. In which case, they did not take part until fully recovered.

As with the IC patients, individual exercise prescriptions were designed to exert patients more than their usual amount. During the exercise test and subsequent exercise sessions, there was the possibility a patient may develop symptoms of angina. Participants who have been prescribed a GTN spray\tablets were asked to bring this with them and in the case of symptoms the GTN protocol was adhered to.

3.9 Refined Aims and Objectives

The primary aim of this thesis was to investigate the feasibility of integrating patients with IC into an already established CRP. The secondary aims were:

i. Investigate the acceptability of trial procedures to patients and staff.
ii. Identify the appropriate outcome measures to use to guide a definitive study of integrated CRP efficacy.

The objectives for next stage of the thesis were:

i. Analyse the results from the feasibility study

Chapter 4 Results

This chapter presents the study findings and highlights trends in the data. The initial section covers the feasibility outcomes of eligibility, consent rate, retention rate, and adverse events. The acceptability of the trial procedures is covered quantitatively through completion rates of outcome measures, and qualitatively through focus groups and individual interviews with participants and CR staff. The acceptability of the treatment – qualitatively assessed during the focus groups and individual interviews - is then presented.

The final section presents the pilot outcome data including sample size calculation for the future RCT on treatment efficacy.

4.1 Participant Characteristics

The baseline characteristics for all three groups in the study is presented in Table 4.1.

4.1.1 Age, Gender, Ethnicity

There were 41 participants who completed the study, 15 in the IC control group, 11 in the IC treatment group, and 15 in the CAD Group. The mean age of participants for the IC treatment group was 68.7 years (SD 12.5; range 48 to 88 years old). The IC control group had a mean age of 67.1 years (SD 10.1; range 43 to 83 years old). The CAD Group had a mean age of 62.3 years (SD 10.5; range 41 to 78 years old). There was no significant difference in age between the three groups ($p = 0.289$). Although there is limited data on the age range of people with PAD in the UK, the mean age of IC patients in this study does reflect the age group with the highest prevalence of PAD in high-income countries (65-69 years old) (Song et al., 2019). The average age of people attending CR programmes in the UK is 67 years old, ranging from 18 to 105 (BHF, 2019c).

There was a high proportion of males in all three groups, with the IC treatment, IC control, and CAD group having 73.3%, 63.5% and 80% male gender, respectively. There was no difference in gender representation across the three groups ($\chi 2 = 0.649$). The CAD data

reflects the NACR 2019 data for participation rates for CR, with female attendance only 28.7% (BHF, 2019c).

The ethnicity of participants was predominantly White-British across all three groups, with only one participant being Black Jamaican and one White-Irish. The ethnicity across the three groups were not different ($\chi 2 = 0.340$). Again, this reflects the under-representation of non-White ethnicities found in those attending CR (BHF, 2019c) and reflects the IC population.

Table 4.1: Baseline characteristics of participants completing each of the Supervised Exercise Programmes broken down by group

Variable	IC Control (n = 15)	IC Intervention (n= 11)	CAD (n= 15)	p value
Mean age (years)	67.1 ± 10.1	68.7 ± 12.5	62.3 ± 10.5	0.289
Gender				
Female	4 (26.7%)	4 (36.4%)	3 (20%)	0.649
Male	11 (73.3%)	7 (63.6%)	15 (80%)	
Ethnicity				
Black Caribbean	1 (6.7%)	0	0	0.340
White British	14 (93.3%)	10 (90.9%)	15 (100%)	
White Irish	0	1 (9.1%)	0	
ABPI[a]	n = 9	n = 11		
>1.4	0	1 = (9.1%)[b]	NA	
1-1.4	0	2 (18.2%)[c]		
0.91-0.99	0	0		
0.9	0	1 (9.1%)		
0.7-0.9	2 (22.2%)	5 (45.5%)		
0.4-0.7	5 (55.6%)	1 (9.1%)		
<0.4	2 (22.2%)	2 (18.2%)		
Mean ABPI[d]	0.53 (range 0.3 to 0.7)	0.67 (range 0.3 to 0.9)		0.149
Unilateral or Bilateral PAD				
Unilateral	7 (46.7%)	5 (45.5%)	NA	
Bilateral	7 (46.7%)	6 (54.5%)		
Missing data	1 (6.6%)	0		
Past Medical History				
IHD	4 (26.7%)	1 (9.1%)	15 (100%)	
CVA (Stroke)	2 (13.3%)	0	0	
COPD	3 (20.0%)	2 (18.2%)	0	
Type 1 DM	1 (6.7%)	1 (9.1%)	0	
Type 2 DM	5 (33.3%)	2 (18.2%)	6 (20.0%)	
Pre-diabetes (IGT)	0	1 (9.1%)	0	
Risk Factors for CVD				
Hypertension	5 (33.3%)	3 (27.3%)	6 (40%)	
Hyperlipidaemia	4 (26.7%)	2 (18.2%)	6 (40%)	
Current Smoker	6 (40.0%)	4 (36.4%)	1 (6.7%)	
Ex-smoker	8 (53.3%)	3 (27.3%)	8 (53.3%)	
Number of comorbidities				
0	2 (13.3%)	3 (27.3%)	2 (13.3%)	
1	2 (13.3%)	3 (27.3%)	4 (26.7%)	
2 or more	11 (73.3.0%)	6 (54.5%)	9 (60%)	
Average no. of comorbidities	2.7 (range 0 to 7)	1.7 (range 0 to 6)	2.1 (range 0 to 4)	

ABPI – Ankle Brachial Pressure Index; COPD – Chronic Obstructive Pulmonary Disorder; CVA – Cerebrovascular Accident; IGT – Impaired Glucose Tolerance, IHD – Ischaemic Heart Disease; PAD – peripheral artery disease; TBPI – Toe Brachial Pressure Index.

[a] If participant had bilateral PAD, then the ABPI from the worse leg was reported

[b] This participant had calcification, so PAD was diagnosed through TBPI (51mmHg and 71mmHg in right and left toes, respectively).

[c] This participant had normal ABPI, so PAD was diagnosed using an exercise test (post-exercise drop ≥20mmHg).

[d] ABPIs above ≥1.0 have not been included in the calculation of this mean.

4.1.2 ABPI and Baseline Walking Capacity (PAD patients)

There was missing ABPI data for 9 of the 15 patients (60%) in the IC control SEP (Table 4.2). All the IC treatment group participants had documented ABPI or TBPI if appropriate. One participant had non-compressible arteries, a sign of calcification, and the resulting ABPI during doppler assessment was >1.4. This patient was therefore diagnosed following TBPI (51 mmHg and 71 mmHg in right and left toes, respectively), using the diagnostic criteria of Conti et al, (2009). Two other participants had normal resting ABPIs but following an exercise challenge there was a BP drop of ≥20 mmHg which confirmed the PAD diagnosis.

A comparison of the mean ABPI of IC control group (0.53) and IC Intervention Group (0.67) showed no significant difference between groups ($p = 0.149$). The number of unilateral and bilateral PAD patients in each group was also not significantly different ($\chi 2 = 0.897$). This showed both groups had comparable disease severity at baseline (Table 4.1). In the case of bilateral disease, the ABPI of the leg most effected by PAD (i.e., lowest ABPI) was used in the comparison.

Although baseline disease severity was similar when measured objectively, there were differences between the group in subjective measurement. A comparison of the baseline walking capacity of the IC control and treatment groups showed differing levels of PFWD. The IC control group's mean PFWD was 95.9 meters (SD 55.7) compared to the IC treatment group's mean PFWD of 176.0 metres (Figure 4.8). This extra 80.1 metres of pain-free walking for the IC treatment group was significantly higher (95% CI [135.4, 24.8 metres], $p = 0.006$). However, this was not the case for the mean MWD for both groups. The IC treatment group's mean MWD of 527 metres (SD 261) was 126 metres longer than the IC control group (M= 386, SD 267), with this difference not being significant ($p = 0.205$) (Figure 4.8).

4.1.3 Past Medical History and Number of Comorbidities

As expected in this patient population, there were many previous diagnoses of related circulatory conditions (Table 4.1) with patients having been diagnosed with ischaemic heart disease and cerebrovascular accidents (stroke). Notably, only 7 of the 41 participants

(17.1%) who completed the study did not have any comorbidities. The average number of comorbidities for the IC treatment, IC control and CAD group, respectively, was 2.7, 1.7, and 2.1. There was no difference in the number of comorbidities (p =0.426). No patient had comorbidity that was more limiting than their referring diagnosis (i.e., IC or CAD).

4.1.4 Missing Baseline and Follow-up Data

The following section shows the completion rate for clinical outcome measures recorded by the PI during the baseline and follow-up assessments. A summary of the baseline and follow-up assessments are presented in Table 4.2 and Table 4.3, respectively. There were stark differences in some outcome measures between the two sites. Nearly 50% of baseline BP, HR, height, weight, BMI, and waist measures were not recorded in the IC control group. The same measures in the IC treatment and CAD group (both completed at the same site) had a 100% completion rate, apart from the waist measurement of the IC treatment group (88.2%)

Table 4.2: Summary of baseline assessments highlighting data collection issues

	Study Group			
	IC Control (n = 19)	IC Intervention (n = 17)	CAD (n = 21)	**Study Total** (n = 57)
Baseline Anthropometrics				
BP				
Completed (n)	9	17	21	47
Missing (n)	10	0	0	10
Recorded (%)	47.4	100	100	82.5
HR				
Completed (n)	9	17	21	47
Missing (n)	10	0	0	10
Recorded (%)	47.4	100	100	82.5
Height, weight, and BMI				
Completed (n)	9	17	21	47
Missing (n)	10	0	0	10
Recorded (%)	47.4	100	100	82.5
Waist				
Completed (n)	9	15	21	45
Missing (n)	10	2	0	12
Recorded (%)	47.4	88.2	100	79.0
ABPI or TBI				
Completed (n)	12	15	NA	27
Missing (n)	7	2	NA	9
Recorded (%)	63.2	88.2	NA	75
Smoking Status				
Completed (n)	17	17	21	55
Missing (n)	2	0	0	2
Recorded (%)	89.5	100	100	96.5
CPD (current smokers only)				
Completed (n)	3	6	1	10
Missing (n)	6	1	0	7
Recorded (%)	50.0	85.7	100	58.8

BP – blood pressure; RHR – resting heart rate; BMI – body mass index; ABPI – ankle-brachial pressure index; TBPI – toe-brachial pressure index. CPD – cigarettes per day

- **Recorded** refers to the percentage of successful data being documented

The completion rate for BP, HR, height, weight, BMI, and waist measures was even lower in the IC control group at follow-up assessment (post-SEP) especially waist measurement which was not recorded in any participant (Table 4.3). A high completion rate for assessment data was achieved in the IC treatment and CAD groups at the separate site. The main reason for this difference was the availability of separate clinic rooms at the hospital site facilitating the control group. There was no scope to book a separate clinic room for the PI to conduct pre-SEP assessments, resulting in baseline data not being collected if no spare clinic room was available on the day. There was also no separate clinic room available on the day of the follow-up assessment of the IC control group participants, due to the location of the rehabilitation facility in the hospital.

Table 4.3: Summary of follow-up assessments highlighting data collection issues

	Study Group			
	IC Control (n = 15)	IC Intervention (n = 11)	CAD (n = 15)	**Study Total** (n = 41)
Follow-up Anthropometrics				
BP				
Completed (n)	5	11	15	40
Missing (n)	10	0	0	1
Recorded (%)	33.3	100	100	97.6
HR				
Completed (n)	5	11	15	25
Missing (n)	10	0	0	1
Recorded (%)	33.3	100	100	96.2
Height, weight, and BMI				
Completed (n)	5	11	15	23
Missing (n)	10	0	0	3
Recorded (%)	33.3	100	100	88.5
Waist				
Completed (n)	0	11	15	40
Missing (n)	15	0	0	1
Recorded (%)	0	100	100	97.6
Smoking Status				
Completed (n)	17	17	15	39
Missing (n)	2	0	0	2
Recorded (%)	89.5	100	100	95.1
CPD smoked				
Completed (n)	3	6	1	36
Missing (n)	6	1	0	5
Recorded (%)	50	85.7	86.7	87.8

BP – blood pressure; RHR – resting heart rate; BMI – body mass index; CPD – cigarettes per day

- **Recorded** refers to the percentage of successful data being documented

4.2 Primary Outcome – Feasibility Measures:

The primary outcome of this study was to assess the feasibility of an integrated CRP for patients with IC and to assess the acceptability of the study protocol. Quantitative measures of feasibility included:

- Eligibility rate
- Consent Rate
- Retention Rate
- Number of adverse events

The acceptability of the study protocol was measured quantitatively through questionnaire return rates and missing data. Qualitative measures were used to assess the acceptability of the study protocol during the focus group and interview stage. Questions on the acceptability of outcome measures such as the thigh-worn accelerometers were included in this qualitative part of the study. Clinicians were invited to attend focus groups and interviews to assess the demands placed on staff for recruitment (pre-screening), and the impact on service delivery due to integrating IC patients into the CR service.

The acceptability of the treatment to both patients and staff was measured during the focus groups and individual interviews to assess their thoughts and opinions of the treatment itself.

Following the CONSORT guidance extension for pilot and feasibility studies (Eldridge et al., 2016) the quantitative feasibility outcomes for each group are covered separately. As three different groups of participants were recruited from two different hospital programmes, and differences in referral and assessment processes were present, this approach allows for individual characteristics and limitations of recruiting at each site and within each group to be more clearly demonstrated.

The IC Intervention Group is presented first, followed by the IC control group, and finally CAD Group following. Descriptive statistics are used to summarise the feasibility outcomes. The qualitative measures of feasibility are then presented as a separate section.

4.2.1 IC Control Group

The flow of participants through the IC control group is presented in Figure 4.1.

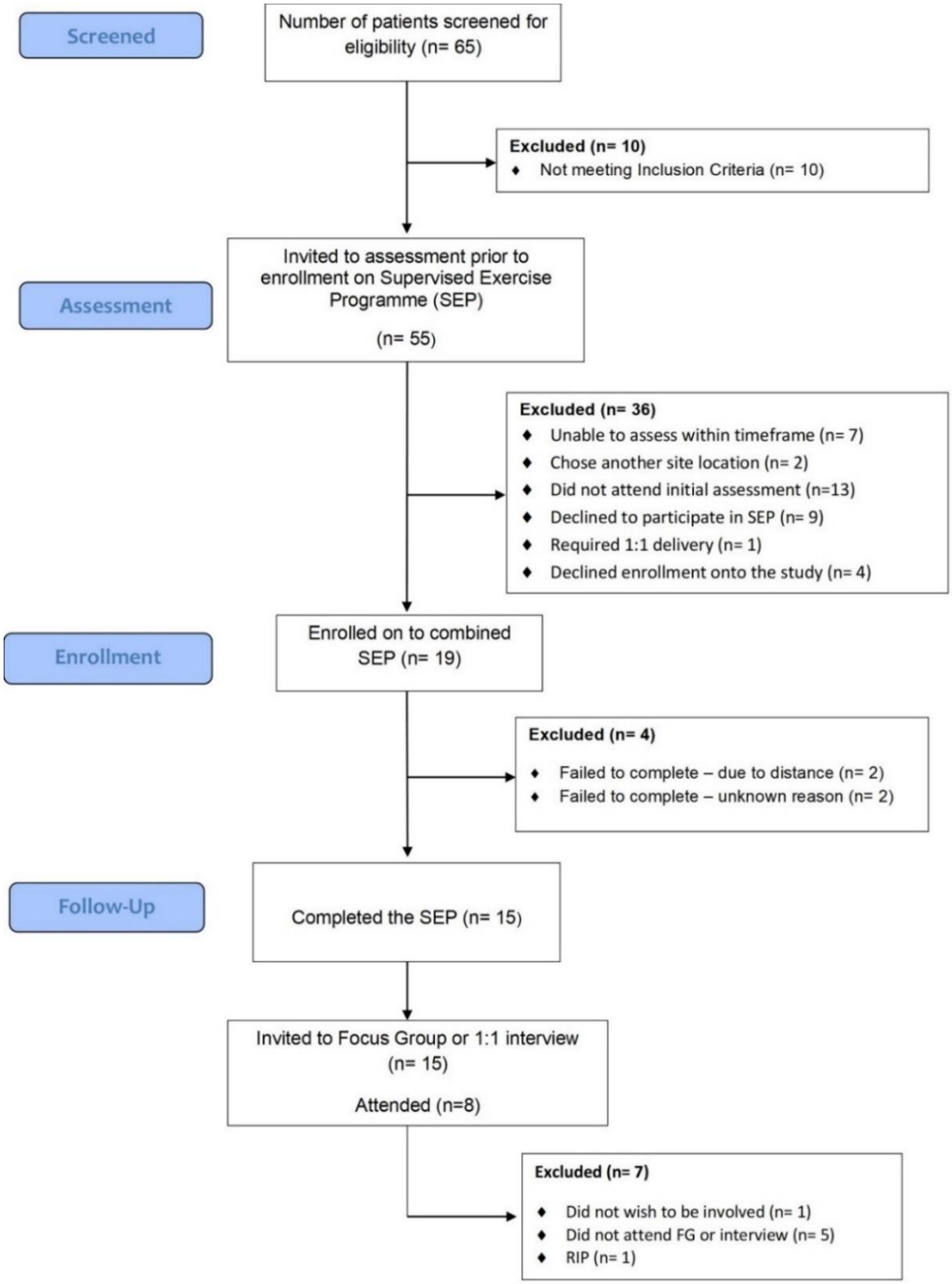


Figure 4.1 CONSORT flow diagram for the IC control group

4.2.1.1 Eligibility of Patients

Over an 8-month period of recruitment (February 2019 to October 2019), 65 patients were referred to the rehabilitation programme that recruited for the IC control group. All 65 patients were screened for eligibility with 10 patients (15.4%) being excluded. The eligibility rate was therefore 84.6%. A summary of the reasons for exclusion is provided in Table 4.4.

Table 4.4 Reasons for patients being excluded from the IC control group during the 'pre-screening' eligibility check

Reason for not meeting inclusion criteria	n
Previous Intervention for PAD (e.g., angioplasty)	5
Previous participation in an SEP	2
Unsuitable – Awaiting surgical repair of AAA	1
Unsuitable – Awaiting orthopaedic surgery	1
Unsuitable – Limiting back pain	1
Total	10

4.2.1.2 Consent Rate

Out of the 55 patients that were identified as eligible, 36 patients (65.5%) were excluded. Seven (12.7%) of the eligible patients could not be offered an assessment within the 3-week cut-off period, therefore could not be invited to the study. Thirteen patients (23.6%) were invited but did not attend their initial assessment appointment.

Out of the patients that did attend their initial assessment, 16 patients (29.1%) declined enrolment on the SEP. The reasons for declining are provided in Table 4.5.

A total of 19 patients were consented to the study, giving a consent rate of 39.5% (19 out of 48). The 7 patients who were not able to be assessed within the 3-week period were not included in this calculation.

Table 4.5 Reason for declining the IC control group supervised exercise programme

Reason given for declining SEP	n
Independent exercise at community-based exercise programme	1
Travel distance – requested SEP closer to their home	2
Unsuitable for group exercise (required 1:1 supervision due to physical limitations)	1
Independent exercise at home or at unspecified location	4
Unable to attend due to work	2
Opted for surgical intervention (angioplasty or bypass)	1
Unknown reason	5
Total	16

4.2.1.3 Retention Rate

The total number of patients recruited to the IC control group was 19. Out of these participants, 4 (21.1%) failed to complete the SEP. Attempts to contact by telephone were made to establish the reason for dropping out. Two participants reported issues with the distances needed to travel to the SEP; however, the other 2 participants could not be reached by telephone, so their reason for dropping out is unknown.

The remaining 15 participants completed the SEP, and all participants performed follow-up assessments. The average number of sessions completed per participant was 11.9 (range 11 to 12, SD 0.4).

The retention rate for this group was 78.9% (15 out of 19).

4.2.1.4 Adverse Events

There were no adverse events reported during the SEP. There was only one patient who died between completion of SEP and invitation to the qualitative arm of the study, which was due to non-CVD causes.

4.2.2 IC Intervention Group

The flow of participants through the IC Intervention Group is presented in Figure 4.2.

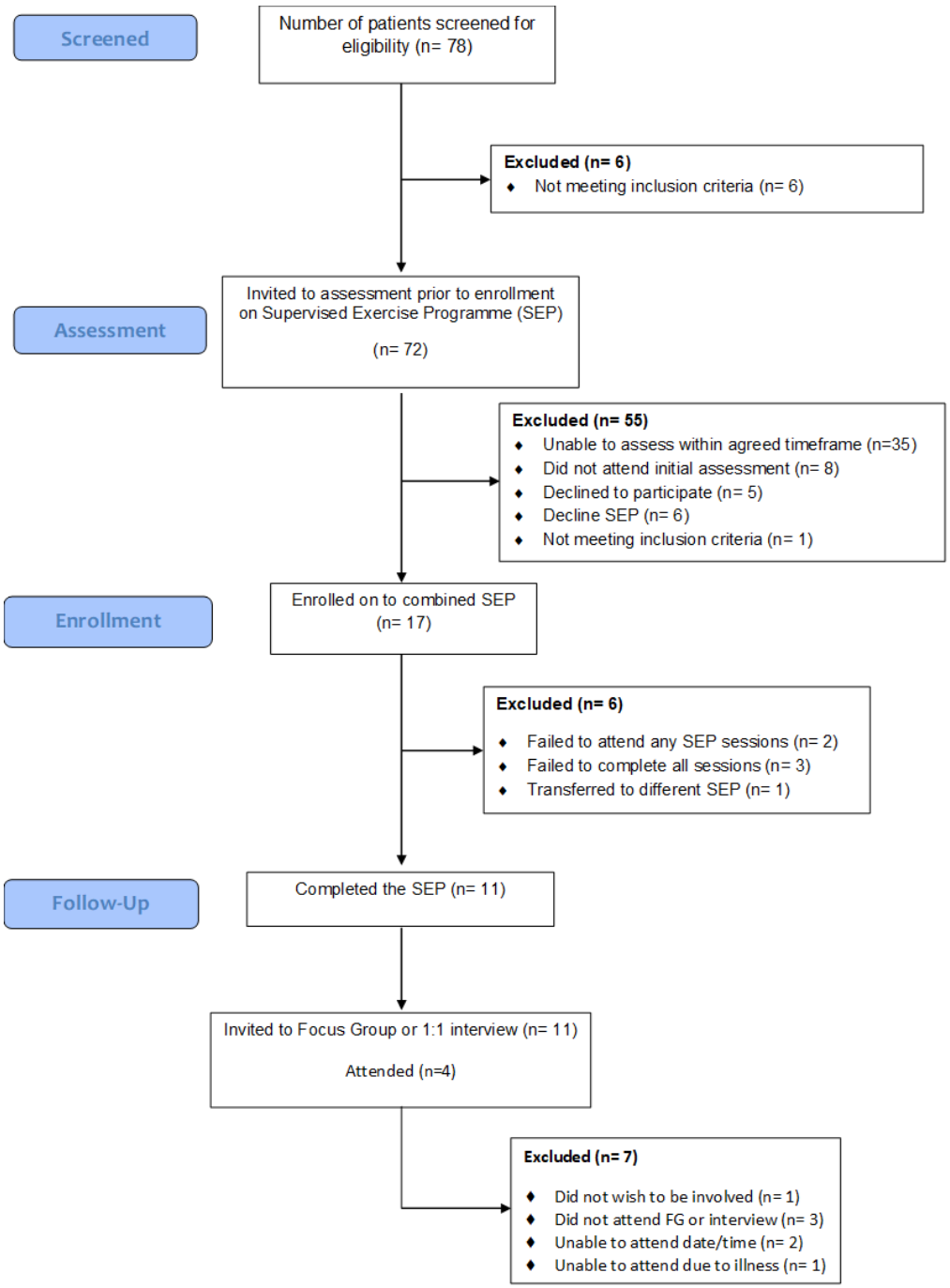


Figure 4.2: CONSORT Flow Diagram for IC Intervention Group

4.2.2.1 Eligibility Rate

Over a 13-month period of recruitment period (August 2018 to September 2019), 78 patients with IC were referred to the Cardiac Rehabilitation Programme (CRP) which was running the combined IC and CAD programme. All 78 patients were screened for eligibility by the Cardiovascular Specialist Nurses, with the PI being consulted if clarification on eligibility was required. Following screening, 6 participants (7.7%) were excluded for not meeting the inclusion criteria, giving an eligibility rate 92.3% (72 out 78). A summary of the reasons for exclusion from the study are provided in Table 4.6.

Table 4.6: Reasons for patients being excluded from the IC control group during the 'pre-screening' eligibility check

Reason for not meeting inclusion criteria	n
Previously attended CR programme for a cardiac condition	1
Recent cancer diagnosis – undergoing treatment	1
Unsuitable – Awaiting surgical repair of AAA	1
Unsuitable – unstable angina – referred for cardiology review	1
Unsuitable – Limiting osteomyelitis	1
Translator Required	1
Total	6

4.2.2.2 Consent Rate

Out of the 72 patients invited to the SEP, 55 (76.4%) were excluded.

A total of 35 eligible patients (48.6%) were excluded from the study due to the PI not being available for pre-SEP assessment within 3 weeks of initial telephone consultation.

Out of the 20 participants who were invited for their initial assessment, 8 (11.1%) did not attend. Eleven patients (15.2%) attended their pre-SEP assessment, but declined the SEP. The reasons for declining are provided in Table 4.7. One patient was excluded from the study due to atypical leg pain that was identified during the pre-SEP assessment.

Table 4.7: Reason for declining the IC treatment Group Supervised Exercise Programme

Reason given for declining SEP	n
Unable to attend - Work commitments	1
Unable to attend - Reason unknown	10
Total	11

Seventeen participants were consented and formally enrolled onto the study. This gave a consent rate of 45.9% (17 out of 37). The 35 patients who were not able to be assessed within the 3-week period were not included in this calculation.

4.2.2.3 Retention Rate

Out of the 17 participants enrolled in the study, 6 participants were excluded prior to the follow-up assessment. A summary of the reasons for participant exclusion prior to follow-up is provided in Table 4.8. One participant could not complete the study due to them being transferred to a more suitable exercise class. During their exercise sessions, it was established that symptoms of shortness of breath limited them due to underlying COPD diagnosis. They were transferred to another class offered at the CR department for patients with low exercise tolerance.

Table 4.8: Reason for exclusion of IC Intervention participants prior to follow-up

Reason for exclusion	n
Failed to attend and SEP sessions	2
Failed to complete at least 8 sessions	3
Transferred to a different SEP	1
Total	6

The remaining 11 participants completed the SEP, and all participants performed follow-up assessments. The average number of sessions completed per participant was 11.4 (range 10 to 12, SD 0.8).

The retention rate for this group was 64.7% (11 out of 17)

4.2.2.4 Adverse Events

There were no adverse events reported in the IC treatment group.

4.2.3 CAD Group

The flow of participants through the CAD Group is presented in Figure 4.3.

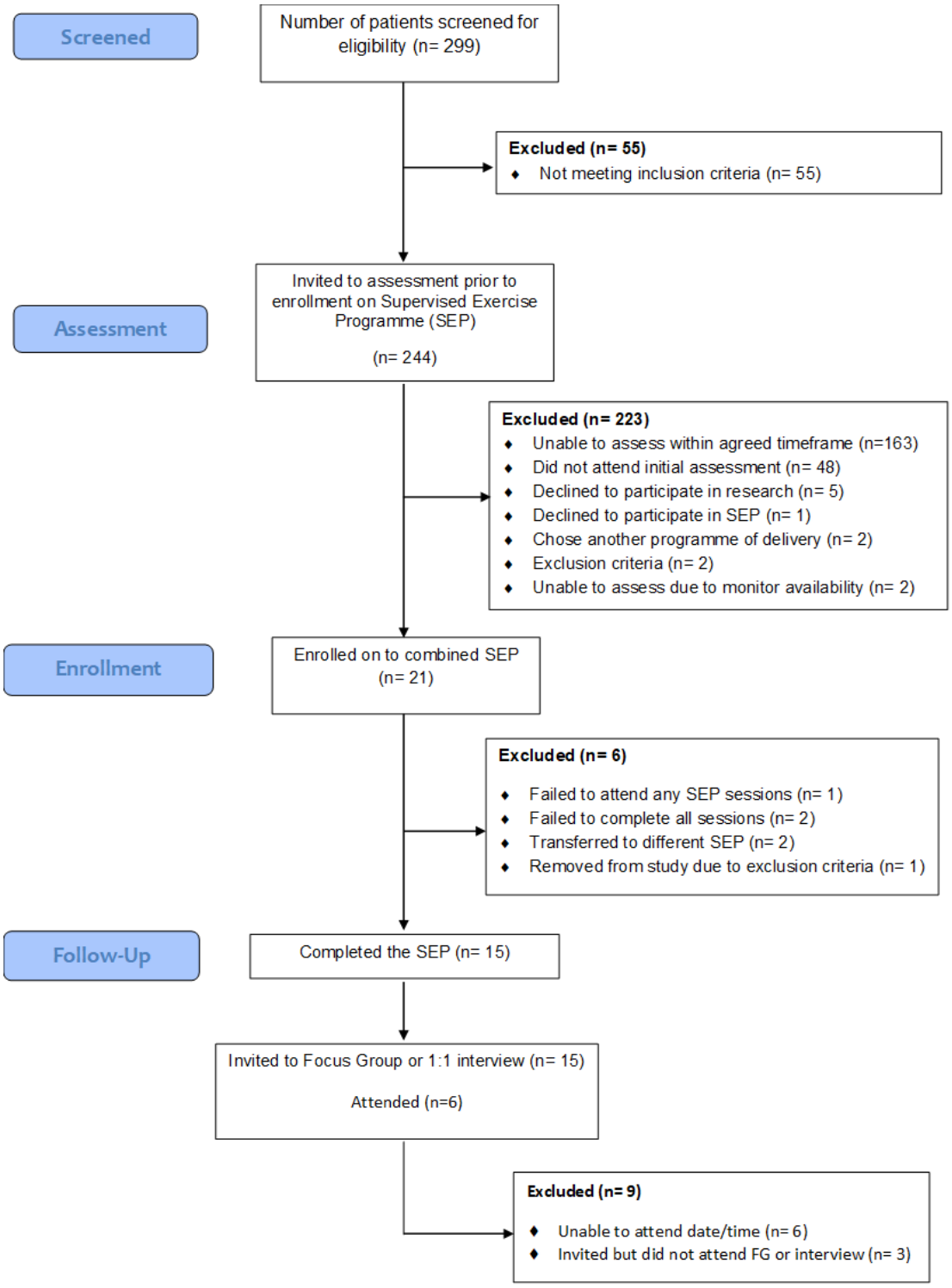


Figure 4.3: CONSORT Flow Diagram for Cardiac Group

4.2.3.1 Eligibility Rate

The recruitment period for the CAD Group was the same as the IC treatment group period (August 2018 to September 2019), as both IC and CAD patients were attending the same rehabilitation programme. During this period, 299 patients were referred to the rehabilitation centre following a diagnosis of a cardiac diagnosis, event, or surgical intervention. All 299 patients were screened for eligibility. Out of this total number, fifty-five patients (18.4%) did not meet the inclusion criteria. Reasons for not meeting the inclusion criteria are detailed in Table 4.9. This gave an eligibility rate of 81% (244 out of 299).

Table 4.9: Reason for cardiac patients referred to CRP not meeting inclusion criteria

Reason for not meeting inclusion criteria	(n)
Heart Failure	31
Primary Diagnosis Not Coronary Artery Disease e.g., valvular or arrhythmias	11
Previous Diagnosis of PAD	7
Currently undergoing dialysis – unable to commit to SEP	1
Ongoing (cardiac) surgical complications	2
Interpreter required	3
Total	55

Seven patients (1.1%) who were diagnosed with a CAD condition had been previously diagnosed and treated for PAD, and therefore could not be included in the study.

4.2.3.2 Consent Rate

Out of the 244 eligible patients, 223 patients were excluded.

A total of 163 patients (66.8%) could not be assessed within 3-weeks of their initial telephone consultations. As previously described, it was deemed unethical to delay patient

start dates, so these patients were excluded from the study. This left 81 remaining patients to recruit from who were all invited for an assessment with the PI. Out of these 81 patients, 60 patients were excluded. Details of the reasons for exclusion are provided in Table 4.10.

Table 4.10: Reason for CAD patients being exclusion from the study

Reason for exclusion	(n)
Did not attend initial assessment	48
Declined to participate in SEP – unknown reason	5
Declined to participate in SEP – anxiety	1
Chose another programme of delivery (twice per week CR Programme)	2
Met exclusion criteria	2
Unable to complete full assessment due to accelerometer availability	2
Total	60

Only 1 of the 5 patient who declined the SEP provided a reason. This patient had high levels of anxiety and felt the research project would add extra personal demands. After the pre-SEP assessment, 2 participants decided they would prefer the twice a week CR programme. Two participants were excluded following their pre-SEP assessment, one for unstable angina and one for lack of capacity due to cognitive impairment following an out of hospital cardiac arrest. Two participants consented to the research; however, there were no accelerometers available for these patients.

Twenty-one participants were consented and formally enrolled onto the study. This gave a consent rate of 25.9% (21 out of 81). The 163 patients who were not able to be assessed within the 3-week period were not included in this calculation.

4.2.3.3 Retention Rate

Out of the 21 consented patients enrolled on the CAD Group, 6 participants were excluded prior to follow-up assessment. A summary of the reasons for exclusion are presented in Table 4.11.

Table 4.11: Reason for exclusion of CAD participants prior to follow-up

Reason for exclusion prior to follow-up – CAD Group	(n)
Failed to attend and SEP sessions	1
Failed to complete at least 8 sessions	2
Chose another programme of delivery	1
Transferred to a different SEP	1
Met exclusion criteria	1
Total	6

One participant failed to attend any of the SEP sessions. Attempts were made to contact the patients, but no response was received. Their reason for not attending the SEP is therefore unknown. Two patients failed to complete the required 8 out of 12 sessions due to work commitments. After starting on the once per week programme, one participant switched to the twice per week programme (6 weeks duration of SEP rather than 12 weeks). This patient was a keen exerciser and wished to return to their local gym as soon as possible. One participant was removed due to meeting the exclusion criteria of a change in medication (beta-blocker dosage was increased mid-way through their programme). As this might have impacted on exercise performance, particularly during their follow-up GXT, they were removed from the study.

Interestingly, one patient experienced lower limb pain during their exercise sessions and was referred to a Vascular Podiatrist for review. Assessment by the podiatrist diagnosed symptom-limiting PAD, and they were switched to the IC rehab programme and removed from the study. Their progression through the IC SEP was not recorded as part of this study.

The remaining 15 participants completed the SEP, and all participants performed follow-up assessments. The average number of sessions completed per participant was 11.7 (range 11 to 12, SD 0.4).

The retention rate for this group was 71.9% (15 out of 21).

4.2.3.4 Adverse Events

There were no adverse events reported in the CAD Group.

4.2.4 Summary of All Groups

A summary of the feasibility measures for each of the 3 groups in the study is presented in Table 4.12. This includes a combined total of all data to give an overview of feasibility of the study as a whole. A total of 442 patients were referred to the rehabilitation programmes. The IC control group had the lowest number of patients referred; however, this was due to a shorter recruitment period compared to the groups involved with the intervention (8 months versus 13 months). All patients referred were screened by rehabilitation staff, with 371 out of the 442 patients (83.9%) eligible for the study. As highlighted in the earlier group breakdowns, there was a large number of eligible patients who were not able to be assessed. The combined figure shows this to be nearly half of the eligible patients. A positive result is the relatively high completion rate for each group, and therefore high rate for the overall study of 71.9% (Table 4.12).

Table 4.12: Summary of the number of patients who were eligible, consented, completed, and who had an adverse event during the study. Data for each group is provided as well as a study total.

Feasibility Measure	IC Control % (n)	IC Treatment % (n)	CAD % (n)	Study Total % (n)
Screened for Eligibility	100 (65)	100 (78)	100 (299)	100 (442)
Eligibility Rate	84.6 (55)	92.3 (72)	81.6 (244)	83.9 (371)
Eligible patients that could not be assessed*	12.7 (7)	48.6 (35)	66.8 (163)	55.6 (205)
Consent Rate	39.5 (19)	45.9 (17)	25.9 (21)	34.3 (57)
Retention Rate	78.9 (15)	64.7 (11)	71.4 (15)	71.9 (41)
Adverse Events	0	0	0	0
* The figures in this row refer to the number of patients who were screened and found to be eligible for the study but could not be offered an assessment with the PI within 3-weeks of their referral to the respective rehabilitation programme.				

4.3 Acceptability of the Study Procedures

In the following section, the completion rates for each outcome measure are presented to show the acceptability of the study's procedures for the participants. The data for the starters and completers for each group is presented separately. This is to show the overall level of acceptability and to highlight any relationship between the study protocol and those who dropped out within and between each of the three groups. Similar to section 4.2 , the individual groups are presented separately followed by a summary of all group data.

4.3.1 IC Control Group – Starters

A summary of the outcome completion and return rates for the IC control group starters is provided in Table 4.13. Each outcome measure is then discussed in more detail individually.

Table 4.13: Outcome measure completion rate for the participants starting the IC control group

IC Control - Starters (n= 19)			
Outcome Measure	Number (n)	Missing data (n)	Completion/Return Rate (%)
GXT	19	0	100
VascuQoL	17	2	89.5
WIQ	19	0	100.0
HADS	18	1	94.7
activPAL	18	1	94.7
Activity diary	16	3	84.2

4.3.1.1 Graded Exercise Tests (GXTs):

All 19 participants underwent a pre-rehabilitation GXT using the Gardner Skinner treadmill protocol. Participants were encouraged to walk through the initial claudication pain (1 out of 4 on 0 - 4 scale rating) and continue to their maximal tolerated claudication pain. The median peak pain during the test 4 (range 2 – 4, SD 0.8).

4.3.1.2 Questionnaires:

The completion rate for the VascuQoL was just under 90%, and the HADS questionnaire was just under 95% completion. There was a high completion rate of questionnaires from the 19 patients recruited for the study. The WIQ was administered by the PI during the initial assessment, which accounted for the 100% completion rate.

4.3.1.3 Accelerometer and Diary:

All 19 participants agreed to wear the accelerometer. Only one participant returned the device without any activity being recorded. They reported wearing the device for the week, and only taking it off to bathe, but upon inspection of the recording, no movement had

been recorded and it was clear that the monitor had not been worn. There was no diary completed by this participant either. This was classed as 'non-compliance' to wearing the accelerometer. Taking this participant into account, the overall consent rate for the accelerometer was 94.7%.

All accelerometers that recorded activity data recorded at least four valid days were classed as successfully recording the required data. The average number of days worn/recorded was 5.9 days. Sixteen participants recorded their wear-time and sleep-times in the diaries provided. No record was made of the reasons why the other three participants did not complete the diary at this point.

4.3.2 IC Control Group – Completers

A summary of the outcome completion and return rates for the IC control group completers is provided in Table 4.14. Each outcome measure is then discussed in more detail individually.

Table 4.14: Outcome measure completion rate for the participants completing the IC control group

IC Control - Completers (n= 15)			
Outcome Measure	Number (n)	Missing data (n)	Percentage (%)
GXT	15	0	100
VascuQoL	14	1	93.3
WIQ	15	0	100
HADS	15	0	100
activPAL	15	0	100
Activity diary	12	3	80
Average Number of sessions completed	11.9	0	99.2

4.3.2.1 Graded Exercise Tests (GXTs):

All 15 participants that completed the programme underwent a follow-up GXT using the Gardner Skinner treadmill protocol. Participants were encouraged to walk through the initial claudication pain (1 out of 4 on 0 - 4 scale rating) and continue to their maximal tolerated claudication pain. The median peak pain reported during the test was 3 (range, 2 – 4, SD 1.0).

4.3.2.2 Questionnaires:

The WIQ was administered by the PI during the follow-up assessment, matching the pre-SEP assessment. The completion rate for WIQ was therefore 100%. The VascuQoL and HADs were given to participants on the penultimate visit with participants being instructed to complete at home and bring to their follow-up assessment (final SEP session). The HADS questionnaire completion rate post-SEP was 100%. Only one participant did not return the post-SEP VascuQoL questionnaire. This participant reported completing the questionnaire but did not bring it to the final session. An envelope was given to post the questionnaire back, but the questionnaire was never received. The VascuQoL return rate was therefore 93.3%.

4.3.2.3 Accelerometer and Diary:

All 15 of the participants who completed the rehabilitation programme agreed to wear the accelerometer again. This was given to the participant on their final rehabilitation session with a pre-paid envelope to post the monitor back following the 7-day wear period. Average recording period was 6.2 days, slightly higher than the pre-rehabilitation wear time, and 12 out of the 15 completed and returned their diaries giving a diary completion rate of 80%.

Three out of the 15 monitors did not record the required four valid days due to technical difficulties, so the data was not included in the final analysis.

4.3.2.4 Adherence to Programme:

The average number of sessions completed was 11.9 out the 12 (range of 11 to 12 sessions) with 86.7% achieving the maximum attendance of twelve sessions.

4.3.3 IC Intervention Group – Starters

A summary of the outcome completion and return rates for the IC Intervention group starters is provided in Table 4.15Table 4.13. Each outcome measure is then discussed in more detail individually.

Table 4.15: Outcome measure completion rate for the participants starting the IC Intervention Group

IC Intervention - Starters (n= 17)			
Outcome Measure	Number (n)	Missing data (n)	Completion/Return Rate (%)
GXT	16	1	94.1
VascuQoL	13	4	76.5
WIQ	14	3	82.4
HADS	15	2	88.2
activPAL	16	1	94.1
Activity diary	15	2	88.2

4.3.3.1 Graded Exercise Test (GXT):

Out of the 17 participants who were enrolled on the study, 16 completed the initial GXT using the Gardner Skinner protocol on the treadmill. One participant was not confident on the treadmill on the day of testing, so a six-minute walk test (6MWT) was performed instead.

Participants completing the Gardner Skinner protocol were encouraged to walk through the initial claudication (1 out of 4 on 0 - 4 scale rating) and continue until their maximal tolerated pain. The median peak pain reported for the group was 3 (range 2 – 4, SD 0.5) at termination of the test.

4.3.3.2 Questionnaires:

The completion rate for the WIQ was only 82.4%. Although the WIQ was administered by the PI to maintain consistency across the reporting, the wrong questionnaire was used on 3 occasions (the first 3 participants recruited). This version did not have the section on stair

climbing. These questionnaires were classed as 'missing', although as the walking distance and speed categories were completed correctly, that data were included in the data analysis.

All participants were given the VascuQoL and HADS questionnaires on their initial assessment and encouraged to complete these at home (due to previously mentioned considerations). There was a 76.5% completion rate for the VascuQoL questionnaire and a slightly higher 88.2% completion rate for the HADS questionnaire.

4.3.3.3 Accelerometer and Diary:

Sixteen of the 17 participants (94.1%) wore the accelerometer following their initial assessment. One participant was given the accelerometer to wear on their initial assessment and then failed to attend any further appointments and were therefore removed from the study. They did not return the accelerometer, so no data or diary were collected. All other participants successfully wore the accelerometer, and the average recorded time was 6.4 valid days. The 15 participants that returned the accelerometer also returned completed diaries showing sleep time and non-wear time. The reason for the one participant not completing the diary was not recorded.

4.3.4 IC Intervention Group – Completers

A summary of the outcome completion and return rates for the IC Intervention group completers is provided in Table 4.16. Each outcome measure is then discussed in more detail individually.

Table 4.16: Outcome measure completion rate for the participants completing the IC Intervention Group

IC Intervention - Completers (n= 11)			
Outcome Measure	Number (n)	Missing (n)	Completion/Return rate (%)
GXT	10	1	90.9
VascuQoL	11	0	100
WIQ	8	3	72.7
HADS	11	0	100
activPAL	11	0	100
Activity diary	11	0	100
Average Number of sessions completed	11.5	NA	95.8

4.3.4.1 Graded Exercise Tests (GXTs):

Out of the 11 participants who completed the SEP, 10 completed the follow-up GXT using the Gardner Skinner protocol. The patient who completed the 6MWT at baseline assessment performed this test again so was not included in the final data analysis for walking capacity. As with the initial GXT, all participants were encouraged to walk through the initial claudication pain and continue until their maximal tolerated pain. The median peak pain during the walking test was 3.0 out of 4 (intense pain) with a range of 2 to 4 (SD 0.9) being reported.

4.3.4.2 Questionnaires:

The follow-up WIQ was administered by the PI for 8 out of the 11 participants. In three cases the WIQ was administered by a member of the rehabilitation team as the PI was not available. The WIQ used by the rehabilitation team was slightly different from the one used in the study as it did not include the section on stair climbing. These three questionnaires have been classed therefore as 'missing'. The distance and speed sections were completed correctly and have been included in the final analysis (secondary outcomes of study).

All 11 participants completed the follow-up VascuQoL and HADS questionnaires (100% completion rate).

4.3.4.3 Accelerometer and Diary:

All participants agreed to wear the accelerometer at the end of their SEP. This was either worn on their penultimate week of the SEP and returned on their last session or given on the last session and posted back to the PI. The average number of valid days recorded was 5.3 (range 5 to 7, SD 2.0). Two accelerometers did not record the required minimum of four valid days so were not included in the final data analysis (secondary outcomes). All participants returned completed diaries containing wear time and sleep time information.

4.3.4.4 Adherence to Programme:

The average number of sessions completed was 11.4 out the 12 (range 10 to 12, SD 0.8) with 72.7% achieving the maximum of 12 sessions.

4.3.5 CAD Group – Starters

A summary of the outcome completion and return rates for the CAD group starter is provided in Table 4.17Table 4.13. Each outcome measure is then discussed in more detail individually.

Table 4.17: Outcome measure completion rate for the participants starting the CAD Group

CAD Group - Starters (n= 21)			
Outcome Measure	Number (n)	Missing data (n)	Completion/Return Rate (%)
GXT	21	0	100
HADS	20	1	95.2
Dartmouth Coop	20	1	95.2
activPAL	20	1	95.2
Activity diary	19	2	90.5

4.3.5.1 Graded Exercise Tests (GXT):

All 21 participants who were enrolled on the study completed an initial GXT with the incremental shuttle walk test (ISWT) performed on the treadmill being the selected protocol.

During the GXT, participants were encouraged to walk for as long as possible. Tests were terminated when the target heart rate reserve (HRR) of 70% maximum or an RPE of 15 ('Hard' on the 6-20 RPE rating scale), or the patient requested for another reason. The median peak RPE reported during the test was 13 (range 11 to 15, SD 1.3).

4.3.5.2 Questionnaires

The pre-SEP HADS and Dartmouth Coop questionnaires were completed by participants using the National Audit of Cardiac Rehabilitation (NACR) Dataset Questionnaires. This is a set of questions given to patients (in paper format) upon referral to the CR programme (initial assessment) that include the HADS and Dartmouth Coop questionnaires along with physical activity recall, prescribed medication recall, and other demographic and anthropometric data (NACR, n.d.). If patients had not returned their initial NACR dataset they were provided with additional copies of the questionnaires and asked to complete as part of the research study.

A high return rate of 95.2% was achieved for both of these quality of life questionnaires.

4.3.5.3 Accelerometer and Diary:

Twenty of the 21 participants starting the programme (95.2%) wore the accelerometer following their initial assessment. One participant was given the accelerometer to wear on their initial assessment and then failed to attend any further appointments and were therefore removed from the study. They did not return the accelerometer, so no activity data or diary were collected. All other participants successfully wore the accelerometer, and the average recorded time was 5.9 valid days (range 5 to 7, SD 0.8) with all devices recording over the required minimum of 4 valid days. Nineteen of the 20 participants (95%) who returned their accelerometer after the initial week wear period also returned completed diaries with sleep time and non-wear time detailed. The reason for the one participant not completing the diary was not recorded.

4.3.6 CAD Group – Completers

A summary of the outcome completion and return rates for the CAD group completers is provided in Table 4.18. Each outcome measure is then discussed in more detail individually.

Table 4.18: Outcome measure completion rate for the participants completing the CAD Group

CAD Group - Completers (n= 15)			
Outcome Measure	Number (n)	Missing data (n)	Completion/Return rate (%)
GXT	15	0	100
HADS	14	1	93.3
Dartmouth	15	0	100
activPAL	13	2	86.7
Activity diary	13	2	86.7
Average Number of sessions completed	11.7	0	97.5

4.3.6.1 Graded Exercise Tests (GXT):

All 15 participants who completed the SEP underwent a follow-up GXT repeating the ISWT protocol performed pre-SEP. Like the initial GXT, participants achieved a median RPE rating of 13 (range 12 to 15, SD 1.1) which approximates to 'somewhat hard' on the 6 to 20 rating scale.

4.3.6.2 Questionnaires

The post-SEP HADS and Dartmouth Coop questionnaires were completed by participants as part of their National Audit of Cardiac Rehabilitation (NACR) Dataset of Questions (Assessment Two) which were given on their penultimate week of their SEP. If patients had not returned their initial NACR dataset, they were provided with additional copies of the questionnaires and asked to complete during their discharge assessment.

A high return rate of 93.3% and 100% was achieved for the HADS questionnaire and the Dartmouth questionnaire, respectively.

4.3.6.3 Accelerometer and Diary:

All 15 participants agreed to wear the accelerometer at the end of their SEP. This was either given to wear on their penultimate week of the SEP and returned on their last session or given on the last session and posted back to the PI. Two accelerometers that were due to be posted back were not received, so the accelerometers and diaries were lost. All the returned devices recorded the required number of days (4 days minimum) with the average number of valid days recorded being 6.2 (range 6 to 7, SD 0.8). All participants returned completed diaries containing wear time and sleep time information, apart from the one that was lost in the post.

4.3.6.4 Adherence to Programme:

The average number of sessions completed was 11.7 out the 12 (range 10 to 12, SD 0.6) with 80% of participants achieving the maximum of twelve sessions.

4.3.7 Summary of Group Acceptability

A summary of the acceptability of study procedures is presented for both starters and completers for each of the 3 groups in Table 4.19 and Table 4.20, respectively. This includes a combined total of all data to give an overview of acceptability for the study procedures as a whole study.

Table 4.19: Acceptability of study procedures reflected in the completion and return rates of the outcome measures for those starting the study. This is presented as the individual groups and as the combined participant data

	Study Group			
	IC Control (n = 19)	IC Intervention (n = 17)	CAD (n = 21)	**Study Total** (n = 57)
Outcome Measure				
GXT				
Completed (n)	19	16	21	56
Missing (n)	0	1	0	1
Completion (%)	100	94.1	100	98.2
VascuQoL				
Completed (n)	17	13	NA	30
Missing (n)	2	4	NA	6
Return rate (%)	89.5	76.5	NA	83.3
WIQ				
Completed (n)	19	14	NA	33
Missing (n)	0	3	NA	3
Completion (%)	100	82.4	NA	91.6
HADS				
Completed (n)	18	15	20	53
Missing (n)	1	2	1	4
Return rate (%)	94.7	88.2	95.2	93.0
activPAL				
Completed (n)	18	16	20	54
Missing (n)	1	1	1	3
Recording rate (%)	94.7	94.1	95.2	94.7
Activity diary				
Completed (n)	16	15	19	50
Missing (n)	3	2	2	7
Return rate (%)	84.2	88.2	90.5	87.7

GXT – graded exercise test; VascuQoL – King's College VascuQoL questionnaire; WIQ – walking impairment questionnaire.

- ***Completion** is used for those measures completed by the PI*
- ***Return rate** is used for those measures that are taken away and then returned by the participant on their next session*
- ***Recording rate** refers to the percentage of successful recordings for the activPALs*

There was a consistently high completion and return rate from those patients starting the study across all outcome measures (Table 4.19). The lowest percentage was for the VascuQoL questionnaire in the IC treatment group. This was one of the questionnaires that was given to patients to complete at home and return on their next session.

Table 4.20: Acceptability of study procedures reflected in the completion and return rates of the outcome measures for those completing the study. This is presented as the individual groups and as the combined participant data

	Study Group			
	IC Control (n = 15)	IC Intervention (n = 11)	CAD (n = 15)	**Study Total** (n = 41)
Outcome Measure				
GXT				
Completed (n)	15	10	15	40
Missing (n)	0	1	0	1
Completion (%)	100	90.9	100	97.6
VascuQoL				
Completed (n)	14	11	NA	25
Missing (n)	1	0	NA	1
Return rate (%)	93.3	100	NA	96.2
WIQ				
Completed (n)	15	8	NA	23
Missing (n)	0	3	NA	3
Completion (%)	100	72.7	NA	88.5
HADS				
Completed (n)	15	11	14	40
Missing (n)	0	0	1	1
Return rate (%)	100	100	93.3	97.6
activPAL				
Completed (n)	15	11	13	39
Missing (n)	0	0	2	2
Recording rate (%)	100	100	86.7	95.1
Activity diary				
Completed (n)	12	11	13	36
Missing (n)	3	0	2	5
Return rate (%)	80	100	86.7	87.8
Sessions completed	11.9 out of 12	11.5 out 12	11.7 out of 12	11.7 out of 12
Completion (%)	99.2	95.8	97.5	

GXT – graded exercise test; VascuQoL – King's College VascuQoL questionnaire; WIQ – walking impairment questionnaire.

- ***Completion** is used for those measures completed by the PI*
- ***Return rate** is used for those measures that are taken away and then returned by the participant on their next session (or returned by post)*
- ***Recording rate** refers to the percentage of successful recordings for the activPALs*

There was also a high completion and return rate from those patients who completed the study (Table 4.20). This was across all outcome measures used, with the lowest being for the WIQ in the IC treatment group. This was due to the incorrect form being used with 3 participants resulting in the data being classed as missing.

4.4 Qualitative Assessment of Acceptability of Intervention and Study Protocol

In this section the results of the focus groups and individual interviews are presented. These interviews focused on the feasibility and acceptability of the study's procedures and of the integrated rehabilitation programme. The aim was to investigate the views and experiences of both the patients and the CRP staff of the trial (e.g., recruitment and assessment procedures) and the intervention (i.e., integrated rehabilitation). The patients' views and experiences are reported separately from the CRP staff views and experiences.

The Consolidated criteria for reporting qualitative research (COREQ) checklist for interviews and focus groups (Tong, Sainsbury, and Craig et al, 2007) was used to guide the structure of this section. This was deemed appropriate after observing its use in similar types of studies to this current one (Hubbard et al, 2015).

4.4.1 Number of Participants

In total, 28 participants were involved in the qualitative arm of the study. The breakdown of each group is presented in the next sections followed by a summary of all groups.

4.4.1.1 IC Control Group:

Out of the 19 participants who enrolled on to the IC control group, 8 (42%) were interviewed. Two focus groups were conducted (one with 4 patients and one with 3 patients) and 1 individual interview. Four participants had withdrawn from the study and were therefore not invited for interview.

Out of those who invited but did not attend for interview, 1 participant (6.7%) did not wish to attend the interview stage, 5 participants (26.3%) did not attend the date given (or

subsequent dates offered), and 1 patient (5%) died of non-CVD related causes prior to invite to an FG or interview (Table 4.21).

Table 4.21: Reason for non-involvement with qualitative arm – IC control group

Reason	(n)
Did not wish to be involved	1
Did not attend FG or interview stage (after being invited)	5
Died prior to FG date	1
Total	7

4.4.1.2 IC Intervention Group:

Out of the 17 participants enrolled on to the IC Intervention Group, 4 (24%) were interviewed. These 4 patients were all interviewed individually with 1 conducted face to face at the recruiting hospital and the other 3 being conducted over the telephone due to COVID-19 restrictions. Six patients (35%) were withdrawn from the study so were not invited to the interview stage. One participant (6%) did not wish to be involved in the interview stage and did not provide a reason. Three participants (18%) were given a date for an FG but did not attend. Invitations for other FGs were sent by post to these patients, but they did not attend these appointments either. They were not followed up after the missed FGs, so their reasons for not attending are unknown. Two participants (12%) could not attend the dates provided due to work or childcare commitments, and 1 patient (6%) was invited but did not feel able to attend due to being recently diagnosed with cancer and awaiting treatment (Table 4.22).

Table 4.22: Reason for non-involvement with qualitative arm – IC treatment group

Reason	(n)
Did not wish to be involved	1
Did not attend FG or interview stage (after being invited)	3
Unable to attend FG/Interview date	2
Unable to attend due to illness	1
Total	7

4.4.1.3 CAD Group

From the 21 patients with CAD enrolled on the study, six (29%) were interviewed. Two focus groups with three participants per group were ran which represents a 40% uptake of the qualitative arm of the study in this group. Six participants (29%) were withdrawn from the study so were not invited to the interview stage. Five participants (24%) were unable to attend any FGs date and times due to work or childcare issues, and one patient (5%) was on a prolonged holiday. Only three participants (14%) that were invited to an FG did not attend on the day. Invitations for other FGs were sent by post, but they did not attend these appointments either. They were not followed up after the missed FGs, so their reasons for not attending are unknown (Table 4.23).

Table 4.23: Reason for non-involvement with qualitative arm – CAD Group

Reason for non-involvement with qualitative arm – CAD Group	(n)
Unable to attend FG/interview date	6
Did not attend – reason unknown	3
Total	9

4.4.1.4 CRP Staff

In total, 10 cardiac rehabilitation clinicians were interviewed during the qualitative arm of the study. Two focus groups were completed (one with 3 staff and one with 5 staff) and one individual interview, all face to face. This represented 67% of all staff employed by the service with all disciplines being represented. The breakdown of roles was as follows:

- CR Manager x 1
- CR Specialist Nurses x 2
- CR Specialist Dietician x 1
- CR Practitioner (dietary and psychological specialist) x 1
- CR Specialist Physiotherapist x 2
- CR Exercise Physiologists x 3

A summary of the number participants in each group, and the type of interview is presented in

Table 4.24. Details of the duration of each interview and the number of weeks after completing the SEP that the interview was held is presented in Table 4.25.

Table 4.24: Summary of participants in qualitative data collection

	Patients with IC			
	Control	Intervention	Patients with CAD	CR Staff
Interview Type				
Focus Group	7	0	6	9
Individual Interview	1	4	0	1
Total	8	4	6	10
Percentage of Total Group Size	42%	24%	29%	67%

Table 4.25 Mean duration of interviews and Mean number of weeks in between completion of SEP and interviews

Interview Group	Mean duration in minutes (range)	Duration between SEP completion and interview in weeks (range)
IC Control	52 (24-55)	6 (1-11)
IC Treatment	26 (18-31)	42 (30-54)
CAD Patients	48 (45-51)	17 (13-23)
CR Staff	52 (34-82)	NA

For all verbatim quotations, the following codes are used along with a unique identification number:

- ICC - intermittent claudication patient in control group
- ICT – intermittent claudication patient in treatment group
- CAD – coronary artery disease patient (in treatment group)
- CRS – cardiac rehabilitation staff

4.4.2 Acceptability of Study Protocol – All Patients

Although each patient group underwent their own focus group or interview (i.e., no focus group contained mixed groups), the topics discussed were so all participant responses have been combined and covered in this next section.

4.4.2.1 Questionnaires:

The high return rate of questionnaires was reflected in the responses from participants during discussion around the study protocol and the perceived burden of enrolment on the study. All participants reported that the questionnaires were not time-consuming and felt they were easy to follow.

> **CAD02:** *Simple, easy, easy to understand. Not difficult to fill out.*
>
> **ICC02:** *It wasn't time consuming*
>
> **ICT01:** *I didn't find it particularly (pause) difficult or extensive or time consuming*.

There were comments that completing the questionnaires at different time points was repetitive:

> **ICT02:** *the only thing that was repetitive was the erm…like the stress and anxiety scoring sheet…I think I had to fill the same one out about 3 times.*

However, this participant did go on to complete a dedicated, 6-week stress management group (Healthy Minds programme) following their SEP, which required them to complete the HADS questionnaire at least one more time. The study only required two HADS questionnaires to be completed (pre and post-SEP).

Participants did not feel that they were being asked to complete anything that would not usually be asked during the standard care.

> **ICC04:** *Yeah. It's just normal. You go at any hospitals, and you get questionnaires, they're all the same thing.*

However, not all participants were entirely comfortable at first, especially with completing the HADS questionnaire with one participant making the following comments during one of the IC control focus groups.

> **ICC05:** *It made me question myself.*
>
> **Interviewer:** *Yeah? (Pause) In what way?*
>
> **ICC05:** *(Pause) Err. Depre...where depression's concerned, and what have you.*

Other participants in that focus group agreed that they were initially concerned by the title of the HADS questionnaire and wondered why they were being given this form, with one participant concerned about what would be the follow on if you did report certain things on the form.

> **ICC07:** *You're gonna go and see a "trick cyclist"!*

This raises some concern regarding the number of participants that might have been discouraged from participating in the research programme due to the nature of the questions being asked.

4.4.2.2 Accelerometer and Diary:

Across the different participants there was a high wear-rate for accelerometers with responses from participants being that it was not burdensome.

> **CAD01:** *It's not like you're carrying a big, like wired up to something you have to carry around. It's just on your leg, isn't it?*
>
> **ICC05:** *You forgot you got it on. The only time I remember that I got it on was when I got up in the night to go to the bathroom and I don't turn the lights on in case it wakes me up…and there's light flashing and I was like, "Oh, what's that?" (Chuckles) But apart from that, it's fine*.

There was also positive feedback about the diary completion with participants being aware of why they were required to complete it. However, there was comments on reporting accurate information was not always possible as participants were unclear what time they went to sleep:

> **ICT03:** *Well, yeah, and they said it was what it was for and the fact that it can't...we had to fill that...when we got up and when we went to bed because it doesn't know the difference between sitting and sleeping, so.*
>
> **ICC07:** *I made one or two up because I couldn't remember. I had to guess when I went to sleep.*

This might not be an issue for future research as the activPAL accelerometers that were used in this study have updated their software and are now able identify sleep time more accurately compared to previous versions.

4.4.3 Acceptability of Aspects of the Study Protocol to Clinicians

There was minimal discussion around the acceptability of the study procedures during the focus groups and individual interviews. The CR specialist nurses involved with the pre-screening did not feel the process was onerous. The need for the PI to clarify on a patient's eligibility was infrequent, although the exact number of times was not recorded.

> **CRS02**: *We had print outs of the inclusion and exclusion criteria which was helpful…but, no, no it was straight forward. We are used to screening the cardiac patients.*

As the PI conducted all pre and post-SEP assessments for those patients enrolled on the study, the CR staff were not involved in the consenting process, or the administration of the research-specific outcome measure they were unfamiliar with i.e. the VascuQoL questionnaire. The WIQ was a familiar tool to the CR team as they had been using it since the 2015 when the expanded their service to IC patients. This was perceived to be an easy-to-use outcome measure.

> **CRS6**: *I found it [the WIQ] a useful form of the assessment. Sometimes I'll start with those impairment questionnaires, and that will help answer a lot of the questions I would have asked anyway. So, I found them quite, quite useful and quite straightforward to do.*

The PI gave out all the accelerometers and activity diaries to patients and provided instruction on their use. The PI secured the accelerometers to the thighs of all male patients. All female participants required a female member of staff to apply the thigh-worn accelerometers. The female members of staff involved in this process found it straight-forward after short instruction from the PI.

Although acceptability of the Gardner Skinner GXT was not specifically mentioned during the staff focus groups and interviews, this treadmill protocol was adopted by the CR exercise team. During the research process, the CR team became familiar with this IC-specific protocol as it was being used by the PI to assess study participants. Prior to that point, the CR team had only used the ISWT with IC patients as this was the standard GXT used at their programme. After observing the protocol being used with study participants, they trialled it out and found it more suitable to the IC patient groups.

CRS7: *I think it took us a while to sort of come to that realisation in terms of the exercise testing that it wasn't quite right. And that did take time. And then trying to decide what was the best replacement or, to use.*

Over time, the CR exercise team began to use this GXT protocol with cardiac patients. More detail is provided on this development in Section 4.10.2.

4.4.4 Acceptability of Treatment - Participants

The following section covers the views and experiences of the treatment. The views of all patients have been represented (IC control and IC intervention, and CAD patients). The inclusion of the IC control group in the qualitative assessment allowed for a comparison of the views and experiences of the IC intervention group to see those receiving standard care. The emerging themes and subthemes (Table 4.26) followed closely to the topics used to guide the interviews, however, there were some differences in some of the responses between the PAD and CAD groups which have been given specific mention.

Table 4.26 Themes and subthemes that emerged from the patient interviews on acceptability of the treatment (i.e., integrated rehabilitation)

Themes	Subthemes
Staff	• Patient-centered support • Reassurance • Providing knowledge
Shared Experience	• Group exercise session • Group education session • Differences between PAD and CAD experiences
Rehabilitation Setting	• Enjoyment of exercise • Benefits of attending
Barriers	• Apprehension • Motivation • Physical Limitation • Travel distance • Work commitments • Lack of support

4.5 Theme: Staff

Throughout all the focus groups and individual interviews, patients reported the important role rehabilitation staff played in their experiences of the programme. The care provided by staff emerged as a key factor in participant attendance and adherence to the programme.

4.5.1 Patient-centred Support

Patients found that staff were friendly and supportive from the beginning of the rehabilitation programme and made them feel at home in the group.

> ***ICT01****: They were kind…And I felt welcomed and gathered in. I felt as though I mattered, which was a very important beginning for any of these things.*

> ***CAD01****: Let's face it, the cardiac team are really, really brilliant company, you are never going to meet a nicer bunch of people…everybody remembers you. And how do they do that? How do they remember who you are?*

> ***CAD04****: They dead friendly, they make you feel you're at home.*

> ***CAD06****: He took me in, and we sat there for an hour and talked about everything. And he told me what the program was about and explained it and answered all the questions. It put me at ease. I went in feeling down and you know (Overlapping Conversation). Exactly! I came out, I was like I've grown two feet.*

All patients perceived that rehabilitation staff enjoyed their job, and a real sense of caring for patients was felt. Patients experienced a sense of belonging to the group and this made them want to engage with the programme further.

> ***ICT03****: …because they are, you (pause) you feel as if you know them…They're like family. They, they enjoy what they're doing…And they care about you and they like to know that everybody's alright. You know, and any problems they'll sort it for you.*

***ICT02**: You know that they're there to help you. They, they're putting in all this effort to try and help you so, you've got to give them a bit back, you know. People have gone to the effort of, of making, making the programme available so…erm…use it.*

***CAD03**: The doctors have done their bit. Let's follow it up. We've spent about 50,000 quid on us, the national health, so let's try and make it worthwhile*

There was a common perception across patient groups that the staff treated them as individuals. Although exercise was performed in a group-based circuit, patients felt it was adapted to suit personal needs when required. Patients recognised the level of support that was required from staff to facilitate the exercise circuit.

***ICC05**: You're not pressurised into...doing each and every one [exercise] you just take them at your own pace and do what you can.*

***CAD02**: Yeah, they tailor the exercise to fit for you…no one says, you know, you've got to do this, you got to do that. Everybody works at their own pace.*

***CAD03**: While we're there, you've got these people with so much one to one tuition at the hospital, isn't it, there's as many people instructing there is people training. But I found that very useful*

4.5.2 Reassurance

An interesting difference that emerged from the CAD patient interviews was the assurance provided from the supervision of staff qualified in emergency life support. There was a concern around adverse events occurring during exercise, and patients gained comfort from having specialist staff there to support them. This concern did not emerge from the interviews with either PAD patient groups.

***CAD02**: If something does happen with our hearts, they [staff] kind of got the training and help us.*

***CAD06**: But I guess that reassurance only comes from their specialist nature and understanding of what's going on. And also their knowledge that what they're putting you through really will benefit you. And you need that reassurance, don't you?*

***CAD04**: I felt reassured. So the worst case scenario if something happens, I'm surrounded by people who know what to do.*

This level of support was also perceived to be important for CAD patients enrolling onto continual exercise programme in the community (Phase IV Cardiac Rehabilitation) following completion of the hospital programme. This further endorsed the view that CAD patients have an added concern over issues that might occur during exercise, due to their specific condition, that PAD patients do not experience.

***CAD06**: All the staff in Fit City Eccles [Staff at community programme] are all trained in life-saving skills. And they've all got the right accreditation for swimming, for cardio. There's defibrillators there as well so I think they're all trained up to those standards.*

***CAD04**: They're [Staff at community programme] all aware as when you scan in, your details come up and the fact you have had a cardio on screen, so anyone who doesn't know you is aware of your conditions because it's on screen…*

4.5.3 Providing Knowledge

Like with the support around the exercise, all patient groups reported the importance of the advice and education provided by rehabilitation staff. They felt it was important to have the chance to ask questions and gain more understanding of their conditions and treatment. A common view across all patients was that staff were specialists in their field and could be approached at any point, which was an important element of the programme.

***ICC04**: …the staff had been good really. If you got any questions, they answer the questions which is, you know, best part about it really, probably educates you a bit more as well.*

***ICT01**: I believe in experts. I was an expert in what I did. I expect you to be an expect in what you do [referring to interviewer]. So, I defer to experts. And if you as the expert, tell me that I need to this then I know I need to do it, so I'll go and do it.*

For the IC treatment and CAD participants, formal education sessions were delivered in groups following the exercise session. This offered any opportunity to provide knowledge and advice to patients in a structured was. A common view was on the importance of these sessions was held.

***ICT01**: There were stuff about the drugs you take. There were stuff about the physical bit...I knew some of it but a lot of it was absolutely new to me.*

***ICT03**: I found them…erm, quite helpful. You know, you…it makes you think about things, erm, you know, you find out things that are useful to you.*

***CAD03**: I loved them [the group education sessions]. They showed all the breakdown of the heart. And then told what to eat and what not to eat, and what damage smoking does. And you see it explained, not just explained, but explained it in a blocked working heart.*

***CAD06**: I was amazed by how much I thought I knew and I didn't. Because I particularly found benefits you mentioned earlier about diet because you changed it.*

The patients found that the talks were delivered in an appropriate way which helped them to engage with the sessions. This was highlighted by the view from patients that those would did not attend the group education sessions were missing out.

***CAD06**: I found the talks, also, not dumbed down, but talking...*

***Interviewer**: Your language.*

***CAD06**: Exactly. That's what I enjoy. I related to it straightaway.*

***ICT01**: Sadly, I noticed that one or two people didn't stay for those. But I think that it was very, very important.*

Many patients who underwent their SEP at the intervention site also took part in other services offered by the CRP such as the stand-alone stress management and healthy eating programmes. Patients found these very useful and enjoyable too.

> ***ICT02****: The support of the eating side of things was for the general health and weight loss which I remember [refers to CR staff member] telling me that if you, if you're not as heavy you're not putting as much strain on your legs. And then obviously the stress side of it was (pause) that wasn't necessarily to do with my legs - that was to do with general lifestyle and things that have been going on for years in the background.*

Interestingly, only the CAD patients discussed the basic life support training. This unique concern for CAD patients expands on the reassurance staff provided around possible life-threatening emergencies during exercise sessions, as discussed in the previous sub-theme (Section 4.5.2).

> ***CAD03****: Yeah, you can ask questions. Say especially in the session where they show you have to use the defibrillator, and how to give CPR. Something which you'd have had no idea before. I've not got much idea now, because I've never done it. But at least we've got basic knowledge. We could probably work at defibrillator. You would be frightened of trying, that's the thing.*

One difference in programme delivery between the control and intervention groups was the lack of formalised, weekly education sessions in the control group. Patients were provided education during their clinic visits, and throughout the programme by the clinicians, however, an interesting finding from the control group interviews was the number of questions patients had regarding their condition. Large parts of the control group FGs ended up being question-and-answer sessions with interviewer.

> ***Interviewer****: Okay, that's grand. Let's move on to the next question then, so what was your experiences of any education or advice that you received about your intermittent claudication?*
>
> *(Pause)*

***ICC03**: I don't really know. (Chuckles)*

***Interviewer**: Did you receive any advice or education on it at all?*

***ICC03**: Well, leaflets more than anything to read…I was told when I was first diagnosed and came to the hospital, and it was explained what was happening, besides the leaflets as well to take home and digest.*

***ICC05:** Yeah, I couldn't fathom out while one day I'm walk, I'm walking up the road, going and doing my usual routine. And the very next day, I'm doing exactly the same thing. And all of a sudden, "what the hell's that in my leg?", cramping up and everything.*

4.6 Theme: Shared Experience

4.6.1 Group Exercise Sessions

During the patient interviews, the acceptability of the exercise circuit was assessed, with most patients finding the group session to be an agreeable format. Patients felt this offered a network of support, separate but comparable to, the support offered by rehabilitation staff.

***ICC04**: Better than doing it at home. Yeah, it's not the same.*

***ICC04**: I think it's having people around you as well.*

***ICC01**: You see, it's not just you.*

Even participants who previously preferred to exercise on their own found attending a group-based class acceptable, and even pushed them further than they would normally do on their own.

***ICT02**: Erm (pause). It was fine. It's (pause) I always find groups uncomfortable anyway I-I always have done but (pause). Once I've done the first week, I was I was alright. This is as I say, someone who doesn't - does exercise doesn't particularly*

enjoy it - er, doesn't particularly enjoy things that cause pain…. Doesn't like group things and I-I…did it all.

Patients enrolled on the integrated rehabilitation were comfortable alongside each other and did not see integration as a negative. This idea of 'peer support' developed during the patient interviews. The view that group rehabilitation meant that patients were sharing an experience, going through the same process together, brought a feeling of camaraderie and support between patients. Interestingly, the shared experience reported by patients was not based on a shared disease or treatment.

***ICT02**: I didn't feel different to anyone else that was in the class. Y'know what I mean. Erm. I was given some slightly different exercises…I never felt different or uncomfortable or not part of the group.*

***ICT03**: I-I just considered them [the CAD patients], they're all like me. They're all coming here and erm…you know, they just doing what they can do…Sometimes, they'd even have a chat about what was wrong with them, and it didn't bother me…I-I thought it was…was good.*

***CAD02**: I think it helps we've all been through something similar.*

***CAD03**: which why I think the hospital one was quite nice, because it is a gym...And it's a lot of people together sharing an experience.*

Patients appreciated there are differences in abilities and people are limited by things outside of their primary diagnosis e.g., comorbidities.

***CAD02**: Because you were saying that everybody's not the same… we're all in for different things.*

***ICT01**: That's really, I think that's the nub of it. It doesn't matter why you're there, whether you had a stroke or heart attack. It doesn't matter. The important thing is you're not doing it on your own…Well, there's a lady there with Parkinson's. And there's a man who had a stroke whose right side won't work, and so on.*

4.6.2 Group Education Sessions

The network of support that was offered through group delivery was not limited to the exercise session, but also occurred during the education sessions. Patients felt they were able to support each other and learn from each other's experiences.

> ***CAD06**: Because I was mindful chatting with the other people…that if I could do well I'd also pass on that kind of confidence to other people, it transmits. We pass that on. I'm sure we all did that. We all did that.*

> ***ICT03**: And…I noticed that one day people were talking and there was a gentleman on his own…and he'd not said anything much before, but then he said, you know, "I feel better." He said "I thought I was on my own with this" you know and then, you're hearing other people's stories, and it's just…I mean you get to know them as well, and I think what they were doing is really good. Absolutely.*

> ***Interviewer**: D-do you think it, in terms of like the group nature, doing it as a group - was that important? Rather than if it, just, you know, doing it on your own at home or something - like?*

> ***ICT03**: …well…you realise how other people feel.*

Although the control group did not integrate with CAD patients, they were asked how they would view a combined PAD and CAD rehabilitation programme. An overview of the programme was given to help them to view what was involved. Although the control group opinion was in response to a hypothetical question, none of the patients in the interviews reported perceived issues with this integration.

> ***ICC04**: I think it would be a great idea, definitely. Because then you can, I mean you might have that problem further down the line, mightn't you.*

> ***ICC05**: It wouldn't bother me at all. No, no. In fact, because it'd be, it'd be beneficial to me as well, wouldn't it?*

> ***ICC06**: All we'd do, we'd just work help each other, in the group. That's what we'd do.*

4.6.3 Difference in Motivation

One difference between the two disease groups was the perception of the difficulty of the exercise, which was focused on the pain experienced during exercise, however, patients viewed this to be necessary for benefits to occur.

> **ICT01**: And they…they have to be demanding because that's what they're there for. They have to push you just a little bit extra all the time. And I always felt, I was tired, but I always felt better afterwards for it.
>
> ***Interviewer**: How did you find that sort of pushing to the pain barrier and then stopping?*
>
> **ICT02**: It's horrible. It's horrible, but it's necessary.

The difficulty of the exercise was reflected in the language used by the PAD patients. Language that was not used by the CAD patients.

> ***ICT04**: It's more my calf than anything… I often felt like it was gonna explode. It's…painful.*
>
> **ICC06**: The tiptoes got, the tiptoes got me. That's a killer that one, in it?!

During the patient focus groups and interviews, it became apparent that there were differences in the reasons for each patient group attending the rehabilitation programmes. This was reflected in the stage of the 'journey' or continuum of care that the patient was on. For example, the CAD patients were undertaking secondary prevention whereas the PAD patients were undergoing treatment to prevent further complications or events. The CAD patients viewed their rehabilitation programme as a second chance after a cardiac event. The language used around the cardiac event reflected this. With the PAD patients, although diagnosed with a limiting condition, they did not perceive themselves as having an event. The reason behind enrolling onto the rehabilitation programme was not consistent across all PAD patients, although the impact of the intermittent claudication (IC) on their life was common throughout.

All PAD patients reported the limiting nature of their condition as having a negative impact on their activities of daily living (ADLs) and quality of life. Many reported this as the reason for attending rehabilitation when they were told that it might improve their walking capacity and improve symptom management.

> ***Interviewer****: In terms on the programme, erm, was there anything that was…making you go back week in, week out?*
>
> ***ICT02****: [I] Didn't want to be in pain anymore. Erm, not being able to walk any distance, has…a massive…not just a massive effect on your physical health but on your mental health and it's, it's very frustrating having to…ch-choose - say you wanted to go out for a walk, and you know you can't go far, you know it's got to be a flat route. It frustrates the people that you're with cos you have to stop all the time. It's, it's actually ruined holidays for me in the past. And I needed, I needed all that to stop, well, every-everyone walks. Everyone needs to be able to walk and when you are restricted it's…it's just not, not nice, it's horrible, as I say it has a massive mental impact.*
>
> ***Interviewer****: Well, nobody wants to suffer with pain if they can help it?*
>
> ***ICC04****: No, I've had enough pain. (Laughs)*
>
> ***ICC03****: I was finding it I was holding everybody back because I couldn't get go as fast and now, they've [family] got a little dog as well, and of course there off even more walking, walking, walking, and I think, "Oh, no, walking."*

For others, the main goal was to improve the quantity and quality of time they can spend with their families. These patients had possibly made the connection between their IC and overall CVD mortality risk.

> ***ICT03****: Er, but, like I say, they've [family] just got me now and…(pause) I mean I'm doing all I can, to, you know…keep up…Nobody knows how long they've got. It's a bit depressing this, but…I do everything I do for my children and my grandchildren, and…I just want to be here for as long as I can to stay with them.*

***ICT04**: I feel a bit of a burden when you're telling everyone, you know, "you're gonna have to wait a minute, you know". They think "aw this old duffer here"*

Although there was a common feeling of frustration amongst the PAD patients around the frequent pain on exertion and how it was limiting them, some patients were also motivated to attend rehabilitation due to a fear of amputation.

***ICC01**: The worry of losing my legs and you know, and they said come and do it and it's an option.*

***ICC04**: Well, [Vascular nurse] just said, "if I were you, I would do some exercises, you don't want to lose the leg." And I said, "lose the leg?!" He said, "well it".(pause) he just went…I said, "well I'll do the exercise then, no problem."*

There was also the fear of requiring a surgical intervention on their leg (e.g., bypass or stent) that made PAD patients take up the rehabilitation programme. The non-invasive treatment option of SEP was favoured over the surgical intervention.

***ICC01**: I'm frightened of what would happen if you don't do it [the rehabilitation programme], so that's what motivates me and the benefit it's given me so that's just it for me.*

***ICC03**: Well, you'd end up having to have an operation, yeah.*

***ICC01**: You absolutely don't want that!*

For one patient, their reason for attending rehabilitation was because they had been told this needed to be completed prior to the vascular surgeon even considering the surgical intervention on their leg.

***ICT04**: Erm…well I was told that-that if I didn't do it [the rehabilitation programme] …I wouldn't get the stent. That you had to do this. So…that sort of set my mind on it. Cos er-really I'm not one for going to the gym an…(pause) you know that sort of training.*

This patient was also concerned that any improvements they had made in walking following the completion of the SEP would prevent them having the operation on their leg.

> ***ICT04****: It's just that-a…I felt while I was doing it, that…when he finally went back to the hospital…you know with their report…they're gonna turn round and say `oh well, he doesn't need this now'…cos I'm-I'm…I really wanted the stent.*
>
> *Interviewer: Right, yeah?*
>
> ***ICT04****: But, I just-I have a feeling I'm not gonna get it after this somehow.*

Although this was only one patient who reported this perception of SEP, it might be a view other PAD patients who see surgical intervention as the only way to improve their symptoms.

A common factor that emerged from the interviews was the role of the vascular specialists in influencing the PAD patient's attendance of the SEP.

> ***ICC05****: I'm with [names surgeon], but he's very loath to go down the surgery. "Before we even go there", he said, "I want to try on this exercise regime to see it has any benefits for you". And I found that it has.*
>
> ***ICC07****: Yeah. For me, it was the specialist who said he would rather do this and see how it goes...rather than do the invasive stuff.*
>
> ***ICC03****: Yeah. The doctor said to me, "if I don't go on, I've got a 50, 50 chance of losing the leg." So that's why they put me on this exercise course. And I think it's the best move I've ever made. I would have loved, I would have loved the operation. But then, then again, it was the doctor who said, "try this out first."*

During analysis of the CAD patient interviews, a key difference in the motivation behind attending rehabilitation emerged. CAD patient wanted to return to ADLs and have increased quantity and quality of life similar to PAD patients, however, the language used by CAD patients reflected their shared opinion on being given another chance after having a cardiac

event that had threatened their life. There was a greater awareness of the causes of their heart conditions, and more of a drive to address these areas of their lifestyle.

> ***CAD06****: For me, it was like I was given the second chance, the second opportunity so grasp it with both hands. I didn't think emotionally I was that scarred but I was, I think I really was. So, it's life changing and possibly life ending, isn't it?*
>
> ***CAD02****: It's made me look at everything…stress, smoking diet. I'm not going to sit and go oh, you know, it wasn't smoking. But stress and no exercise.*
>
> ***CAD03****: When I went to the [rehabilitation] gym, I said to my wife, "well look, I've had a near miss now", because when I went to Wigan and they looked at the angiogram they said: "You've probably had about four or five small heart attacks, over the last year." I said to her "life's given me the chance to start again now." The first place to start is in the gym isn't it.*

Although PAD and CAD patients integrated well and supported each other, it was evident that there were some key differences. For both patient groups, fear was a common factor influencing attendance of an SEP. The root of that fear, however, was different, with PAD patients fearful of surgical interventions, or the ultimate risk of amputation and CAD patients were fearful of a further cardiac event that they would not survive.

4.7 Theme: Rehabilitation Setting

4.7.1 Enjoyment of Exercise

Both the PAD and CAD patients reported enjoying the exercise sessions. This is not surprising considering those involved in the interview stage had completed the full 12-week programme of exercise. There was a common view of the fun and social aspect of the exercise sessions, which patients felt supported their engagement.

> **ICC03**: I enjoyed it, I enjoyed it. That's why I say I was sorry when it ended really.

ICC06: I loved it when I come. It was hard at first, but when, when the weeks going, going by, then you was enjoying it, enjoying it more.

CAD03: Yeah, but like I say, we have a laugh and that. It's more like a little bit of a social thing.

CAD04: And you have fun, that's the important thing.

Interestingly, the PAD patients reported the circuit exercises to be an ideal format. Patients felt the variety of exercise was good, and the fact they could select the order they performed the exercises was also favourable. This was an interesting area of discussion to emerge as many of the modes of exercise utilised in the PAD-exercise literature is non-circuit based, often limited to just treadmill walking only.

ICC04: It was nice choosing what you wanted to do.

ICC07: I found it was best to go on the treadmill first. When I went on the bike first, then I couldn't do the treadmill. So, you go on the treadmill first, I was alright.

ICC05*: There's no, no set routine to it. You don't, you don't have to do from start from 1, 2, 3, go through them all. You do as each and every one, "right, I'll do that one. Then go on this one." And then when you if you get yourself a little bit tired out, which you think "five-minute rest, we'll go for the next one. An easier one."*

4.7.2 Benefits of Attending

Both PAD and CAD patient groups reported benefits of completing their respective rehabilitation programmes, however, the specific areas of these perceived improvements differed between the two disease groups. The PAD patients reported improvements in their walking capacity and how this allowed them to return to their leisure activities. There were also improvements in the blood flow to their legs and the sensations that had been found through follow-up reviews with their specialists.

***ICC02**: When I first started, I couldn't walk from the car park to the gym without stopping about four or five times and now I can do it without stopping…You find through the whole course that you gain each week really, you feel that bit better.*

***ICC05**: I've been able to (pause) I've actually, my feet are actually warm. So, something's happening. It must be because there's no discoloration to me leg or my feet, or anything like that. I'm getting like a, a crawling sensation on the skin like a muscular...like a spasm. Where that's coming from, I'm not too sure what it's like, it's just telling me something's happening down there.*

***ICC04**: She [diabetic nurse] said, "I can feel your pulse". And my sensitivity or whatever it's called…*

***Interviewer**: Is coming back?*

***ICC04**: …is great anyway.*

***ICC07**: Well, it's a lot better now actually. It was the exercises that's done it. You didn't think it would.*

For the CAD patients, however, the focus was more on the improvements in their lifestyle and how they were reducing their risk of having another cardiac event that emerged from the discussions, rather than improvements in physical function.

***CAD02**: I am a lot calmer than I used to be. I used to be much less calm shall we say. It's made me look at everything.*

***CAD06**: And I think it went a very long way in improving my own physicality, mentally, emotionally, spiritually, in every way.*

4.8 Theme: Barriers

Although participants in the focus groups and individual interviews were all patients who had completed the rehabilitation programme, they did offer thoughts on the potential barriers other people might have to attending. There were similarities between the different

patient groups such as travel distance and parking, but perception on rehabilitation as a treatment option was different between the groups.

4.8.1 Apprehension

PAD patients were apprehensive about the programme based on scepticism regarding the effectiveness of the exercise as a treatment. Many PAD patients reported not knowing if, or how the programme would work.

> ***Interviewer**: Yeah. So, before you came along to the class, were you aware of the benefits of exercise for rehabilitation?*
>
> ***ICC01**: No.*
>
> ***ICC03**: No.*
>
> ***ICT02**: I told you I went in with the opinion that I couldn't see how it was going to work…and then the results at the end were quite shocking - to me…on how, how much I'd improved at the end.*
>
> ***ICC01**: I mean, I couldn't believe at first when I were in exercise class because I don't really understand it totally, I thought, "Is it really going to make a difference?"*

Rather than doubting the effectiveness of the treatment, CAD patients reported feelings of apprehension about the exercise programme due to fear not being physically able to complete, or what might happen during the exercise. Patients thought this might be present a barrier to others. This further highlighted the different views on treatment the two patient groups had.

> ***CAD05**: So, you're scared at first. What can I do, what can I do?*
>
> ***CAD06**: Of course, I was afraid (Overlapping Conversation). You don't like admitting it. You don't like admitting it. It was just like the first day of school, you know, the big school.*

***CAD01**: Yeah. I think some people might be a bit scared of gyms and gym after illness, because thinking they may overdo it, and damage themselves in some way. Or just frightened of the whole idea of that of gyms,*

The group-based nature of the programme was also a consideration for patients. There was an element of having to overcome barriers with both PAD and CAD patients, such as motivation, that might have caused other people to not attend in the first place.

***ICT02**: Erm (pause). It was fine. It's (pause) I always find groups uncomfortable anyway I-I always have done but… once I've done the first week, I was I was alright*

***CAD06:** When I first came for [exercise class], walking into a room with all these people, it's a bit daunting isn't it?*

***ICT04**: Yeah, I think, there's some people that find it very hard to communicate with other people, you know…or (pause), just socialising in general…They [non-attenders] might be a bit self-conscious or uncomfortable, but yeah.*

4.8.2 Motivation

Patients also found that motivation was a necessary requirement for enrolling and adhering to the rehabilitation programme. Patients from both groups recognised that they themselves had reasonable levels of motivation which influenced their attendance and viewed this to be lacking in patients who did not attend.

***ICC03**: Yeah. I mean, like you and I have said, we kept going because we got that motivation to do it but it's the people that haven't...*

***ICC01**: I think you just got to have the desire to want to do it, that's what I think the main motivating thing is. If you're half-hearted about it, it doesn't matter what exercises they offer you, you won't do it. That's what I think anyway, I don't know about you? You've got to want to do it.*

***CAD02**: I mean, there's obviously going to be some people that are going to go "Well, I can't be bothered" or "Don't want to do it".*

***ICC03**: Yeah, but there are people that think, "I can't be bothered, I can't bother going, I can't bother doing it."*

Patients appreciated that past experiences of exercise might influence uptake and attendance, and one patient reported a personal example of a bad experience with previous exercise to illustrate this. This patient obviously still attended the rehabilitation programme, but it did highlight a possible barrier for attendance:

***ICT04**: Well, I used to do the, go to the gym years ago with a friend of mine. And er (pause). It's just a memory now, the state I was in when I used to come out, I used to feel like I wanted to be sick. I could hardly walk… and I thought, I thought this was supposed to be doing me good, but I'm coming out feeling even worse than when I went in…So, it-it-it's just never been something that…would enter my head to `ooh yeah, I'd love the gym today'.*

4.8.3 Physical Limitation

Although participants on the programme found that exercise sessions were tailored to the needs of each individual, they perceived that physical limitation might be a barrier to other patients attending.

***ICC05**: They could have a condition that is so severe that prevents them from doing the exercises.*

***CAD02**: I imagine, the people having mobility issues,*

Interestingly, participants on this study did not feel their own limitations had stopped them from exercising, they did feel that mobility might be an issue for others, particularly around their motivation to attend the programme. Patients felt that others might not be willing to come in and exercise alongside people that they thought were more physically able than them.

***CAD06**: I said I feel a bit self-conscious because I come in, I came with my kit on, like I said, I treated it like a race, on the treadmill straight away, and people were looking at me. I felt awkward that I was able to, you know. Yeah, I felt a bit…*

***CAD05**: Guilty*

***CAD06**: Yeah, that's the word, guilty that I was able to do that.*

***CAD05**: Yeah. And I feel a bit guilty…because other people that are there, they're about 80 and they said to me at the start "Don't be showing us up"! (Laughter)*

4.8.4 Travel Distance

Several patients felt that the location of their hospital programmes presented a barrier for some people to attend. They felt that providing multiple settings to attend at easily accessible locations may have increased uptake and attendance.

***ICC03**: It is a bit awkward to get to. It's a shame that we can't like, have it at Trafford General. There is one at Wythenshawe, a nice big one there. There's nothing at Trafford General, you've got to come here. You know.*

***ICC02**: There's one at Altrincham…Community hospital… a gym. I know because my partner goes there, and... it'd be better if we could go to local hospitals.*

***ICC04**: Erm…Probably the time I would have thought because yeah, you hear to people out there that have to get busses and stuff like that. You know? You might get more people think "well I'm not going [to the hospital] if I have to get in two buses."*

There was also the issue around parking at the hospital sites.

***ICT01**: There's problem about coming to the hospital, it's getting here and the parking. I was fortunate because I got a friend to drop me off…There is parking but you're lucky if there's any when you got there.*

***CAD03**: I think, the only problem I had a [name] Hospital was parking. When I first went, I give that up after the first day after that, I just got the wife to drop me off. It was an easy problem to solve because my wife drives. So, I just got dropped off and picked me up two hours later, but parking at [name] Hospital is...*

LAUGHTER

***CAD01**: Terrible. I can't walk very far, because obviously I've got arthritic hips and so I've got a disabled pass for my car. And there's no disabled spaces there at all. Always full, 24 hours a day*

***CAD04**: At 10 o'clock on a Friday morning, people just park on yellow lines…*

***CAD01:** Everywhere. But walking back after you've, you know, done a pile of gym stuff that you're not used to and you've got arthritic hips, it's a long walk up that hill, trust me. It's uncomfortable. So yeah, better parking would be ideal in Hope hospital generally, everybody would say better parking. Free parking. Better parking.*

4.8.5 Work Commitments

Another area emerging form the patient interviews was the barrier of work. Patients appreciated that patients who were currently employed may have difficulties in committing to rehabilitation sessions that always took place during the standard working day.

***ICC04**: I mean people, when I was working, they would give the time off to go and do it but it was right in the middle of my shift so I wouldn't go back after. And they weren't overly happy about it. They said well, have they got later one?*

***CAD01**: I suspect a lot of it will be work.*

***CAD02**: Work, yeah. I was lucky, they allowed me to have the time off work… so they would have allowed me to do it.*

CAD01: *I mean, there's obviously going to be some people that are going to go "Well, I can't be bothered" or "Don't want to do it". I know a lot of it will be related to work, it's really bad. To not let people have sick time off, when they need it.*

CAD05*: It's a big ask when you ask them to do it after work and maybe that could be a barrier for some (Overlapping Conversation). Many know they…My bosses've been really good with me, if anything that I've had to go to, but I can imagine for others it might be hard.*

ICT02*: you, you may struggle if you were employed, and your employer wasn't particularly (pause) helpful…Erm. (pause) Evening, if, if people were prepared to do things erm- some of the staff were prepared sort of do stuff in the evening that-that may help.*

4.8.6 Lack of Support

Patients from both groups also viewed lack of support from family and friends as a possible barrier to people attending rehabilitation.

CAD01*: Maybe they haven't got any family to encourage them? Or, no, no, no local family? Because I mean, it certainly is your partner or your children encourage you to, if you have them, I suspect to go and help you to be motivated to go.*

CAD06*: You asked of barriers - I couldn't think of one except what you said before about people who are living on their own and, as (refers to* ***CAD04****) and (refers to* ***CAD05****) both said when we were chatting, that you can, if you don't have someone to….*

Interviewer*: To chivvy you along?*

CAD06: *Exactly…And if I didn't have my wife, family support at home, chances are I might not have done them (the rehabilitation sessions).*

Although all patients had attended the rehabilitation programme, some did give personal examples when they had not been supported by people close to them, further highlighting the barrier of lack of support.

> ***CAD06****: Family and friends took the opportunity - not callously but they meant well when saying: "I told you that at your age you - at 64 - shouldn't be doing it." I needed to hear from someone that I was doing the right thing…listening to everyone telling me that I'll never do it. I'll never be the same again.*

> ***CAD04****: My sister-in-law, she is just like, does nothing and…a couple of years ago, I had a bit of trouble with my knee and "that's it" she said…" you're finished".*

4.9 CRP Staff Interviews

The following section covers the acceptability of the trial and treatment processes and procedures to the CRP clinicians. The views of all staff have been represented. The emerging themes and subthemes (Table 4.27) followed closely to the topics used to guide the interviews.

Table 4.27: Themes and subthemes that emerged from the CRP staff interviews on acceptability of the treatment (i.e., integrated rehabilitation)

Themes	Subthemes
Adaptations to Service	Getting the service ready
	Assessment adaptations
	Exercise adaptations
	Lifestyle advice adaptations
	Extra demands on the service
Differences between patient groups	Risk factor challenge
	Patient motivation
Making a difference	Benefits of an integrated CRP
	Improved service provision for PAD patients
	Professional Development and Job Satisfaction
	Future proofing

4.10 Theme: Adaptations to Service

The following section explores the range of changes to the CRP that were requires to ensure appropriate integration of the IC patients. The CR team had extended their service to incorporate IC patients prior to the start of this study, which means that their experiences the 'treatment' being investigated in this study spread beyond the 13-month study recruitment period. This offered the opportunity for a deeper understanding of the feasibility of the integrated rehabilitation and the adaptations required by another CRP to be achieved. The strengthens the decisions on methodological changes made for the future definitive RCT into treatment efficacy.

It emerged that initial changes to referral pathways and the upskilling of staff were required prior to accepting IC patient onto the programme. Changes were by made to the assessment process and to the delivery of exercise and education sessions. These are covered in detail below.

4.10.1 Getting the Service Ready

Initially, the CR manager needed to gauge the willingness of all team members to take on the new patient group.

> ***CRS1:*** *So, the sort of first step was really to have a chat with the rest of the team, in terms of was it practical? So, you know, the wide range of clinicians ranging from the nursing staff to the exercise professionals.*

Referral pathways were created so that vascular specialists had easy access into the CR service with clear lines of communication to ensure suitable patients were referred and appropriate information included on the referral form. The new IC patients required changes to service delivery with an extension to the length of the rehabilitation programme from eight weeks to twelve weeks to meet the NICE guidance CG147 for IC patients. As this affected all clinicians in the service, the CR manager felt all staff needed to be consulted to ensure they were willing.

Feedback from the CR clinicians was that they wanted to become acquainted with the IC patient journey prior to them starting the CR programme. Observation of podiatry run vascular clinics was arranged so that CAD could see how PAD was diagnosed and how the decision between whether to refer into rehabilitation or to immediate surgical intervention (using disease severity) was made. The team felt this gave them a better awareness of the signs and symptoms of worsening disease and when to refer back to the vascular specialists if evidence of worsening PAD (critical limb ischaemia) was identified.

> ***CRS7:*** *I think the big, big learning thing for me, it is the hard thing to get your head around, is the processes outside of what we do. So, the referral into the programme,*

and what the potential pathways are out of our programme in terms of vascular surgery, and that sort of side thing.

***CRS10**: And we've got…the emergencies. So, we, you know, as long as you know, in what circumstances when to send direct somebody that way [back to surgeons]. But we've got that, I think that's really important for setting up a service that you get them channels of communication.*

The CR team were experienced in screening cardiac patients for signs and symptoms of worsening cardiovascular disease, and they had clear pathways in place for when urgent cardiology review was required. They believed that similar pathways were required for the PAD patients, and they felt reassured having these in place. Prior to delivery of the rehabilitation to the new IC patients, a range of in-house training was delivered to help improve knowledge of PAD and its treatment.

***CRS3:** I mean, fantastic members of the team that researched it [PAD] quite heavily, you know, and sort of filter that information back through to us, we could then easily, you know, sort of embed and help, you know, at a basic level, help that patient understand.*

***CRS2:** The exercise, the exercise team did updates, several updates...and they did them on an individual basis for us you know, so they tailored that information to, to the different specialties within the team.*

The responses from all members of the CR Team highlighted their view that the integration of IC patients was not something that could be without time invested in the preparation stage. There was also a requirement for ongoing learning once the IC patients has begun attending the CR programme.

***CRS7:** There was definitely an example that I can remember of doing the…CVD talk….there was a particular patient that was really set on collateral circulation: "what is it?" And you couldn't just give them the basics of it, it had to be very sort of detailed level, and it was a level that I didn't know. I literally couldn't answer his*

questions in the class, I literally had to go away and research it myself and come back and talk to him in a little bit more depth about it.

However, this is not unique to the CR staff and they had to do this with the cardiac patients too.

***CRS7**: Some of the cardiac patients will ask me specific stuff about specific conditions that I won't know about. And I'll go away, I'll read, and come back to them.*

As it became clear that there was a requirement for new learning and experience within the team to help the integrated service work well, the possibility of a formal training course was raised during the focus group and interview process.

***CRS9**: Obviously cardiac, I think is something that's installed at university a little bit more. But in terms of the PADs, from when I was coming through, it wasn't, so I wasn't really as aware of what, of what it was. So, I think reading, obviously, is one. I don't know if there are any courses or anything to go on for it?*

4.10.2 Assessment Adaptations:

When the IC patients were referred into the CRP, they began on the standard assessment process used with the cardiac patients: an initial telephone interview, face to face assessment prior to SEP (including exercise test), and then discharge assessment (after completion of SEP). Although the assessment journey was not adapted for the new patients, there were noticeable variations between the assessment process for the two patient groups.

***CRS3:** There are similarities, but it's very, it is different, you know? When we, when we get a PAD patient to, to do the initial assessment [initial nurse telephone assessment] you could be, you could be through it in a matter of 20 minutes, if you know if there's no other issues at that time, or you could be on the phone for an hour and a half because you suddenly unpeel, from that practical experience: "I can't walk this far. I'll go and get something done about it."*

Clinicians found that their assessment questions identified other issues that had not been included on the initial referral to the CR service such as exertional angina, or other important comorbidities. Although they did not perceive the complexity of the new IC patients to be significantly greater than the cardiac patients, there was a lack of information compared to the that included on cardiac patient referrals. This was also an issue for the next stage of the assessment process – the face-to-face pre-SEP assessment. The exercise specialists in the CR team who conducted the pre-SEP assessments highlighted an issue specifically with their risk stratification process. For heart patients, a standard cardiac-specific risk stratification tool is used. The IC patients did not have their own specific risk stratification tool, so CR staff utilised the cardiac-specific tool. However, missing information made this process of risk stratification of IC patients difficult.

> ***CRS7:*** *The information that we get on our cardiac patients is geared towards that risk stratification. Whereas…compared to the information you get for the PAD patients, so things like PADs won't typically have an echocardiogram, but that's a big part of our risk stratification.*

In the case of information missing from the cardiac patient's hospital notes or referral form, the default position is to classify the patient as high risk and start their exercise prescription at the lowest intensity (as per ACPICR guidance). For IC patients, this information was not missing due to incomplete notes or referral forms but due to the investigations required not being performed as part of the standard care of the IC patients (i.e., an electrocardiograph or echocardiogram). The cardiac risk stratification tool was deemed inappropriate for IC patients, but staff were still using it as they felt some form of screening process was required, and they felt vulnerable if they had not screened and stratified each patient. A solution to this issue had not been found by the CR Team.

> ***CRS7:*** *But that would be the query in terms of do you need to adopt your risk stratification to make a purely for PAD, based on information that you will, you will have for that patient, and not cardiac-specific?*

Changes were also made in how the CR exercise specialists assessed the functional capacity and exercise tolerance of the IC patients. The research protocol used the Gardner-Skinner GXT when assessing IC patients due to its wide use across the literature. This test was different to the standard exercise tests used by the CR Team to assess cardiac patients: the Incremental Shuttle Walk Test (ISWT) and six-minute walk test (6MWT). Prior to the research project, the CR Team had been using the ISWT with IC patients, however, they began to perform the PAD-specific GS test with all IC patients not enrolled on the research. This was after seeing its use with IC research participants and deeming it more appropriate.

> ***CRS6****: I think sometimes we can risk false readings [with the ISWT] because patients would want to stop due to the speed…rather than claudication pain. So that's one of the reasons why we change, we changed that test.*

This adoption of the PAD-specific exercise test was also made across the wider CR programme, with the Gardner Skinner GXT being used for some cardiac patients. It was considered easy to use and a beneficial addition to the existing exercise test options for staff.

> ***Interviewer****: So, you swapped incremental shuttle walk, which is standard cardiac, to the Gardner Skinner with the cardiacs?*
>
> ***CRS10****: We still use it [the ISWT], but we tend to use more of the Gardner Skinner now…because they [the patients] don't like to get into that running speed you know, they don't.*
>
> ***CRS6:*** *It's become more of a toolbox, hasn't it? Because we use the bike test now, the six-minute walk test [with cardiac patients]. We've got a couple of treadmill tests. So rather, again it's that individualization, it's getting, is getting the most appropriate test for that patient.*

4.10.3 Exercise Adaptations:

The area that required the most adaptation, as reflected in the duration of discussion on this topic, was the changes to the exercise sessions required to integrate the IC patients.

Although the same equipment was used during the exercise sessions, the mode of exercise differed between patient groups. The exercise modality for cardiac patients was low to moderate interval training with an intensity of exercise below any symptom thresholds (e.g., angina threshold), however, the IC patients were encouraged to exercise through any symptoms (i.e., claudication pain). There was also additional monitoring of the IC patients as they were required to record the duration of each exercise and the level of claudication pain achieved. Not all aspects of the exercise integration were described as easy.

> ***CRS7:*** *In terms of, erm, from the exercise prescription point of view… to be honest, fairly straightforward.*

> ***CRS10****: The exercises are quite simple. Calf raises. Marching on the spot and things like that. Really simple to use exercises.*

> ***CRS6:*** *I think the thing is, the circuit and the exercise session was initially set up for cardiac patients. You can't put a PAD patient into that and say that's gonna work for you. So, I think, to start off with we did have to adapt a lot.*

One concern of integrating the IC patients, perceived by members of the exercise team, was the level of supervision required with the new population group and how it negatively impacted on the usual cardiac population.

> ***CRS10:*** *I think they [the IC patients] can take away from the cardiac patients, because I remember classes where you'd have one to one about five one to one PAD patients.*

> ***CRS6:*** *That's what I was gonna say. I mean, it's like, for other services, if you're bringing PAD patients in, you can't just think "I'm gonna stick them straight into cardiac circuit" and off you go.*

This further highlighted the mixed views with the CR Team on how straightforward the exercise delivery was.

CRS6: *The exercise program is very different to maybe a standard, set cardiac rehab programme. You know, it does [the circuit of exercise] have to be more individualised.*

The CR Team did reflect on the fact that the nature of the IC patients was not necessarily more complex than the cardiac patients, however, there was a noticeable additional impact of bringing them into the exercise sessions. Aspects such as the exercise record sheet that IC patients used added an extra demand to the service as patients had to be supported with completing this.

CRS9: *Some people it worked really well [the exercise record sheet]. Some people it didn't at all! (laughter). You know, so.*

CRS10: *Because if they're very low functioning, there's, they're never going to fill that in (referring to the exercise record sheet), and that's for sure. So, if you need to make sure they're progressing, you'd have to be doing it with them.*

The extra requirement of the exercise record sheet was not perceived to be solely negative. The CR Team began to offer an exercise log to cardiac patients, as a closer way of monitoring them during their rehabilitation programme.

CRS2: *Because it was just such a, you know, it was that immediate feedback that the patients were getting…it was their ownership as well. And it, and we needed to pass that option back over to the cardiac patients… And it was it, it became increasingly obvious that actually, the cardiac patients didn't have that same structure.*

Interviewer: *So, it's gone the other way? In terms of something for the PADs has actually...*

CRS2: *It went from PAD patients having their clipboard and writing it down, to actually everybody had, had that format.*

The experiences of exercise delivery from the other specialities within the CR Team, those who were not exercise specialists, was also explored during the staff interviews. Some of

the non-exercise clinicians supporting the exercise classes found the new mode of exercise difficult to adjust to, initially. There was also acknowledgement of the difference in advice given to IC patients compared to cardiac patients, the usual patient group that is catered for by CR staff.

> ***CRS5:*** *At first, you're a bit nervous, because obviously, there's a big difference when a person's telling you they've got pain, because in a cardiac patient with chest pain, that is really significant. So, you, you automatically spring into action then and it's like, "Well, you know, let's get your obs. (observations) done", you know. How many times do we have to go to A&E sometimes with a [cardiac] patient? With a PAD patient…they, they had to sit down and let the pain go completely. And then we could carry on. We didn't do that with a heart patient, obviously. So, I had to kind of adjust to that.*

Interestingly, the CR staff found that the NICE guidance for IC exercise was restrictive compared to the cardiac recommendations and noted that this might have impacted on uptake and adherence. Also, it was acknowledged that the current evidence base supporting exercise for IC patients focused on the lower limb issues and adaptions to exercise only and did not consider other comorbidities or goals that patients have. This perceived limited focus of the guidance did not match with CR Team's approach to rehabilitation, so adaptations were made which differed from the 'classic' IC exercise prescription, such as the use of upper body exercises. It is important to note this was a recent change and had not been done with patients enrolled on the research project.

> ***CRS7****: The research is based on someone going and sitting beside a treadmill, "Walk till you have to stop. Sit until you can go. And do that for an hour." It sounds like punishment. But we are starting to filter in some of the more non, non-weight bearing stuff, focusing purely on improving cardiovascular fitness…trying to be a little bit more holistic with every patient.*
>
> ***CRS10****: Yeah.*

> ***CRS9****: It's like reading similar evidence wasn't it, about how erm, the erm, PADs had done the arm ergs (upper body cycle machine) to improve fitness and actually got improvements in walking distance.*

Other areas of focus such as balance issues and muscular strength were deemed appropriate, with clinicians taking the approach that addressed the patient's goals were sometimes more important than simply tackling their claudication pain.

> ***CRS7****: And just because the patient is diagnosed with PAD, the PAD exercise guidance…isn't necessarily what we think is the best exercise for them.*

> ***CRS8****: They've generally deteriorated, haven't they? Their whole body, so. And I usually kind of get them doing that [standard PAD exercise] and then offer that there is more we can do to get their fitness up. And they'd like to do more usually, well a lot of them do.*

The CR Team felt that stepping away from the recommended exercise protocol for IC and having a holistic approach to exercise was more appropriate for patients.

The CR Team felt that the new patient groups brought challenges, and a range of adaptations were required to successfully integrate IC patients into the exercise sessions. This was also experienced by the team when providing education and advice on lifestyle modification and risk factor reduction.

4.10.4 Education Adaptations

As part of their CR programme, patients were given advice on lifestyle modification and risk factor reduction to lower the likelihood of a deterioration in their cardiovascular condition. This was given through formal or structured sessions e.g., group education, or given *ad hoc* e.g., conversations during exercise sessions. The CR Team identified adaptations that were required to ensure the correct advice was provided to the new patient group during their rehabilitation. Due to the nature of the underlying pathophysiology of the CAD and PAD being the same – atherosclerosis – most of the established content of the CR educational

talks could be kept. It was accepted however, that key changes needed to be made for certain educational talks to cater for the new patient groups.

> ***CRS6:*** *Some of the education sessions are really appropriate for both patient groups. So, things like your risk factor talk, your diet and things like that worked really, really well.*
>
> ***CRS7:*** *All those risk factors are the same. Like I say, I was unexpected and how much it would impact with the PADs, but all the risk factors are the same.*

However, it was recognised by the CR Team that combining the two patient groups into one education session did not always work due to differences in the treatment options used for different diagnoses.

> ***CRS6:*** *I say maybe doing you know, the talk on, I don't know, maybe tests and investigations, it's mainly all cardiac, that's probably why you lose them [IC patients not attending].*
>
> ***CRS9: I****f the nurses do the medications talk and you had two PADs [patients] sat in front of you, are you going to go through all the cardiac medications?*

The CR Team noticed that there were issues with the attendance of the educational talks that followed the exercise session. Not all patients attended, and there were concerns that if patients thought the first talk was focused more on the other patient group, they might not attend future talks.

> ***CRS6:*** *So, I think probably…for a heart patient, do they really want to sit and learn about, you know, circulation for PAD? I think some of the things that would be for cardiac patients…aren't completely appropriate for the PAD patients.*
>
> ***CRS10:*** *Yeah, we could be better at doing that, couldn't we? We struggle anyway with education sessions.*

The attendance of the education sessions by research participants was not monitored during this study, so this area has not been fully evaluated. Suggestions were made by the CR Team as to how the education sessions could be adapted to best suit the integrated rehabilitation approach. This was similar to the exercise approach of having options available rather than one strict method of delivery.

> ***CRS7:*** *We definitely want to do group education. But I think one thing that was definitely said we want to do more of in the group education is having it less prescriptive about what we are telling them and try and make it more conversational in terms of gearing it more towards the people that are in the room, that day.*

4.10.5 Extra Demands on Service

During the staff focus groups and interviews, the challenges of integrating IC patients on all elements of the CR service were explored. The CR Team consisted of a range of specialities that could provide advice and support to patients at any point during their programme, if required. These included specialist nurses, a dietician, a counsellor, and an occupational therapist offering cognitive behavioural therapy (CBT). This was referred to by the CR Team as their 'Menu of Options' and all specialists were made available to IC patients, as per their standard CR policy. Although the exercise team had recognised the extra level of supervision required during the exercise session, the other clinicians found only a slight impact on their part of the service.

> ***CRS5:*** *Can't say I really noticed any difference…I didn't personally see that there was loads more patients, they just got absorbed into the service and came through in the normal way.*

When asked about the treatment plans for PAD patients, both from a dietary and mental health intervention perspective, there was mixed opinion on the presenting needs for this new patient group.

> ***CRS4****: No. I think, obviously, you've got patients that are different, because they've got other conditions, whether it's COPD…whether it's just a PAD or whether it's PAD*

on CHD. …it's about identifying which weight loss method is going to work for them as an individual not, not particularly based on whether they've got PAD or not PAD.

***CRS5**: No, they didn't come in with the same set of issues. The heart patients, generally speaking, are far more anxious. And I think that's just, you know…normal thing, to feel very fearful, when it's your heart. Having said that, the PAD patients came in very upset because they, they have a lot of pain. You know, a pain, you know, if you think of psychological pain, they tend to get a lot more pain than the cardiac patients. The cardiac patient's pain is their thoughts. So, their fearful thoughts…The heart patients, fear doing something, so it's their anticipation of doing something. So, they kind of limit themselves sometimes by their thoughts, rather than their physical pain, the heart patients, whereas the PAD patients are physically limited. So, treating them is different, but the CBT is the same.*

The CR Team found that despite there being a range of adaptations required, it was a straightforward and natural thing to integrate the IC patients into the CR service. One area they felt important to note for other teams looking to integrate IC patients into their service was the commissioning side of the service.

***CRS1:** It was, it was, it was hard work, the business case I have to say, but I just feel now it's kind of like totally embedded in the team I and I don't feel it was that painful in terms of that embedding process either. I think it was more of a stress in terms of: "Are we going to get funding for it? Is that, is that side of it Okay?"*

Support from the commissioners was provided when initially setting up the integrated service, however, it was noted that this might not always be the case in different Trusts.

4.11 Theme: Differences Between Patient Groups

4.11.1 Risk Factor Challenge

One area of difference between the two groups was the lifestyle modifications required to reduce the risk factors for CVD of the IC patients. The CR team noted that there were significant differences in the number of risk factors IC patients had and to the degree that these were being monitored by healthcare professionals outside of the CR team.

> ***CRS7:*** *The cardiac ones…that complexity tends to come from the cardiac diagnosis… Whereas the PAD ones, the complexities tends to be from those surrounding risk factors, rather than the actual PAD condition.*

> ***CRS6****: So, things like you might get someone that has had a heart attack that stopped smoking, a PAD patient wouldn't have stopped smoking. There lots of things like that…and initially, the risk factors probably aren't as well controlled.*

> ***CRS7****: So, in terms of systolic blood pressure, in terms of smoking status, in terms of BMI, all those sort of traditional risk factors, matching, it's hard to match like for like, but in general, our PAD actually have higher levels of CVD risk factors.*

The difference between the risk factor profiles between the two groups was attributed to their specific diagnosis and treatment. The cardiac patients were referred for exercise after having a cardiac event and invasive investigations or surgical intervention. The IC patients, however, were referred prior to having surgical treatment. They may have been started on the 'best medical therapy' to prevent the atherosclerosis in the legs worsening – anti-platelets and statin medication – but they were yet to have an invasive intervention. Indeed, the goal of the IC rehabilitation programme to prevent the need for further intervention, and CR staff perceived this to be a determinant factor.

> ***CRS6****: I think, maybe a lot of time it can be because they [the PAD patients] haven't had that event, if you like. You know if you're going like, STEMI primary PCI, you have had that event, while the PAD patient often seen as: "you got a bit of pain in your legs when you walk", so it's not that dramatic, at the moment, I suppose.*

CRS3: *And a lot of patients that come through with PAD were quite happy smokers as well, and still smoking, because like you said earlier, they might not have had that necessary shock that was enough for them to stop.*

CRS10*: …they [the cardiac patients] have already been dealt with cardiac-wise by the time they come to us. So, they may well have had those risk factors that were exactly the same, but they've already been controlled. So, we're getting them at a different point.*

4.11.2 Patient Motivation

CR Team members reported differences in the motivational levels between the two patient groups that were linked to difference in their conditions and treatment journeys. IC patients were found to be motivated to participate and complete the CRP specifically to avoid further surgery.

CRS7*: There's definitely quite a few of them said that they'll do whatever it takes not to have to go for the surgery.*

However, CR staff noticed that other PAD patients did not have the required motivation when it came to making lifestyle changes to reduce risk factors for CVD, due to the lack of immediacy of these CVD-related complications and mortality.

CRS7*: They maybe only have a mild to moderate degree of PAD, it's probably not going to develop to anything in the next four or five years. How can you motivate them to say, come, put yourself through pain for 12 weeks, because it might prevent any problems in 10 years' time? I think that's the hard thing with motivating them and getting the adherence.*

Due to the amount of risk factor modification required by PAD patients, the CR Team viewed their inclusion into the standard CR programme as a logical thing to do. Tackling this issue of uncontrolled risk factors was something that the CR Team felt they were well-suited to support.

***CRS7**: I came from working in different services and didn't have any experience working with PADs. I remember my mindset "why do they need to come through a level three [hospital-based] service?" …Why can they not just be passed straight into, like our active lifestyles [community] programme or those long-term exercise programs? Working in it now, I know exactly why!*

***CRS10:** I think there is a probably a general opinion that they're [the PAD patients] going to be very straightforward patients and low risk, and there won't be any issues with them. And some are, but a large number of them are not. They're far more complex with comorbidities than I expected. I think we've come to learn that, with time.*

4.12 Theme: Making a Difference

4.12.1 Improved Service Provision – for PAD Patients

During the clinician interviews, it became apparent that the CR Team recognised the gap in service provision that was being filled by the integrated rehabilitation programme. Before this integrated service was available, IC patients in Salford had limited options. Access to a generic exercise referral programme was available. This was run in the local leisure centres. The CR team considered that a rehabilitation programme that focused on IC-specific limitations was more appropriate than a generic programme. Patients attending the integrated CRP were felt to require high levels of supervision, and this was seen by staff as an essential part of building of rapport with patients. Staff felt this gave the opportunity for developing trust in the exercise that was being prescribed as IC patients were required to push through initial claudication pain to the point of maximal or near maximal pain. The CR exercise team appreciated the importance of patients trusting them that this exertional pain was safe, and indeed necessary for improvements in walking ability and symptom reduction – something that might not be offered in a generic programme with limited supervision. The CR Team did not feel that the patients would be likely to push themselves to the required level without the support and encouragement provided during the supervised rehabilitation.

CRS7: *And trying to motivate yourself to do that independently is very hard. Coming to a class where someone standing beside you and saying: "Yeah, I know, you're feeling pain, but do a little bit more."*

CRS9*: Just naturally, no one would want to take himself past that point [of pain]. But, also, I think being here…at the hospital, gives patients a bit more confidence to push themselves a little bit more…that confidence that someone's telling me, "I'm not doing any damage."*

The exercise team also recognised that any improvements would not occur immediately, so patients needed to persevere with the exercise to see improvements, which again emphasised the need for a group therapeutic relationship with the CR staff and continual close supervision during the programme.

CRS7*: But you're not going to see improvement straight away. So, they're going to have to trust us for at least the first few weeks, until they actually start seeing those improvements.*

Not only did the CR Team highlight the perceived benefits of addressing apprehension towards pushing through claudication pain, but they also felt the need to address the fear patients had of losing their legs. Patients reported being told that they might lose their leg during the initial consultation with their vascular specialist, and this had built fear for the future. Staff felt that addressing this fear during the CRP helped patients to engage with the programme; something that would not be available in an exercise-based programme such as the exercise referral in the community.

CRS2 *Taking away those fears, those legitimate fears..."Well, what are you worried about that will happen? "Well, I'm worried that my leg is going to you know…drop off".*

CRS3 *So yeah, absolutely. Just that little bit of education really can change someone's understanding and outcomes.*

There was no perceived negative to the new Salford programme being an CR-based programme and not an IC-only group, like the one in Manchester. It was perceived to be ground-breaking, which the team viewed positively.

> ***CRS1:*** *We were doing something really quite unique and different. I, we like doing that, we like innovating, we like developing, we like sort of pushing those boundaries. There's a separate [rehabilitation] programme, but nobody else had done this [combined programme].*

The CR Team felt that this would be a better alternative to the current 'walking advice only' that was currently being offered to patients diagnosed with symptomatic PAD. Their experience of how close supervision and encouragement of cardiac patients improved their outcomes was viewed as the most suitable approach for the new PAD patients especially because the mode of exercise involved pushing through claudication pain.

> ***CRS7****: Coming to a class where someone is standing beside you and saying: "Yeah, I know, you're feeling pain, but do a little bit more."*
>
> ***Interviewer****: Yeah?*
>
> ***CRS7****: That's what makes the big difference. That guy yesterday was a classic example of that. He was going to the gym. He was doing all the exercises. But what you have done with him here was a step above what he was doing.*

The CR Team acknowledged that this was not limited to the exercise intervention. As an aggressive approach to lifestyle modification is required with PAD patients, according to NICE (2012) guidance, having a multi-disciplinary team of staff within the programme was perceived to be a positive for PAD patients. Rather than general practitioners having to complete multiple referrals to different specialisms, it can be covered in one programme.

> ***CRS5****: If you think if there was no rehab…and you had to see a dietitian and go to community dieticians. If you then wanted mental health support, and you had to wait for CBT. If you look at our umbrella that we have, you know, we have our sub-teams:*

psychological, we have our dietetic team, we have physios, we have physiologists, we have our nurses who specialize in it [cardiovascular disease]. What's not to like?

The CR staff perceived that the current provision of these individual services might not currently be in place, through an already established infrastructure, and that this might negatively impact the PAD patients of Salford.

***CRS8**: If you think we weren't doing this [rehab] and then carried on? I wonder how many patients then go on to have heart issues.*

***CRS5**: Because that's going to be less burdensome on other services. It's less burdensome on the GP and other services. And that's only going to help the NHS and the patients. So, I think it's more cost effective.*

***CRS10**: There's no clinics like Heart Failure clinics or cardiac clinics where [PAD] people are maybe up titrated [referring to medication]…After they've been seen by a podiatrist who recommends [medication]…without being awful but, you know, GPs, are so very busy…are they going to review them again? Very unlikely.*

***CRS7**: In terms of PAD...they wouldn't get this level of input anywhere else. Whereas the cardiacs, would probably still get their follow-ups from cardiology and get education from different places and have different exercise opportunities, and stuff like that. Your PADs wouldn't get that.*

The CR Team felt that the PAD patients required supervised rehabilitation as it is not something they could manage sufficiently on their own.

***CRS8:** I think a lot of the few of the ones I've had are just stuck in a rut, and they don't know how to get out of it…And they get down.*

***CRS9:** They're so grateful, aren't they, when they come along.*

***CRS8:** Even to just do a bit more or walk around the shops without it all.*

***CRS10**: They haven't got a clue what to do with painful legs, have they?*

4.12.2 Benefits of An Integrated CRP

One key strength to of PAD patients mixing with the CAD patients was the increased awareness of their risks of CVD, particularly cardiac events. CR staff noticed that PAD patients were not aware of the link between their lower limb issues and the risk of cardiac events when entering the programme.

> ***CRS5****: I noticed that the PAD patients maybe they were a little bit more complacent [with lifestyle modifications]…some PAD patients I think, saw it as less important because it wasn't their heart.*

Patients with IC did not appreciate their risk of a major cardiac event and could not visualise what a cardiac event might look or feel like, and what further limitations this introduce. Integration with CAD patients allowed for this increased awareness in a unique way.

> ***CRS10:*** *They [PAD patients] are seeing the cardiac patients there as the sort of end results, what may happen if perhaps they don't give up smoking. Whereas they've got some pain in the legs. They're not, if it was purely PADs you might not see the potential end result of: "Oh, my goodness, I might be with a heart attack if I don't give up smoking."*

> ***CRS3****. …as they realized what else that [smoking] was doing to the body, it wasn't just the circulation in the legs, it's the circulation to the heart, the brain, the whole of the body, they would then come forward and say, "Well, how do I access smoking cessation support?".*

> ***CRS9:*** *I think it's important to have PADs in cardiac rehab, because …cardiac rehab is primary and secondary prevention. So, like I say…have that opportunity to almost prevent it happening. A bit like prehab, type of thing.*

The CR staff also felt that CAD patients benefitted from the integration as they too were at risk of atherosclerosis of the lower limbs, and this was often spotted during their rehabilitation journey.

CRS1: *Pathways are still working really, really well with the vascular surgery and the podiatrists, we've got numbers of patients who are cardiac perspective we refer into podiatry, they've got PAD which they didn't know and haven't been diagnosed, but they can be properly reviewed on an ongoing basis.*

This benefit also was present during the educational talks when patients could offer peer support to lifestyle changes.

CRS2: *And they could hear each other's stories as well...that was a really important part of the education talks…that the patients, they're sharing their stories, and they recognize similarities in their different history, or, you know, one would say "I was a heavy smoker until this and then that I was like...nothing made a difference until I had this"…That was really, that was really pleasing to see in the education sessions. You just feel like...Yes, run with that. And you kind of angle the discussion so that, you knew what their background stories were because we have assessed them, and we are involved in, but for them to tell each other...*

CRS1: *You've got two patients sat next to each other. And then all of a sudden, they think, "Crikey, if I don't do something, I could end up with that." And "if I don't do something, I could end up with that" [referring to PAD and CAD].*

As previously identified by the CR Team, providing the service to symptomatic PAD patients not only improved the chances of them getting the lifestyle modification advice and the best medical therapy, but it also offered an opportunity for clinicians to identify other comorbidities, particularly cardiac ones.

CRS3*: In some PAD patients…were found that actually, it sounds like you might be getting a bit of angina here, but that might not have been as obvious before, because they didn't walk that far. But then when they start walking further, the symptoms of the heart start.*

> ***CRS7**: There's quite a few that we've come in and said, "You've got angina", or with had a few with arrhythmias and have ended up with pacemakers, only from coming to us.*

Clinicians were then able to refer through to the cardiology team that they work closely with so that the IC patients could get the necessary investigations. The CR staff noted that the process worked well the other way when cardiac patients began to report symptoms of intermittent claudication.

> ***CRS5**: Because let's face it with some times, we've got heart patients who then they've only come in as a heart patient, but, we pick them up then and they'll, erm, "I've got pains in my leg," and then we say "Right, we can refer them on", whereas that would have been another trip to the GP. So, we pick things up. So, the benefits of being under that one umbrella is that you can pick up all these other things.*

> ***CRS7:** The amount of cardiac patients that we can see straight away: "This person has PAD", they've never been diagnosed, and no we're having the referral pathways that, literally, I'll send an email. We'll have an assessment with podiatry within two weeks and they'll have a diagnosis.*

It became clear that the CR Team noticed the integrated rehabilitation had benefits for both the PAD and CAD patient groups. Staff also spoke about the perceived impact of the expanded service on them as clinicians and their own personal development and job satisfaction.

4.12.3 Professional Development and Job Satisfaction

During the initial stages of the integrated service, the CR Team spent time with the clinicians who were referring the IC patients. This was to understand the patient journey, and to gain knowledge and experience of the condition. Although this naturally placed extra demands on staff, this was not seen to be negative. Expanding the service to a new patient group was seen by staff as an opportunity for professional development.

***CRS5**: Yeah, I enjoyed it. I enjoyed going out to the clinics and learning, you know, in the in the advanced podiatry clinics…Also, we can all get very bored. I don't want to be rude. But you can get a bit bored in your role. And you do the same things every day, don't you. You see different people, but it's the same thing. You know, sometimes it's quite, I think it's very good to exercise your brain.*

***CRS10**: Well, it makes our job more interesting as well. If you look at it from the pros from our side, it's very motivating for us and it makes it more interesting...You've got variety of patients.*

During the interviews, a real sense of making a difference to patients and their families developed from the CR staff. They found the programme to offer tangible improvements to patients that were followed by positive feedback.

***CRS3**: But it was really lovely to see patients, erm, patients' confidence improving, so they felt more comfortable and confident to maybe go on and join a local gym or join a local walking group, you know, things that they probably didn't have the confidence to do before.*

***CRS2**: The patients tended to be the younger age groups, as well. Working. And the actual practical difference that that would mean for them, whether that was being able to take kids on the school runs.*

***CRS3**: I had one that was a security guard…So, he was toing and froing going up and down and his legs were just causing him horrendous pain and he couldn't believe you know how well he done and how good you know, these outcomes were and it changed his life.*

There was a clear sense of job satisfaction that emerged from the CR staff focus groups and interviews. Despite the adaptations and challenges taking on a new patient group entailed, they CR staff perceived the benefits of running the programme outweighed and negatives.

***CRS1**: I feel we've made a massive difference to patients in Salford. I think I've always said, if we walk away tomorrow, it's kind of like something's been set up, by us, you know, as a service that has made a really big difference.*

***CRS7:** I think if you're asking that question, would you do it again? The reason we'd do it again, is because we see such massive impact for some of the patients.*

***CRS10**: Yes. It's very motivating for us, isn't it?*

***CRS7:** If you're, if you're talking to me about, for an easy life? And for just coming and getting out on, and making a decision as easy and straightforward as PADs? Would I do it? Potentially not. But the reason that we would do it is because the massive impact that we do have with a lot of these patients...*

***CRS8:** It's when they start doing...living again.*

***CRS7:** Well, it's life changing for some of them. And that's why we do it. It's not an easy option.*

***CRS10**: No.*

***CRS7**: But it's definitely worthwhile.*

Members of the team perceived the programme to be something they would do again, and they acknowledged that it had already generated interest from other rehabilitation programmes in the UK. The expansion in service provision was also perceived to be a strength in terms of recommissioning of the CR service.

4.12.4 Future Proofing

Clinicians viewed an expanded service as less likely to be withdrawn or service provision to be transferred to a different provider, a perceived threat of the current 'business-like' approach to how the NHS is currently operated. The combined programme was not just felt to be an opportunity to do something new with the CR service, but also to protect staff. This

sense of ‘future-proofing’ in part came from the positive financial impact the service had on the local NHS.

> ***CRS1****: And we were also looking at a cost savings because the numbers of these patients weren't going back for vascular surgery. And even for an outpatient appointment, you know, the savings were in excess of £200, £300 just for an outpatient appointment. So, the cost savings in itself are kind of it's a no brainer.*

> ***CRS1****: And then I think it was also about future proofing was as a service. We were, you know, we're still a commissioned service, we can quite easily be decommissioned or another, you know, area can come in.*

4.13 Secondary Outcome Measures

This section of the Results starts by showing the changes in graded exercise test (GXT) in the IC control and IC treatment groups, highlighting the impact of the SEP on each of the two groups. The IC control and treatment group results are then contrasted to review how the IC treatment Group compares to current standard care for the claudication population (IC control group). Following this, all three group's GXT results are then compared using the change in Metabolic Equivalents of Task (METs) pre and post-SEP to assess the level of change across all groups. The results of the CAD Group are presented and compared both pre and post-SEP and against the data from the National Audit of Cardiac Rehabilitation (NACR).

4.13.1 Pre and Post Pain-free Walking Distance (PFWD) and Maximal Walking Distance (MWD)

4.13.1.1 IC Control Group

At baseline assessment, the IC control group had a mean pre-SEP PFWD of 95.9 metres (SD 55.7). Upon completion of the SEP, the mean PFWD improved to 293.9 metres (SD 192.7). This represents a 206.5% improvement in pain-free walking time in the control group (Figure 4.4). This difference of 198 metres (95% CI [130.6 to 279.6 metres]) was significant (p = <.001) and represented a very large effect size (d = 3.55).

The IC control group had a mean pre-SEP MWD of 344.3 metres (SD 238.2). Upon completion of the SEP, this increased to 563.3 metres (SD 227.1) representing a 63.8% improvement in MWD (Figure 4.5**Error! Reference source not found.**). This difference of 219 metres was significant (95% CI [130.9 to 307.1 metres], p = <.001), and represented a large effect size (d = 0.92).

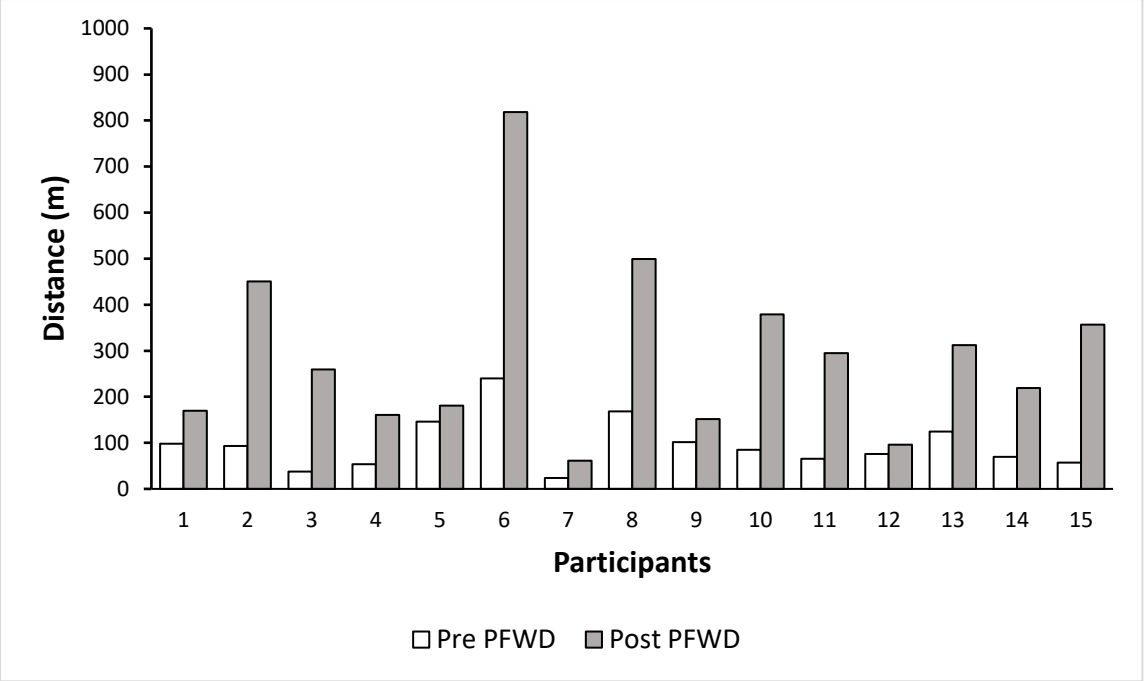


Figure 4.4: The pre and post-SEP pain-free walking distance (PFWD) for intermittent claudication (IC) participants in the control (IC only) group. The PFWD is given in meters.

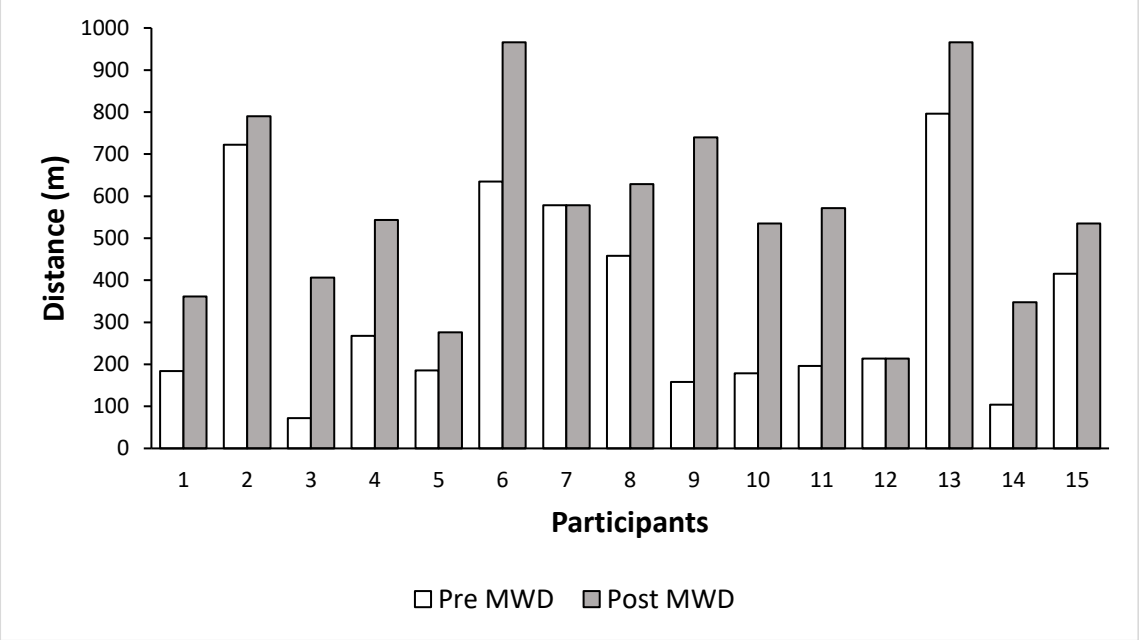


Figure 4.5: The pre and post-rehabilitation Maximal Walking Distance (MWD) for intermittent claudication (IC) participants in the control (IC-only) programme. The MWD is given in metres.

4.13.1.2 IC Treatment Group:

The IC treatment group had a mean pre-SEP PFWD of 176.0 metres (SD 78.4). Upon completion of the SEP, this increased to 366.4 metres (SD 116.9), representing a 108% increase in pain-free walking distance (Figure 4.6). This difference of 190.4 metres was significant (95% CI [114.8 to 266.0 metres, p = <.001). This represented a large effect size (d= 2.4).

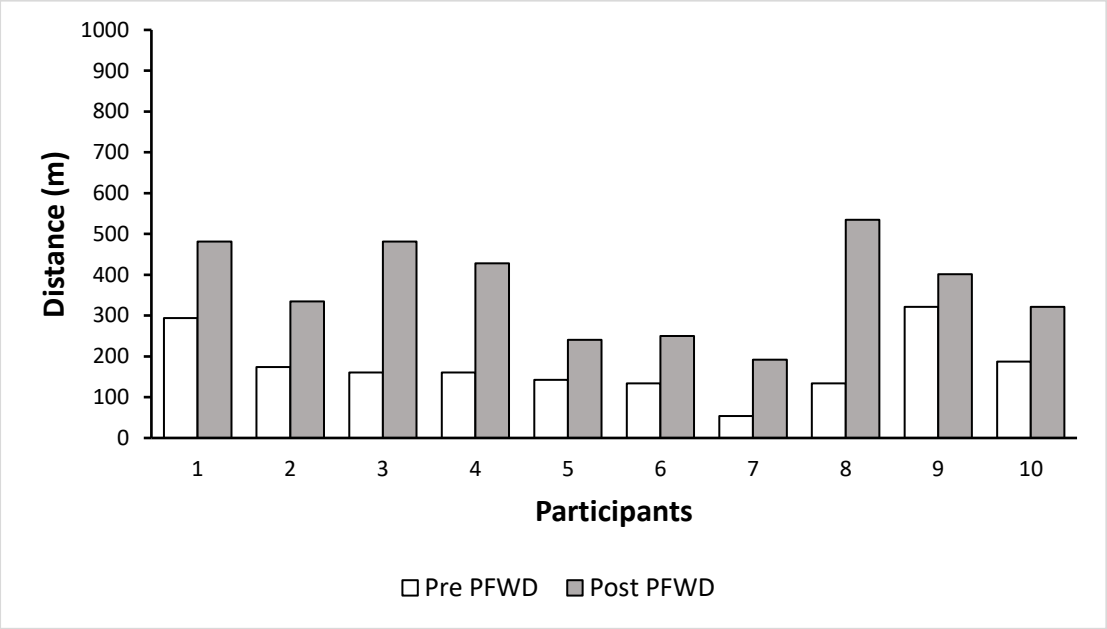


Figure 4.6: The pre and post-treatment pain-free walking distance (PFWD) for intermittent claudication (IC) participants in the integrated cardiac rehabilitation programme (CRP). The PFWD is given in metres.

The IC treatment group had a mean MWD pre-SEP of 470.5 metres (SD 233.7). Upon completion of the SEP, this increased to 754.2 metres (SD 244.0), representing a 60.3% improvement in MWD. This difference of 283.7 metres was significant (95% CI [99.7 to 467.7 metres], p = .007), and represented a large effect size (d = 1.21).

The one participant (participant 10) who did not change their MWD post-rehabilitation was the participant who had completed the treadmill test on their initial assessment. They reported the same peak claudication pain of 3 out 4 at the point of test completion (Figure 4.7).

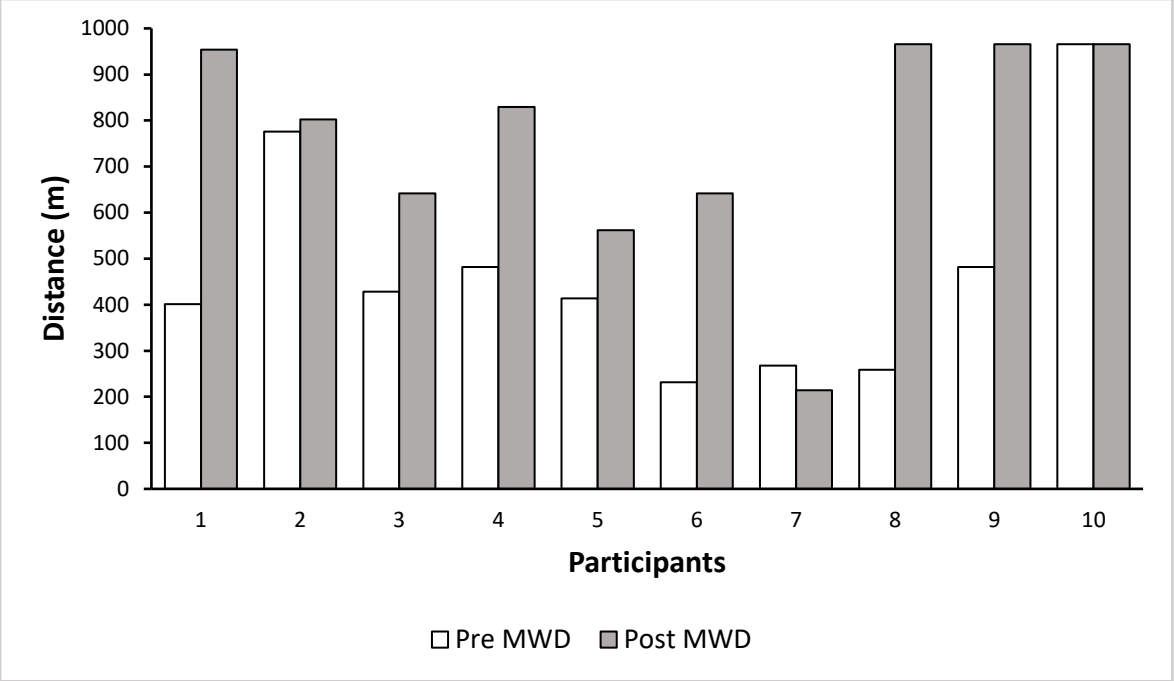


Figure 4.7: The pre and post-rehabilitation Maximal Walking Distance (MWD) for intermittent claudication (IC) participants integrated cardiac rehabilitation programme (CRP). The MWD is given in metres

4.13.2 Comparison between IC Treatment and IC Control Groups

4.13.2.1 Pre-SEP Comparison

The IC control and treatment groups showed a difference in onset of claudication at baseline assessment with PFWDs of 95.9 metres and 176.0 metres, respectively (Figure 4.8). The IC treatment group's extra 80.1 metres of pain-free distance was significantly higher than the control group's (95% CI [24.8 to 135.5 metres], p = 0.006). There was also a difference between groups in their baseline MWD, with the IC treatment group's MWD being 126 metres longer than the IC control Group, however, this difference was not significant (p = 0.204) (Figure 4.8).

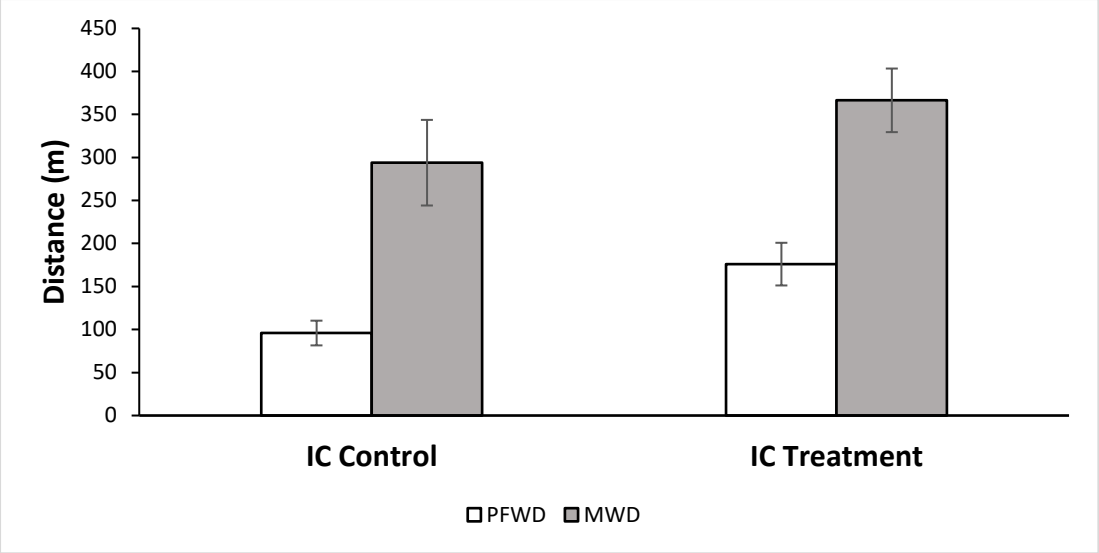


Figure 4.8: Comparison of the IC control and IC treatment groups pre and post-SEP PFWD

4.13.2.2 Post-SEP Comparison

Previous results have demonstrated that both the IC control and IC treatment groups improved significantly in PFWD and MWD. However, the mean change in PFWD between the two groups following completion of the SEP were only 8 metres and was not significant (p = .849), (Figure 4.9).

Although the IC treatment group post-SEP MWD was on average 64 metres more than the control group, this difference was not significant (95% CI [-246.4 to 110.2 metres], p = .490) (Figure 4.10).

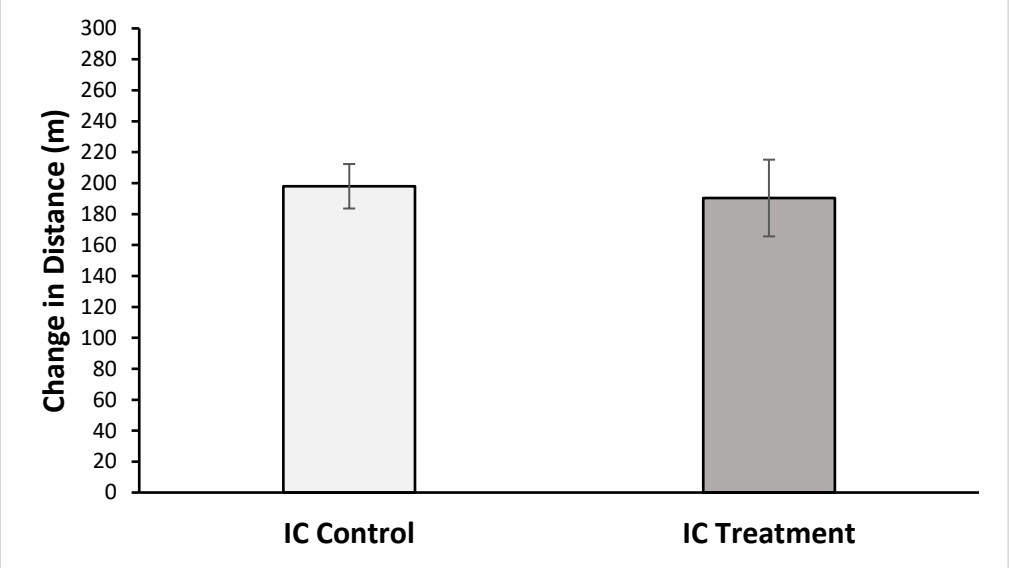


Figure 4.9 Comparison between the mean change in PFWD between the IC control group and the IC treatment group following completion of the SEP

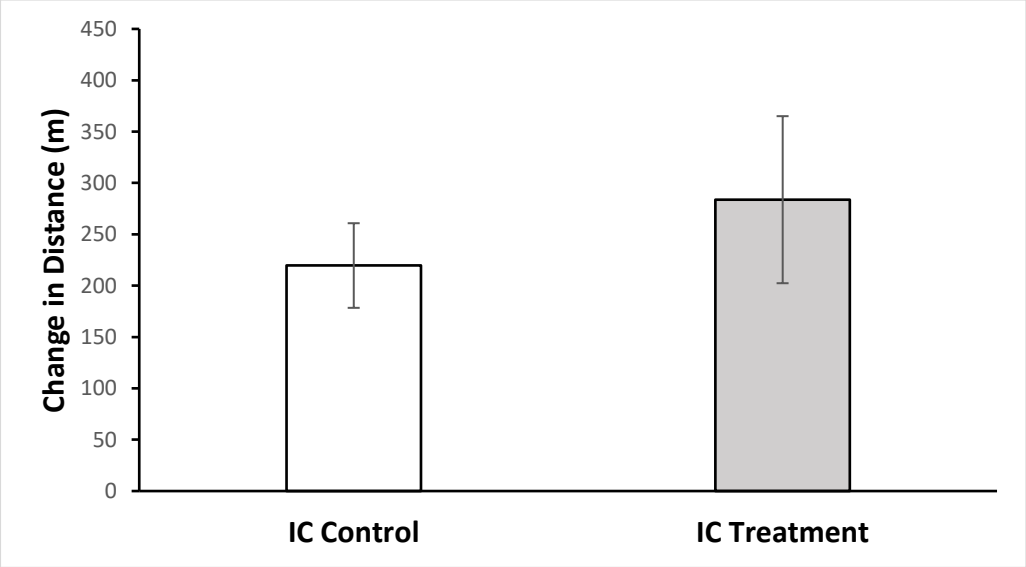


Figure 4.10 Comparison between the mean change in MWD between the IC control group and the IC treatment group following completion of the SEP

4.13.3 Impact on of SEP on METs

4.13.3.1 IC Control Pre- and Post-SEP METs

At baseline assessment, the average METs achieved during the GXT for the control group was 3.8 METs (SD 1.2). This increased to 4.9 METs (SD 1.1) upon completion of the SEP, representing an increase of 28.9% (Figure 4.11). This difference of 1.1 METs was significant (95% CI [0.6 to 1.6 METs], p = <.001), and represented a large effect size (d = 0.92).

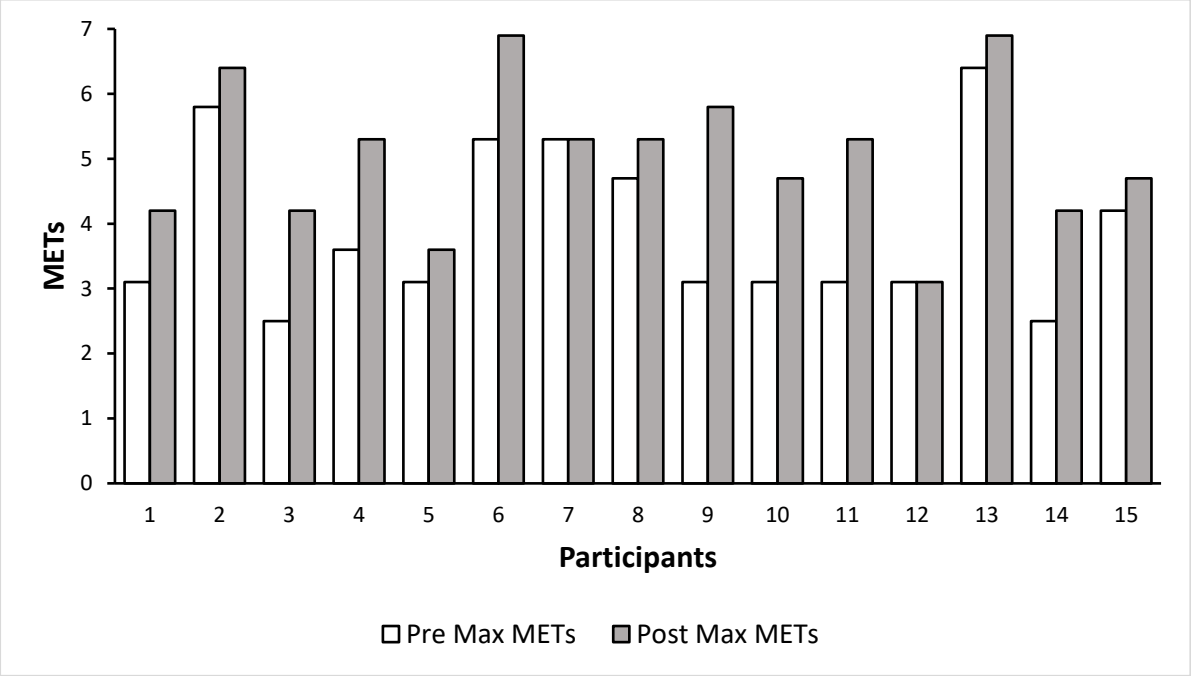


Figure 4.11 The pre and post-rehabilitation METs achieved by the intermittent claudication (IC) participants in the control (IC-only) rehabilitation programme.

4.13.4 IC Treatment Group Pre and Post-SEP METs

At baseline assessment, the average METs achieved during the GXT for the IC treatment group was 4.4 METs (SD 0.4). This increased to 5.7 METs (SD 1.1) following the 12-week SEP, representing an improvement of 29.5% (Figure 4.12). This increase of 1.3 METs was significant (95% CI [0.6 to 2.1 METs], p = .004), representing a large effect size (d = 3.25).

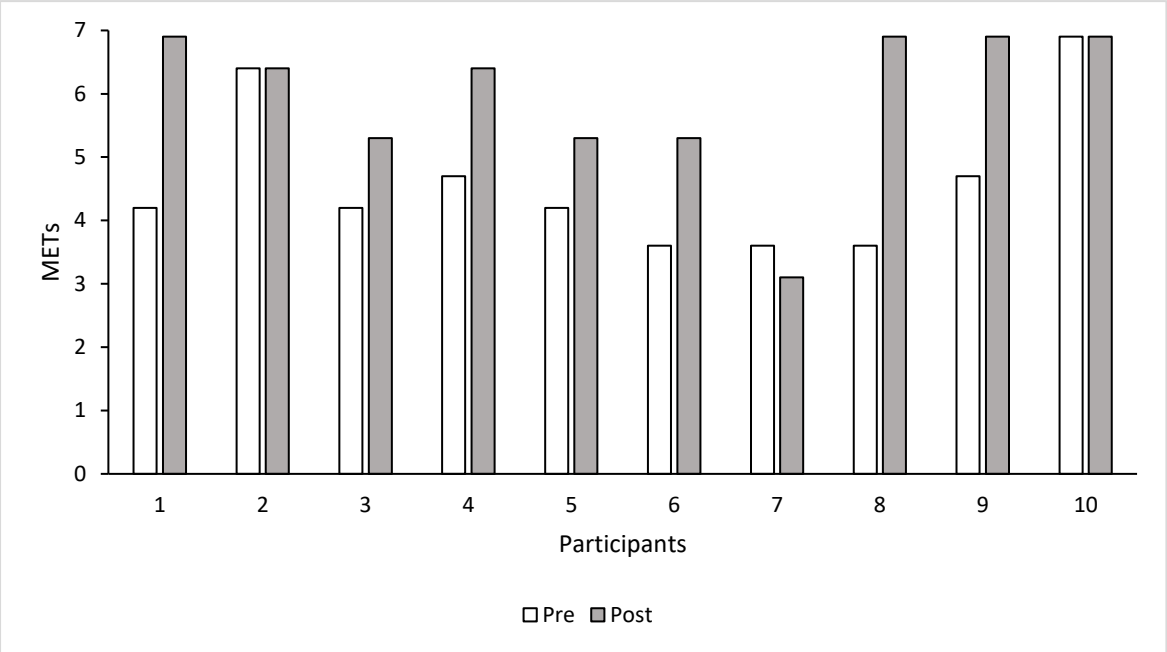


Figure 4.12: The pre and post-rehabilitation METs achieved by the intermittent claudication (IC) participants in the IC control group

4.13.5 CAD Group Pre and Post-SEP METS

The CAD Group had a pre-SEP METs of 5.0 (SD = 1.2). Upon completion of the SEP, this increased to 6.1 METs (SD 1.8) representing a 22% improvement in exercise capacity (Figure 4.13). This difference of 1.1 METs was significantly different (p = .002) and represented a large effect size (d = 0.92).

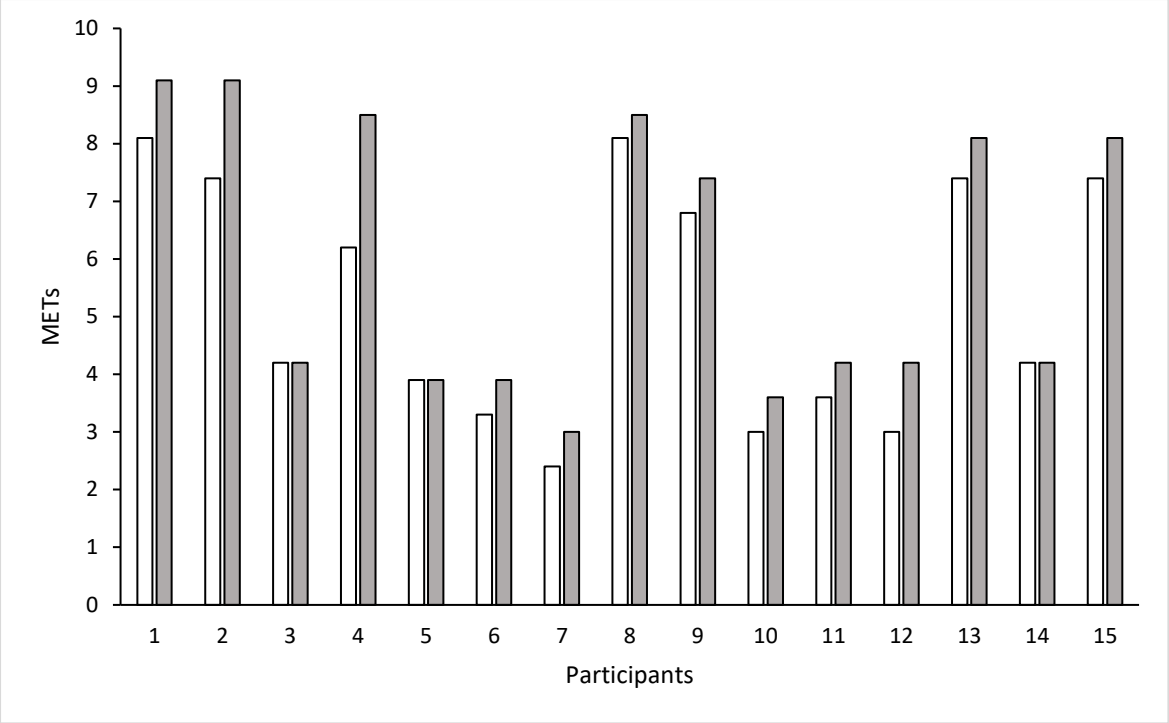


Figure 4.13 The pre and post-rehabilitation METs achieved by the coronary artery disease (CAD) participants in the combined rehabilitation programme

4.13.6 Comparison of Change in METs Across All Three Groups

Although two different exercise tests were used in this study (i.e., Gardner-Skinner Treadmill Test for IC participants, and Incremental Shuttle Walk Test for CAD participants), a comparison of the changes in functional capacity post-SEP can be made between the three groups using the outcome measure of METs. A comparison of the average change in METs of all three groups showed no difference in the level of change achieved ($p = .722$) with all three groups increasing their mean METs by a similar amount (Figure 4.14).

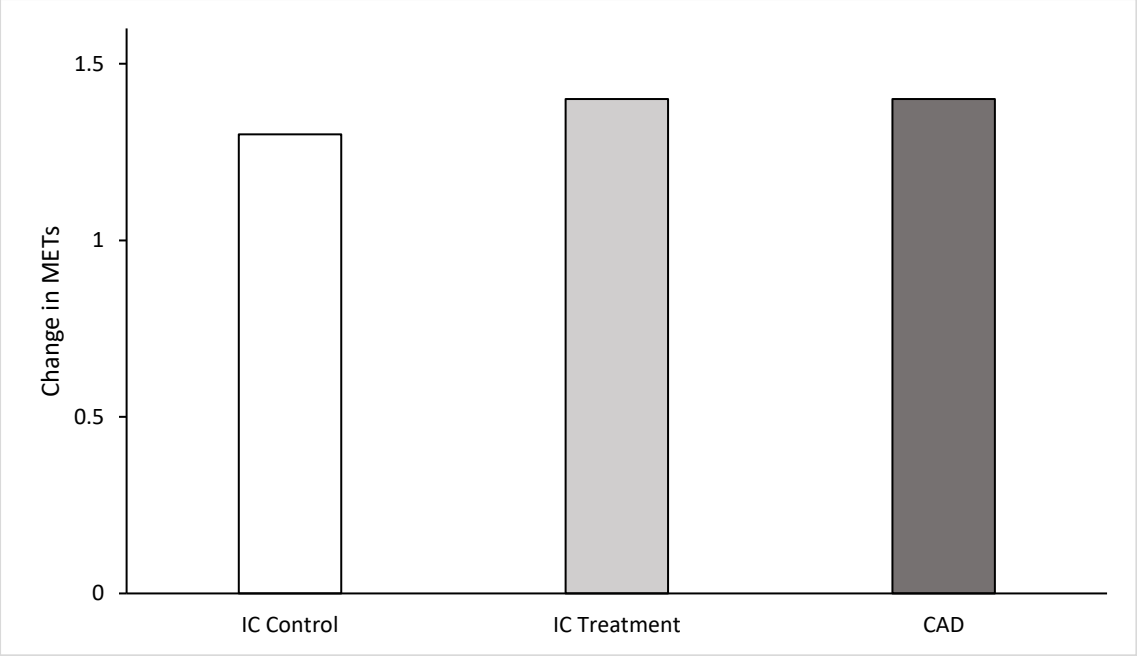


Figure 4.14: Average change in Metabolic Equivalents of Task (METs) for all three groups following completion of the SEP

4.13.7 CAD Group Compared to Known National Average

The results from the CAD Group were compared to the National Audit of Cardiac Rehabilitation (NACR) data. Originally, it was stated that the most recent NACR data would be used for comparison, which would have been the 2021 publication. However, due to COVID-19 restrictions, CR programmes in the UK switched to home-based and online provision with little face to face delivery. As this delivery is vastly different in nature to that of the programmes delivered in this study, the pragmatic decision was made to compare to the NACR 2019 data as this was the last full year of data without changes in service delivery due to COVID-19.

The NACR report the functional capacity (as recorded by ISWT) changes in two separate ways: the percentage of patients achieving a clinically meaningful change of >70 metres, and the percentage of patients completing one additional stage of the ISWT on their follow-up test (post-CRP test) (NACR 2019). The NACR further break the results down into male and female patients and then sub-divides into number of comorbidities (0, 1, and 2 or more). Due to the small number of participants in this study, this makes a direct comparison between this study data and the NACR 2019 data difficult. For example, out of 3,845 male

patients completing pre and post-ISWT in the NACR 2019, 69.8%, 65.4%, and 64.9% achieved an improvement of >70 metres in the 0, 1, and 2 or more comorbidities group, respectively (Figure 4.15).

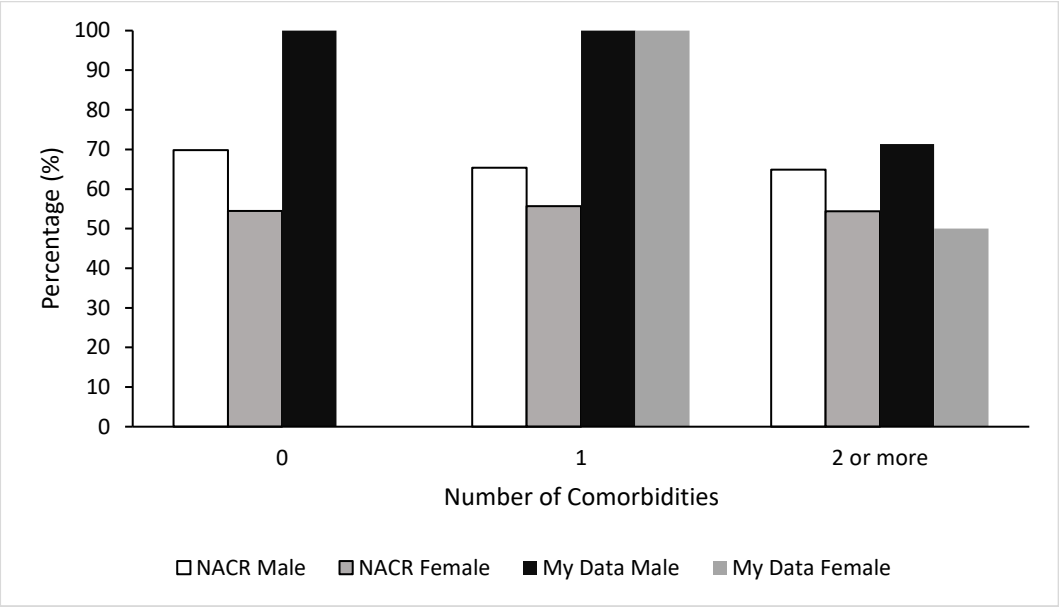


Figure 4.15 Comparison of percentage of patients achieving a meaningful difference in ISWT

A direct comparison to this current study would be a 100%, 100% and 71.4% achievement of >70 metres in the 0, 1, and 2 or more comorbidities categories, respectively. However, there are limited participants in each sub-group of comorbidities as only 12 male participants were recruited to the Cardiac Group in this study. Combining the data for all male cardiac participants, and disregarding the number of comorbidities, gives an 83.3% achievement rate for a clinically meaningful improvement in their functional capacity, as measured by the ISWT (Table 4.28). However, overall, it does reflect a positive trend of improvement in cardiac patient functional capacity post-SEP when compared to national audit data.

Although the generally positive results, the methods for comparing cardiac patients to national audit data need reviewing to try and establish a more accurate way of assessing what impact integrating IC patients into CR has in cardiac patient groups.

Table 4.28: Comparison of study participant graded exercise test changes post-SEP to national audit data. National audit data taken from NACR 2019.

ISWT	Comorbidity	0	1	2 or more	Combined Data
>70 metres	Male (n= 3,845)	69.8	65.4	64.9	
	Female (n= 1,154)	54.5	55.7	54.4	
	Study Data (Male n= 12)	100	100	71.4	83.3
	Study Data (Female n= 3)	NA	100	50	66.6

4.13.8 Quality of Life Measures

4.13.8.1 Walking Impairment Questionnaire

Although there were statistically significant improvements in PFWD and MWD across both the IC treatment and the IC control groups, it needs to be established if this translates into a perceived improvement in walking ability for the participants through the use of patient-reported outcomes measures (PROMs). To establish this, the Walking Impairment Questionnaire (WIQ) was used at baseline and following completion of the SEP. Participants gave their perceived walking ability in terms of walking distance, walking speeds, and stair climbing. The scores for each of the three areas were then calculated as a percentage, with 100% showing no perceived impairment in that area, and 0% being unable to do due to limitations due to claudication or another limiting factor. Changes are therefore given in percentage points.

4.13.8.1.1 IC Control Group

The data for pre and post-SEP WIQ, as well as the mean change in scores, are presented in Table 4.29. The mean change in WIQ subgroup scores for each participant in the IC control group is presented in Figure 4.16.

At baseline assessment, the IC control group had a mean perceived walking distance of 32.7% (SD 30.8). Upon completion of the SEP, this increased to 45.3% (SD 30.2). This

difference of 14.5% was significant (p= 0.006) and represented a medium to large effect size (d = 0.47).

Table 4.29: Results of post-SEP Walking Impairment Questionnaire (WIQ) in the IC control group

	Pre-SEP Mean (SD)	Post-SEP Mean (SD)	Change Mean (SD)	P value	Effect Size
Walking Impairment Questionnaire					
Distance	32.7 (30.8)	45.3 (30.2)	12.6 (15.6)	0.006	*d*= 0.47
Speed	24.8 (18.5)	39.7 (18.2)	14.9 (13.8)	0.008	*d*= 0.8
Stairs	56.4 (23.2)	66.7 (26.6)	10.3 (15.5)	0.034	*d*= 0.44

The same was seen for perceived walking speed with an increase from a baseline mean of 24.8% (SD 18.46) to a post-SEP of 39.7% (SD 18.2). This difference of 14.9% was significant (p= 0.008), representing a large effect size (d = 0.8). Finally, the perceived ability of stair climbing increased from a mean of pre-SEP of 56.4% (SD 23.2) to 66.7% (SD 26.6) post-SEP. This improvement of 10.3% was significantly different (95% CI [0.541, 0.931], p= 0.034), representing a medium effect size (d= 0.44).

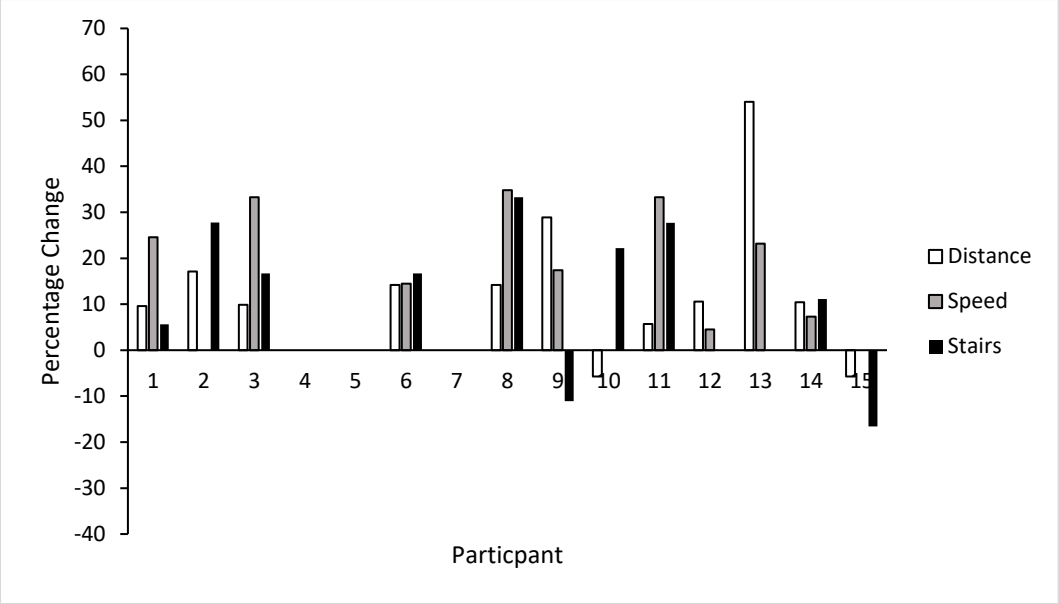


Figure 4.16: The mean change in the three WIQ subgroups (Distance, Speed and Stairs) for participants in the IC control group following completion of the SEP

4.13.8.1.2 IC Treatment Group

The data for pre and post-SEP WIQ, as well as the mean change in scores, are presented in Table 4.30. The mean change in WIQ subgroup scores for each participant in the IC control group is presented in Figure 4.17.

At baseline assessment, the IC treatment group had a mean perceived walking distance of 35.3% (SD 31.8). This increased to 62.4% (SD 36.4) following completion of the SEP. This improvement of 27.1% was significantly (95% CI [-0.2, 0.9], p= 0.027), representing a large effect size(d= 0.85). The same was seen for the perceived walking speed with an increase from baseline of 25.9% (SD 18.6) to 45.0% (SD 18.1) post-SEP. This improvement of 19% was significant (95% CI [3.4 to 6.4], p= 0.007), representing a large effect size (d= 1.02).

Table 4.30: Effect of the SEP on Walking Impairment Questionnaire (WIQ) in the IC treatment group

	Pre-SEP Mean (SD)	Post-SEP Mean (SD)	Change Mean (SD)	P value	Effect Size
Walking Impairment Questionnaire					
Distance	35.3 (9.58)	62.4 (11.0)	27.1 (38.9)	0.027	*d*= 0.85
Speed	25.9 (5.6)	45 (5.45)	19.1 (18.9)	0.007	*d*= 1.03
Stairs	85.7	85.7	0	NA	NA

There was no change from baseline to post-SEP in the perceived stair climbing ability, although the mean of 85.7% was higher than the IC control group at both pre- and post-SEP. This may have been limited by the 3 missing sets of data for this sub-group of the WIQ.

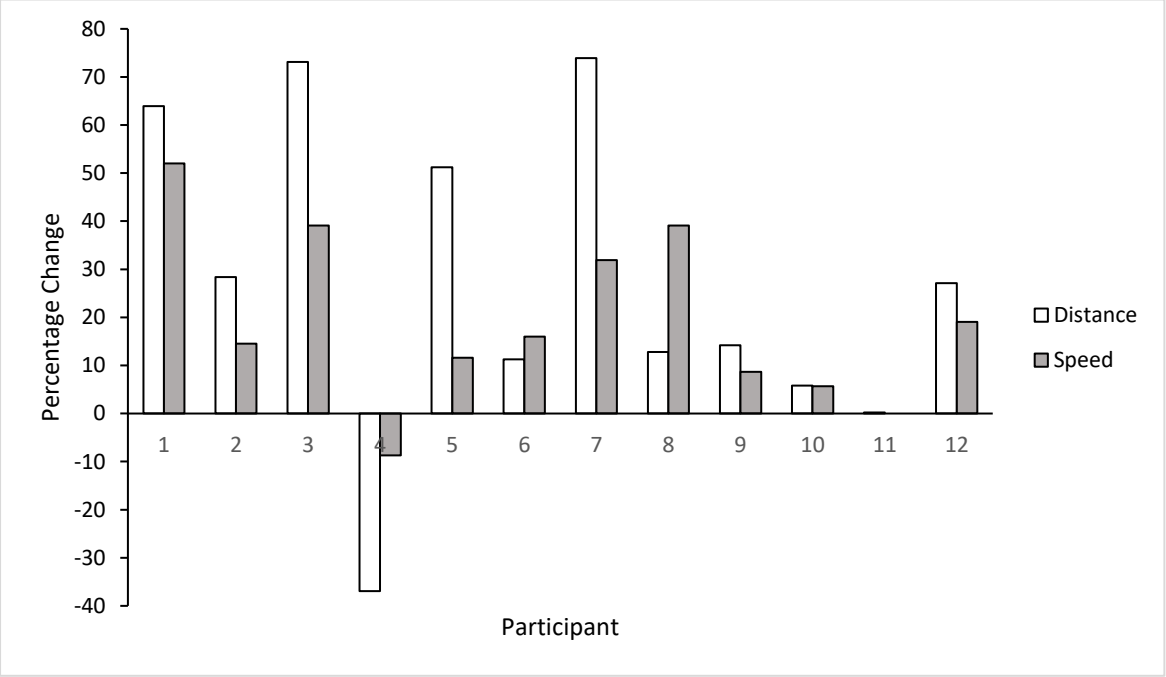


Figure 4.17: The mean change in the three WIQ subgroups (Distance, Speed) for participants in the IC treatment group following completion of the SEP. The Stairs category has not been included as no change occurred.

4.13.8.2 Comparison of IC Control and IC Treatment Groups WIQ Results

The IC treatment and IC control groups both had statistically significant improvements in WIQ scores following completion of the SEP, except for the perceived stair climbing, which did not change in the IC treatment group. To compare the change in WIQ between the two IC groups, Mann Whitney U tests were performed to establish whether the treatment group change was comparable to the 'standard care' provided in the IC control group. The comparison of the mean change across all three subgroups of the WIQ (distance, speed, and stairs) did not show any statistically significant differences (Distance: p= 0.569, Speed: p= 0.569, Stairs: p=0.097) showing both IC groups improved by a similar amount post-SEP.

4.13.8.3 VascuQoL Results

4.13.8.3.1 IC Control Group – Total VascuQoL Score

At baseline assessment, the average VascuQoL score for the IC control group was 5.1 (SD 0.88). Upon completion of the SEP, this had increased to 5.6 (SD 0.97). This difference of 0.5, was significant (95% CI [0.2 to1.0], p = 0.013), and represented a medium to large effect size (d = 0.56) (Table 4.31).

Table 4.31 Effect of SEP on quality of life in the IC control group

King's College VASCQOL	Pre-SEP Mean (SD)	Post-SEP Mean (SD)	Change Mean (SD)	P value	Effect Size
Total Score	5.1 (0.9)	5.6 (1.0)	0.5 (0.6)	0.013	*d* = 0.56
Pain	4.5 (1.1)	5.0 (1.2)	0.5 (0.9)	0.67	*d*= 0.45
Activity	4.9 (0.9)	5.5 (1.1)	0.6 (0.7)	0.012	*d*= 0.60
Emotional	5.3 (1.3)	5.8 (1.2)	0.5 (0.7)	0.025	*d* = 0.38
Symptom	5.5 (0.7)	5.8 (0.8)	0.4 (0.5)	0.021	*d*= 0.58
Social	6.0 (1.2)	5.9 (1.3)	-0.1 (0.6)	0.487	*d* = 0.08

4.13.8.3.2 IC Control Group – VascuQoL Domain Scores

When considering the individual domain scores (Pain, Activity, Emotional, Symptom and Social) there were improvements in four of the five domains from baseline to post-SEP in the IC control group - the Social domain being the only one to decrease (Table 4.31). At

baseline assessment, the mean pre-SEP Activity score was 4.9 (SD 0.89). Upon completion of the SEP this increased to 5.5 (SD 1.1). This difference of 0.6 was (p= 0.028), representing a medium to large effect size (d= 0.67).

The mean pre-SEP Emotional score at baseline assessment was 5.3 (SD 1.3). This increased post-SEP to 5.8 (SD 1.1). This difference of 0.5 was significant (p= 0.025), representing a small to medium effect size (d = 0.38).

The mean pre-SEP Symptom score at baseline assessment was 5.5 (SD 0.67) which increased post-SEP to 5.8 (SD 0.81). This improvement of 0.4 was significant (p= 0.021), representing a medium effect size (d= 0.60).

Although there was an improvement in Pain score from the pre-SEP mean of 4.5 (1.1) to 5.0 post-SEP (SD 1.2), the difference, 0.5 (95% CI [0.2 to 0.9]) was not significant (p= 0.67). The only domain to have a reduction in score post-SEP was Social which dropped from a pre-SEP mean of 6.0 (SD, 1.2) to 5.9 (SD, 1.3). This reduction of 0.1 (95% CI [-0.1 to 0.3]) was not significant (p= 0.487) and represented a small effect size (d = 0.08).

4.13.8.3.3 IC Treatment Group – Total VascuQoL Score

At baseline assessment, the mean Total VascuQoL score for the IC treatment group was 5.16 (SD 0.93). Upon completion of the SEP, this increased to 6.07 (SD 0.99) (Table 4.32). This improvement of 0.97, (95% CI [0.2 to 1.0]) was significant (p = 0.001) and represented a large effect size (d = 0.97).

Table 4.32 Effect of SEP on Quality of Life in the IC treatment group

King's College VASCQOL	Pre-SEP Mean (SD)	Post-SEP Mean (SD)	Change Mean (SD)	P value	Effect Size
Total Score	5.2 (0.9)	6.1 (1.0)	0.9 (0.5)	0.001	*d* = 0.97
Pain	4.8 (1.0)	5.6 (0.9)	0.8 (0.5)	0.001	*d* = 0.84
Activity	4.7 (0.9)	6.0 (1.2)	1.3 (0.9)	0.003	*d* = 1.15
Emotional	5.5 (1.2)	6.2 (1.1)	0.7 (0.6)	0.008	*d* = 0.63
Symptom	5.8 (0.9)	6.3 (0.7)	0.5 (0.5)	0.015	*d* = 0.56
Social	5.1 (1.6)	6.2 (1.2)	1.1 (1.1)	0.023	*d* = 0.71

4.13.8.3.4 IC Treatment Group – VascuQoL Domain Scores

When considering the individual Domain scores (Pain, Activity, Emotional, Symptom and Social) there were improvements across all domains for participants completing the SEP (Table 4.32). At baseline assessment, the mean pre-SEP Pain score 4.8 (SD 0.98). Upon completion of the SEP, this increased to a mean of 5.6 (SD 0.91). This improvement of 0.83, (95% CI [0.6 to 1.0]) was significant (p= 0.001), representing a large effect size (d = 0.84).

The pre-SEP Activity mean score was 4.7 (SD 0.94). This increased to 6.0 (SD 1.21) following the completion of the SEP. This improvement of 1.4 (95% CI [0.8 to 2.0]) was significant (p= 0.03), representing a large effect (d= 1.15).

The pre-SEP Emotional mean score was 5.6 (SD 1.21). Upon completion of the SEP this increased to 6.2 (SD 1.12). This improvement of 0.7 (95% CI [1.0 to 3.4]) was significant (p= 0.08), representing a medium effect size (d = 0.63).

The pre-SEP Symptom mean score was 5.9 (SD 0.90). This increased to 6.33 (SD 0.72) upon completion of the SEP. This improvement of 0.5, (95% CI [0.8 to 0.2]) was a significant improvement (p= 0.015), representing a medium effect size (d= 0.56).

The pre-SEP Social domain mean score was 5.2 (SD 1.56). Upon completion of the SEP this increased to 6.22 (SD, 1.23) upon completion of the SEP. This increase of 1.1 (95% CI [0.3 to 1.7]) was significant (p= 0.023) and represented a medium effect size (d = 0.71).

4.13.8.4 Comparison Between IC Treatment and IC Control - VascuQoL

After establishing the statistically significant improvements in VascuQoL Score for both the IC treatment and the IC control groups, it is important to ascertain whether there was any difference between the baseline and post-SEP Total Scores. At baseline assessment, the mean VascuQoL score for the IC treatment and IC control groups were 5.2 (SD 0.88) and 5.1 (SD 0.93), respectively. When comparing the means of these two groups, they were shown not to be significantly different from each other (p= 0.950). This was also the case for the post-SEP Total VascuQoL Scores. The IC treatment group mean of 6.1 (SD 0.99) and the IC control group mean of 5.6 (SD 0.97) were not different from each other (p= 0.249). The mean change in the Total Score between the two groups following completion of the SEP

also was not significant (p= 0.60). This indicates that the IC treatment group, receiving the novel intervention, had similar improvements in the VascuQoL score to standard care control group.

Analysis of the pre-SEP scores for each of the five Domains, and post-SEP change showed a similar trend to Total VascuQoL scores. The mean scores for Pain, Activity, Emotional, Symptoms, and Social domains between the two groups of IC participants were not found to be significantly different (Pain p= 0.632; Activity p= 0.531, Emotional p= 0.631, Symptom p= 0.268, Social p= 0.181), signalling a similar starting point for both groups in terms of disease-specific quality of life. The IC treatment group did have an improvement in mean Activity Score that was significantly greater than the IC control group (p= 0.025) as well as in mean Social domain score (p= 0.016). As previously stated, the Social Domain was the only Domain in the IC control group that showed a decrease post-SEP, whereas the IC treatment Group had a mean improvement of 1.1 which was the second highest improvement across all domains. There was no significant difference between the two IC groups in mean change in the three other Domain scores (Pain: p= 0.298; Emotional: p= 0.586; Symptom: p= 0.577).

4.13.9 Free-Living Activity

As shown from the GXT and WIQ results, there were improvements in both acute treadmill-based walking ability and perceived walking ability. Another area investigated in this study was the amount of free-living activity the participants performed outside of the rehabilitation setting. This comparison is important to establish if improvements found in measured and perceived walking ability impacted day-to-day activity levels.

4.13.9.1 IC Control Group – Daily Step Count

The participant data for pre and post-SEP daily steps is presented in Figure 4.18.

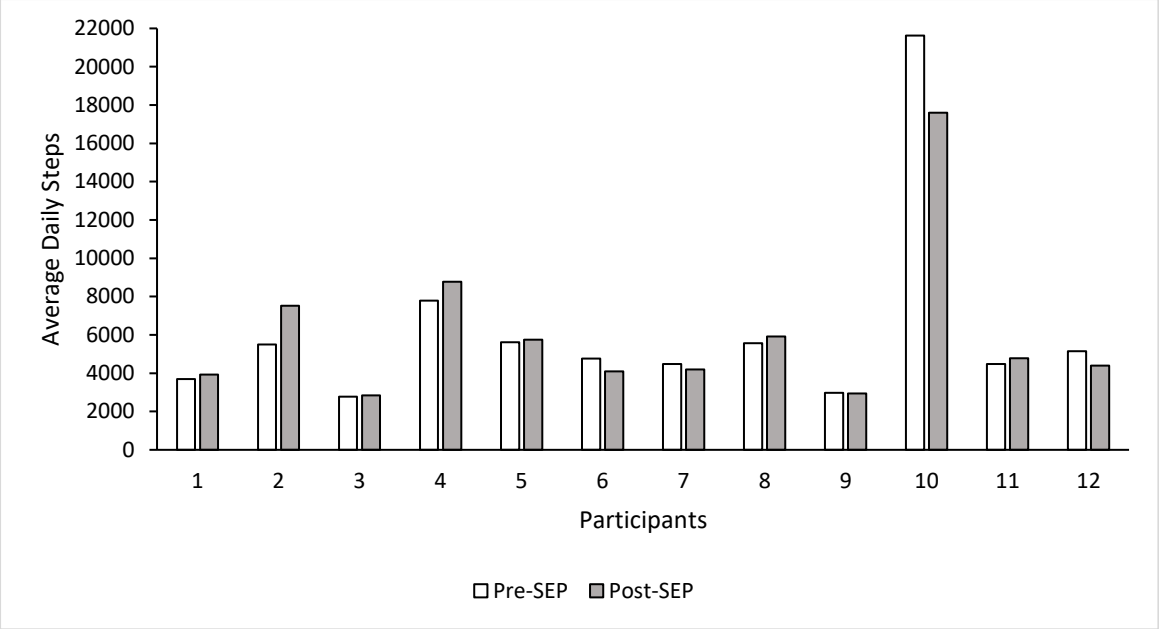


Figure 4.18: Individual pre and post-SEP daily step count for the IC control group

At baseline assessment, the IC Control participants had a mean daily step count of 6200 (SD 5036.6). Following completion of the SEP there was a reduction in daily steps to 6063 (SD 4036.1). This difference of 137 steps (95% CI [-768.7 to 1041.9 steps) was not significant (p= 0.564). The change in average daily steps count for each individual patient is presented in Figure 4.19.

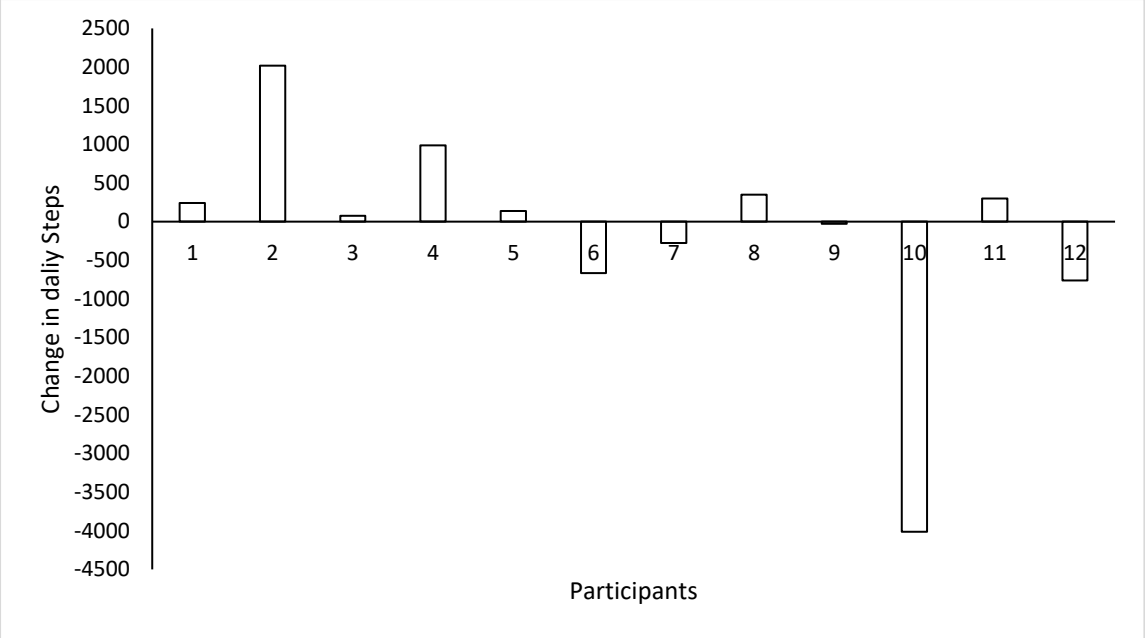


Figure 4.19: Change in daily steps for individuals in the IC control group

4.13.9.2 IC Treatment Group – Daily Step Count

The participant data for pre and post-SEP daily steps is presented in Figure 4.20.

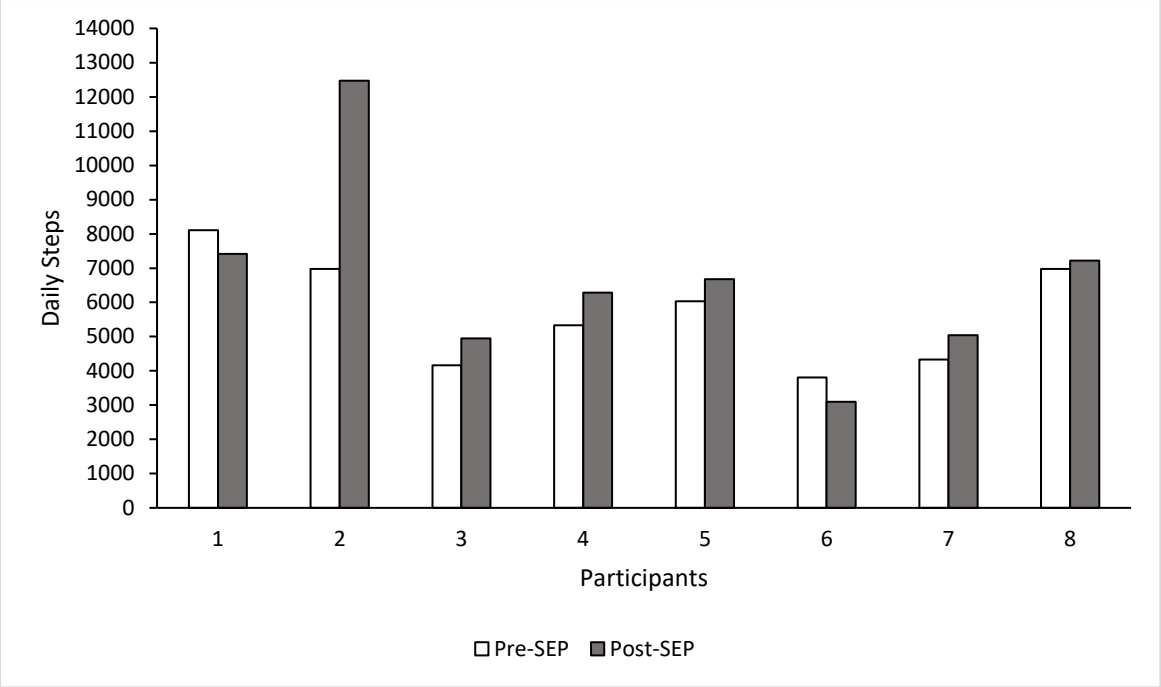


Figure 4.20: Individual pre and post-SEP daily step count for the IC treatment group

At baseline assessment, the IC treatment group had a slightly lower mean daily step count of 5715 (SD 1564.2) compared to the IC control group (6200 steps, SD 5036.6). Notably the maximum daily steps achieved by a participant in the treatment group was 8108 which was considerably lower than the maximum daily steps of 17604 steps achieved in the IC control group (Figure 4.18). Following completion of the SEP, the mean daily steps increased to 6646 (SD 2753.8) which was an increase of 931 steps (95% CI [-706.8 to 2569.6 steps). This difference was not significant (p= 0.161). The change in average daily steps count for each individual patient is presented in Figure 4.21.

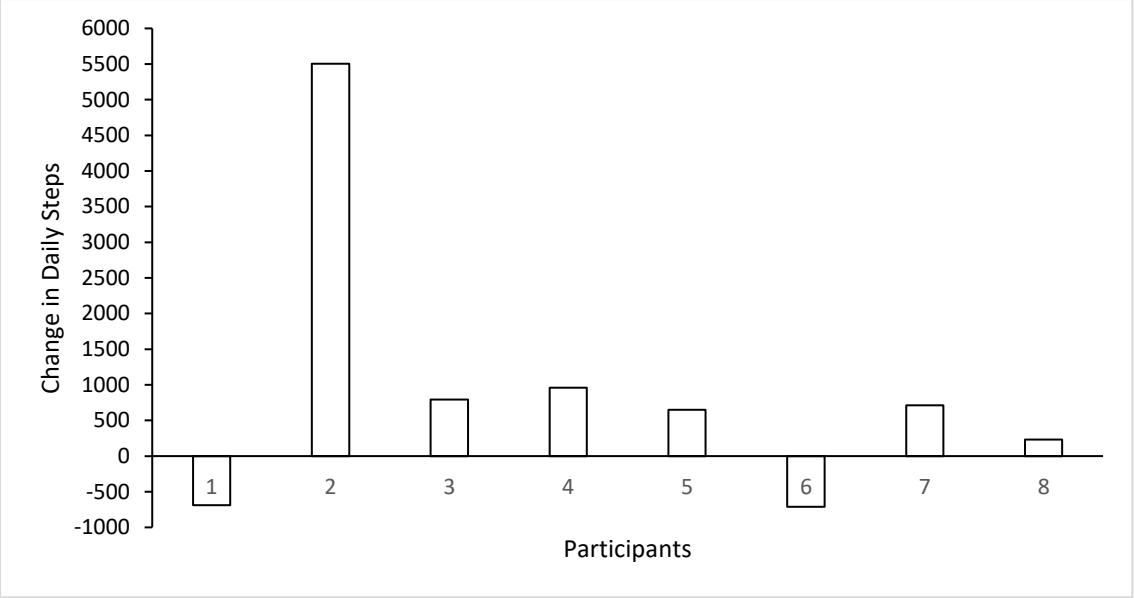


Figure 4.21: Change in daily steps for individuals in the IC treatment group

4.13.9.3 CAD Group – Daily Steps

The participant data for pre and post-SEP daily steps is presented in Figure 4.22.

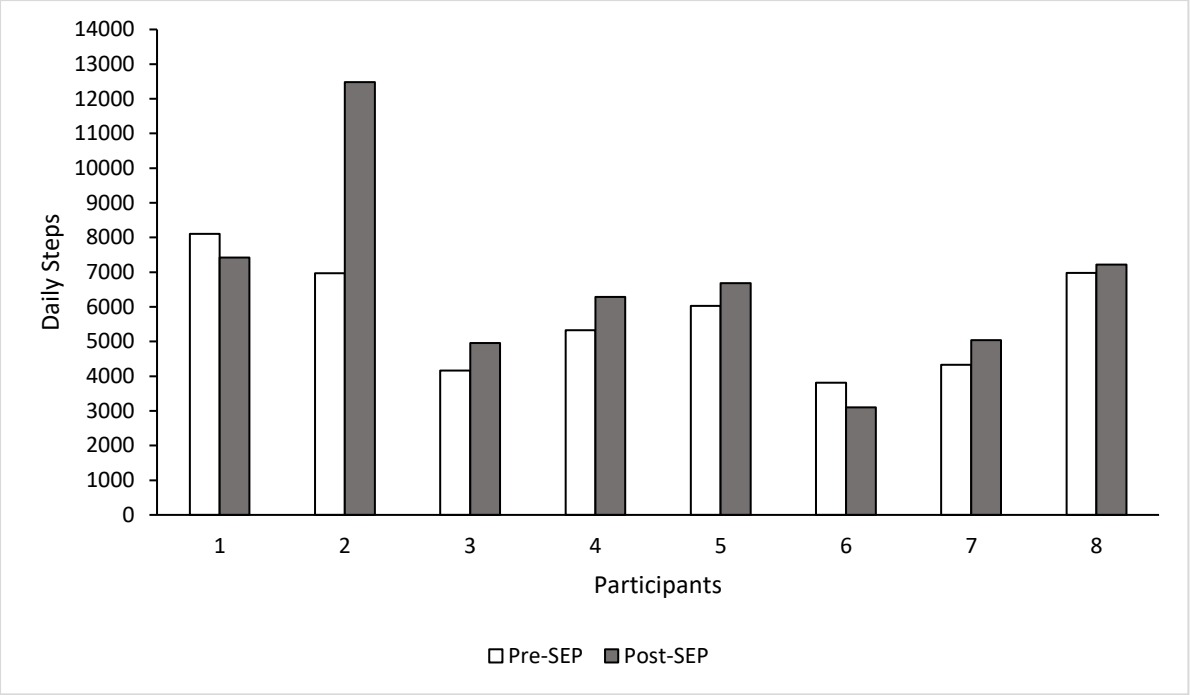


Figure 4.22: Individual pre and post-SEP daily step count for the CAD Group

At baseline assessment, the average daily steps for the CAD group was 7724 steps per day (SD, 3279.2). Following completion of the SEP, this increased to 8840 steps (SD, 3554.8). This difference of 1116 steps per day, (95% CI [-418.6 to 2650.2 steps] was not significant (p= 0.139). The change in average daily steps count for each individual patient is presented in Figure 4.23

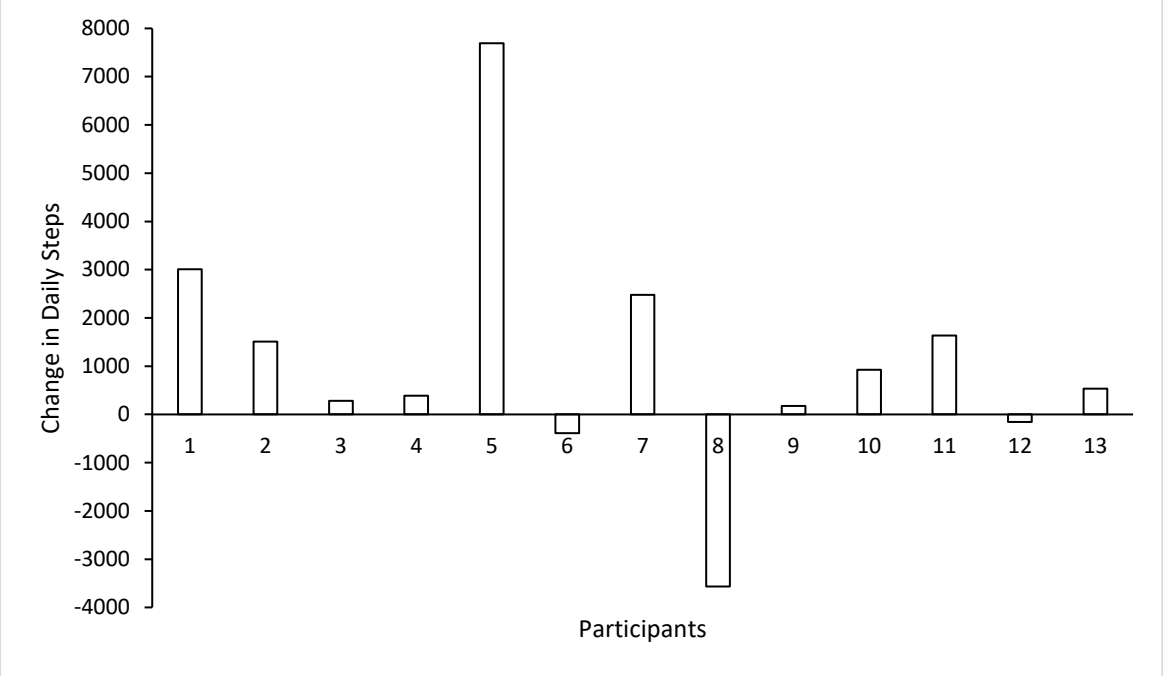


Figure 4.23: Change in daily steps for individuals in the CAD Group

4.13.9.4 Sedentary Behaviour

4.13.9.4.1 IC Control Group

The participant data for pre and post-SEP sedentary time is presented in (Figure 4.24). At baseline, the IC control group participants had a mean sedentary time of 527.9 minutes (SD 152.2). Following completion of the SEP this reduced to 494.0 (SD 150.1). This reduction in sedentary time of 0.6 hours (95% CI [0.008 to 1.3 hours]) was not significant (p= 0.107).

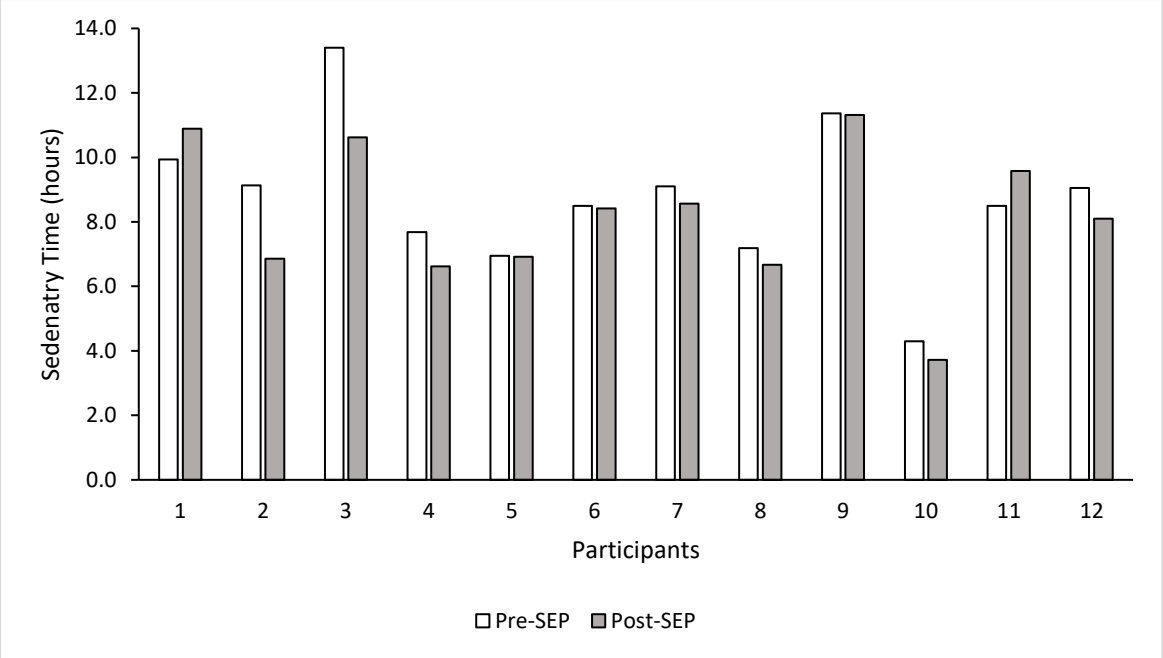


Figure 4.24 Pre and post-SEP sedentary time (hours) for participants completing the IC control group

4.13.9.4.2 IC Treatment Group

The participant data for pre and post-SEP sedentary time is presented in (Figure 4.25). At baseline, the IC treatment group had a mean daily sedentary time of 9.9 hours (SD 1.9). Following completion of the SEP this reduced to 9.2 hours (SD 2.4). This reduction of sedentary of 0.7 hours per day (95% CI [0.5 to 1.3 hours]) was not significant (p= 0.072).

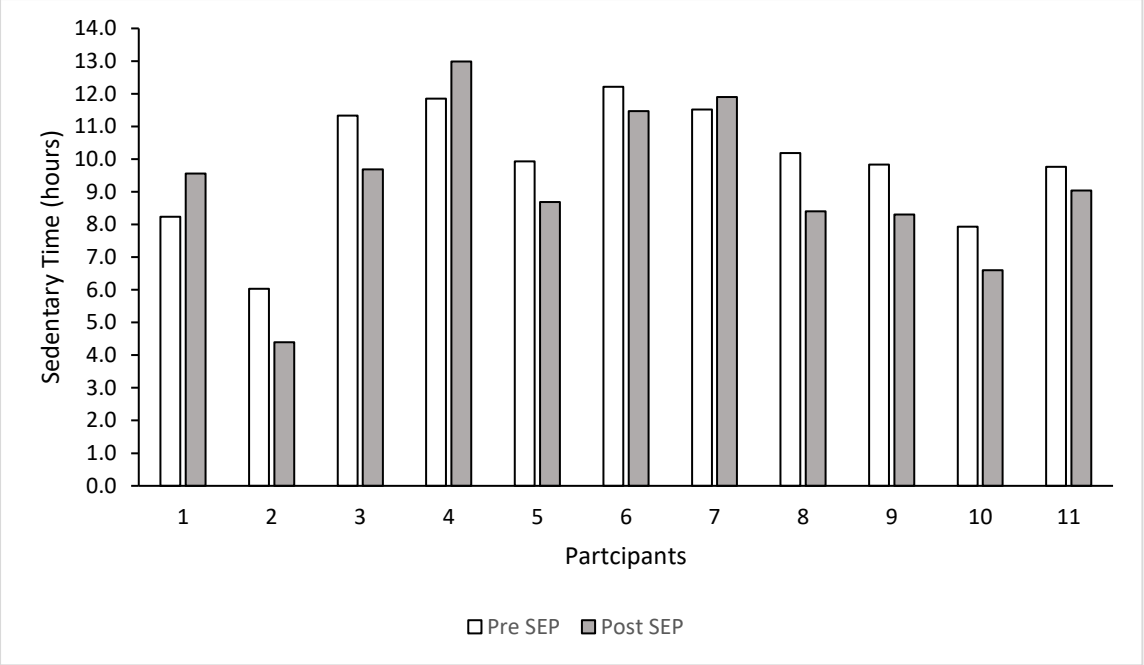


Figure 4.25 Pre and post-SEP sedentary time (hours) for participants completing the IC treatment group

4.13.9.4.3 CAD Group

The participant data for pre and post-SEP sedentary time is presented in (Figure 4.26). At baseline, the CAD Group has a baseline mean sedentary time of 9.2 hours (SD 2.1). After completion of the SEP, this reduced to 8.9 hours (SD 1.8). This reduction in daily sedentary time of 0.3 hours per day, (95% CI [-0.1 to 0.8 hours]) was not significant (p= 0.224)

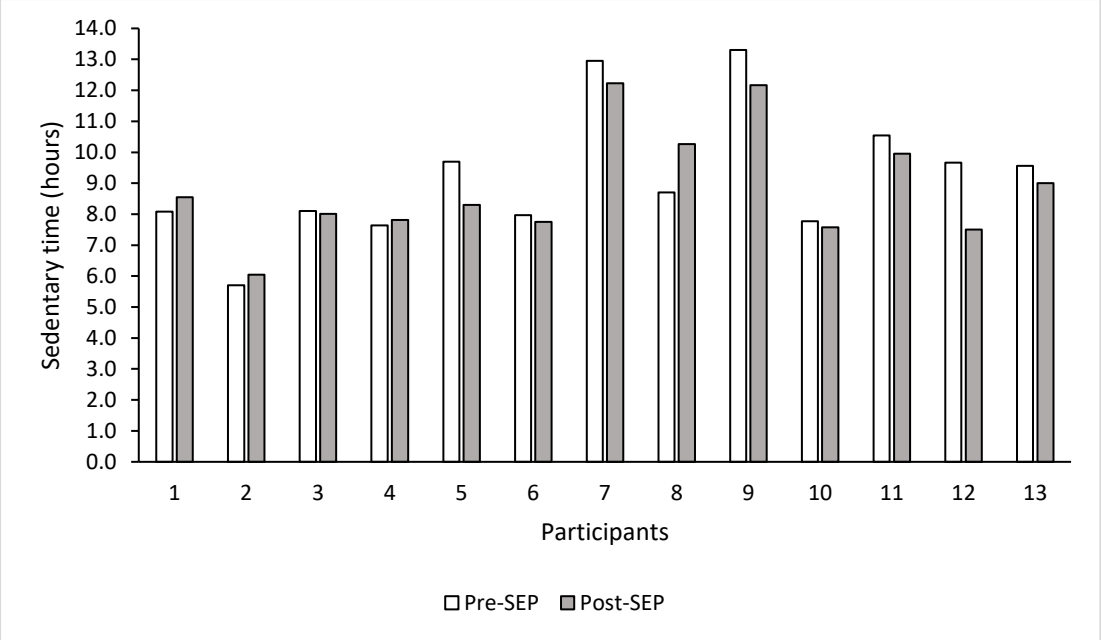


Figure 4.26 Pre and post-SEP sedentary time (hours) for participants completing the CAD Group

4.14 Power Calculations

It was decided that both the MWD data and total VascuQoL score data from the treatment group would be used in the power calculations. This is because improving these outcomes are the main focus of interventions for the management of IC (Ibeggazene et al., 2022). The test with the highest recommended sample would be used to guide the future study.

4.14.1 Maximal Walking Distance (MWD) Data

Using the G*Power Software (Version 3.1.9.7), the achieved power for the MWD was first determined using the *post hoc* power calculation. Using the effect size of d = 1.21, the α level of 0.05, and sample size of 10, the achieved power was 0.92. From this, the *a prior* sample size calculation was performed. The selected statistical test was an independent t-test (2-tailed), as the future trial will compare the means of the control and intervention groups. This gave a total sample size of 34, with 17 participants in each group.

4.14.2 Total VascuQoL Score Data

The same process was followed to calculate the sample size based on the outcome of the VascuQoL questionnaire (total score) in the IC treatment group. Using the effect size of d = 0.97, the α level of 0.05, and a sample size of 11, the achieved power was 0.82 (using the *post hoc* power calculation). As with the MWD-based calculation, the selected test was an independent t-test (2-tailed). This gave a total sample size of 38, with 19 participants in each group.

4.14.3 Recommended Sample Size & Recruitment Target

There was little difference between the sample size calculations using the MWD and VascuQoL outcomes. As originally stated in the methodology, the highest sample size recommendation from the two tests would be used, therefore the aim for the future trial should be 38 participants with IC. Due to the dropout rate found in this study, it is advised to over-recruit by 30%. This is supported by another study protocol involving IC patients (Whorlton-Jones et al., 2022). To achieve the required 38 IC participants, a total of 50 should be recruited, with 25 in each group.

For the CAD group, the recruitment aim should be the same number of patients as the IC groups. There is no function in the G*Power software to calculate out the sample size for three different groups, and the outcome measures used were not CAD-related. Therefore, the recommendation is for 25 aged-matched CAD patients to be recruited to investigate the efficacy of the integrated CRP for this patient group.

Chapter 5 Discussion

The primary aim of the thesis was to investigate the feasibility of integrating patients with intermittent claudication (IC) into an already established cardiac rehabilitation programme (CRP). A non-randomised control trial was conducted over two sites: one site recruited IC patients and coronary artery disease (CAD) patients for the combined treatment group, and a second site recruited IC patients only to act as the control group. The feasibility of the integrated CRP was assessed quantitatively using eligibility rates, consent rates, retention rates, and the number of adverse events. The acceptability of the novel treatment to patients was qualitatively evaluated through the use of focus groups and individual interviews. Both IC patients and CAD patients were involved in the qualitative stage to assess the feasibility and acceptability of the treatment for both patient groups. The quantitative and qualitative feasibility measures were also collected for the IC control group to act as a comparison. The study showed the integrated CRP to be feasible with eligibility rates, consent rates, and retention rates similar across all three groups (IC control, IC treatment, and CAD group). The novel programme was also found to be acceptable to both IC and CAD patients, with patients feeling they could provide support to each other regardless of their underlying health condition.

The secondary aim of the study was to collect data from the integrated programme to guide the design of a definitive efficacy study of the integrated CRP. This was achieved by embedding a pilot study into the feasibility study. Data on walking capacity, quality of life, and free-living activity was collected for all patient groups. There were high completion rates across the exercise tests, quality of life questionnaires, and free-living activity assessments. However, there was a large amount of missing data from the baseline and follow-up assessments such as blood pressure, resting heart rate, height, weight, and waist circumference. This highlighted differences in the pre- and post-SEP assessments that will need to be addressed in the future definitive trial.

This chapter discusses the findings of this study in detail to show how the aims and objectives of the thesis have been met.

5.1 Feasibility Evaluation

The following section evaluates the feasibility of the integrated Cardiac Rehabilitation Programme (CRP) for people with intermittent claudication (IC) using the findings of this study. A systematic approach by Bowen et al. (2008) has been used to present this feasibility evaluation in a clear and logical manner. Bowen et al.'s eight areas of focus for evaluating an intervention's feasibility are presented in Table 5.1.

Table 5.1 Bowen et al.'s areas of focus for evaluating intervention feasibility

Acceptability	To what extent is a new idea, program, process, or measure judged as suitable, satisfying, or attractive to program deliverers? To program recipients?
Demand	To what extent is a new idea, program, process, or measure likely to be used (i.e., how much demand is likely to exist)?
Implementation	To what extent can a new idea, program, process, or measure be successfully delivered to intended participants in some defined, but not fully controlled, context?
Practicality	To what extent can an idea, program, process, or measure be carried out with intended participants using existing means, resources, and circumstances and without outside intervention?
Adaptation	To what extent does an existing idea, program, process, or measure perform when changes are made for a new format or with a different population?
Integration	To what extent can a new idea, program, process, or measure be integrated within an existing system?
Expansion	To what extent can a previously tested program, process, approach, or system be expanded to provide a new program or service?
Limited-efficacy testing	Does the new idea, program, process, or measure show promise of being successful with the intended population, even in a highly controlled setting?

5.1.1 Acceptability of the Integrated CRP

For a new intervention to be deemed feasible, Bowen et al. (2008) recommend measuring the level of suitability or attractiveness of the novel intervention to both those delivering the service, and those receiving it. This is presented in the following two subsections.

5.1.1.1 Service Users

The study showed that both the IC and the CAD patients found the integrated CRP acceptable. The consent rate for the IC treatment group was similar to the that in the IC control group (45.9% and 39.5%, respectively). The retention rate for the IC treatment group was also similar to those in the IC control group (64.7% and 78.9%, respectively). During the focus groups and individual interviews IC patients reported that they did not feel 'out of place' in a cardiac exercise programme. Although they were performing different exercises to the CAD group, this was not perceived negatively. Patients did not separate themselves into IC and CAD groups. Instead perceived themselves as individuals going through a treatment programme with the common aim of improving their condition, whatever that condition may be. This was reflected in the views of the CAD patients who saw the IC patients as another group of people who were just trying to make a positive impact on their health and lifestyle via the same rehabilitation programme. These findings are supported by a study by Desveaux et al. (2017) which found that patients with heart failure (HF) and chronic obstructive pulmonary disease (COPD) enrolled on a mixed exercise programme viewed that they were all there for the same purpose and did not differentiate each other by condition.

In this current study, both IC patient and CAD patients felt they could not only exercise alongside each other but could also offer each other peer support regardless of their individual conditions. Other research has supported this view of patients providing a support network that is based on a shared experience of rehabilitation, and not a shared disease. In the Cardiac Rehabilitation in Bowel Cancer (CRIB) study (Hubbard, Munro, et al., 2016), patients following bowel cancer surgery were incorporated with cardiac patients in a CRP. Both patient groups reported supporting each other through their rehabilitation journey with individual diagnoses not being a barrier to integration.

Data from this study does raise an area for concern on the initial view expressed by IC patients on how effective the treatment would be. Patients in both IC groups were doubtful the exercise therapy would reduce their symptoms and increase their walking, compared to the alternative of revascularisation. This suggests that participants in this research were already highly motivated to participate despite their perception of the treatment. Other less-motivated patients may not share this view of treatment acceptability. This was echoed in the view some IC treatment patients had of the combined education sessions. They did not see the relevance of some of the topics discussed in the education sessions, particularly those they felt were cardiac-focused.

5.1.1.2 Cardiac Rehabilitation Staff

During the focus groups and individual interviews with CR staff, the integration of IC patients into their programme was found to be acceptable. Although adaptations to the service were required, once these were made the integration was deemed appropriate and logical by the CR Staff. It was deemed logical due to the higher prevalence of uncontrolled risk factors for cardiovascular disease (CVD) found in the IC group. Since PAD patients go on to develop cardiac disease, and often die prematurely of a cardiac cause, staff believed they were offering a primary prevention programme to this population, as well as treating their PAD. Importantly, CR staff identified a lack of available support for PAD patients in the wider healthcare system compared to what is offered to cardiac patients. They attributed this to the prevalence of uncontrolled CVD risk factors within the IC patients. Staff felt that the IC patient's motivation levels to make lifestyle changes was poor because they had not had a major cardiac event, such as an MI, so providing support to modify these risk factors was essential. CR staff felt their service provided support to IC patients that was not limited to the reduced need for surgical intervention.

CR staff also identified the challenge of motivating patients with IC to engage with the programme, particularly walking to maximal pain. However, they thought these challenges were outweighed by seeing the patient realise the benefits upon completion of the programme, such as improved walking ability and improved quality of life. This, combined with the perceived impact on reducing the risk of future cardiac events, gave CRP staff a

feeling they were making an impact on IC patients' lives. This has been reflected in other similar studies of integrated rehabilitation programmes. An investigation into the experiences of rehabilitation staff running the Healthy and Active Rehabilitation Programme (HARP) in Ayrshire, Scotland, an integrated multimorbidity rehabilitation programme, found staff could offer a service to patients that would normally not be able to access (Cowie et al., 2021; Cowie et al., 2018). Like with this study, there was adaptations required to the programme, and there was apprehension from some staff, however, staff felt the developed professionally through this integrated programme.

5.1.2 Demand for the Novel Intervention

To fully evaluate a novel intervention's feasibility, the demand for the programme needs to be established (Bowen et al., 2008). To establish demand, the feasibility outcomes of eligibility rate and consent rate can be used. This section discusses the results of those feasibility measures for this study and compares them to the results of similar studies of exercise-based interventions. This information will also be useful for other CRPs interested in expanding their services to IC patients, to get an estimate of the number of additional patients to expect. An overview of the results of the studies used is presented in Table 5.2.

The eligibility rate of IC patients and CAD patients referred to the integrated CRP was 92.3% and 81.6%, respectively. This shows a small proportion of patients diagnosed with IC are unsuitable for the CRP. In comparison to this, in a study of community-based walking therapy for patients with IC, the eligibility rate for the intervention was only 36% (Müller-Bühl et al., 2012). This is markedly lower that the current study and is potentially due to the nature of the exercise delivery used in CRPs being suitable to a large proportion of referred patients. The classic manifestation of disease means that extended walking periods are not comfortable or even possible for most IC patients. A circuit-based programme that offers easy transition from exercise to seated rest might be more accessible to the majority of patients with IC, compared to a community-based walking programme.

Table 5.2: Comparison of the feasibility outcomes of this study to other studies into exercise-based interventions

	IC Control Group (current study)	IC Treatment Group (current study)	Harwood et al. (2016) Systematic Review of SEP for IC	Muller-Buhl et al. (2012) Community Walking Programme	Hubbard et al. (2016) CRIB
	% (eligible/total referred)	% (eligible/total referred)	% (eligible/total referred)	% (eligible/total referred)	% (eligible/total referred)
Eligibility Rate	84.6 (55/65)	89 (127/143)	Data unavailable	36 (166/462)	67 (133/198)
Consent Rate	39.5 (19/55)	28 (36/127)	24 (1820/7517)	66 (110/166)	31 (41/133)
Retention Rate	78.9 (19/19)	72 (26/36)	75 (3015/4012)	32.7 (36/110)	93 (38/41)

A study into the feasibility of an integrated CRP for patients with bowel cancer (the CRIB study) had an eligibility rate of 67% (Hubbard et al., 2015). As this study was also investigating an integrated CRP, the comparison to the current study may be more appropriate as the same programme of delivery was used. However, the CRIB study involved a different and arguably more complex group of patients. Reasons for declining SEP in the CRIB study were protracted recovery post-surgery, poor mobility, and cancer-related fatigue. Also, patients were undergoing concurrent cancer treatment which was a barrier to attending. The IC population used in this study were not post-treatment, as in the CRIB study.

The consent rate for the integrated CRP is also important to establish as this provides a more accurate figure of the potential level of demand for the new intervention. There might be a large number of patients that are eligible for the programme, but if there is a small number of patients who actually take up this option, this will reduce the feasibility of this treatment option. The consent rate for IC patients to the integrated CRP was 45.9%. A systematic review of the uptake and adherence rates to SEPs for IC patients (23 studies with 7517 participants), the overall consent rate was 24% which is much lower than this study. In the community walking programme study by Müller-Bühl et al. (2012), the consent rate was 66% which is markedly higher. However, this was followed by a poor retention rate, which will be covered later in the discussion. In the CRIB study by Hubbard, Adams, et al. (2016), the consent rate was 31%. The data from Harwood et al. (2016) and Hubbard et al. (2016) both show lower consent rates to this study. However, this could be due to the way that consent rate was calculated in this study. In this study, patients who were eligible but were not able to be assessed in time were not included in the consent rate calculations.

5.1.3 Implementation

This study shows that an integrated CRP for IC patients can be successfully implemented with a high number of IC patient referrals received in the 13-month recruitment period (78 to the integrated CRP), and successful delivery of IC-specific exercise within the established CRP circuit. Implementation involved the initiation of a new referral pathway, and eligible patients were successfully screened and enrolled on to the new intervention. The consent

rate for IC treatment group was comparable to the IC control group (45.9% and 39.5%, respectively), and above the levels usually quoted in the literature (Table 5.2). There was a high adherence rate to the integrated programme with the average number of sessions completed by the IC patients being 11.5 out of 12 sessions. The fidelity to the exercise guidance was kept, as IC patients were able to exercise to maximal or near to maximal claudication pain. Education on CVD risk factors had support on lifestyle modification was successfully offered as part of the programme. These findings show that the new programme can successfully deliver the intended programme to the intended participants.

Clear lines of communication were established with the vascular specialists so that CR staff were able to easily discuss complex patients or raise concerns about patients who showed signs of deterioration in their condition, such as resting leg pain. This was key to the implementation process as this matched the communication lines present for CRP staff to refer to Cardiology review for cardiac patients who deteriorate whilst accessing their service.

The CR team reported that additional education and support was required to successfully deliver the programme, but most of this was delivered through in-house training. There was no requirement for formalised training to be provided by external companies. Although, staff did feel they benefitted from visits to the Specialist Podiatry service, who diagnosed and referred the IC patients into their service. This helped them gain an insight into the IC patient journey. In the CRIB study (Hubbard, Adams, et al., 2016), members of the CR team completed a specialist cancer training programme prior to the integrated programme. This would have incurred costs, both financial and staff time. Due to the similarities between IC and CAD pathophysiology, staff did not feel there was a large personal burden on developing their knowledge and skills to cater for the IC patients. Some staff found it very interesting to upskill themselves in PAD and saw it as an opportunity for personal development.

5.1.4 Practicality

To fully evaluate feasibility, the extent to which IC patients can be incorporated within the resources of the CRP needed to be established. The degree to which outside support or intervention is required needs to be assessed to determine the likelihood of other CRPs operating in the UK being able to follow suite. This study showed that it is feasible for CR staff to deliver the integrated programme within their programme infrastructure (e.g., standard exercise circuit), and within their scope of practice due to the limited requirement for training and development prior to accepting IC patients.

Outside of the PI conducting the pre and post-SEP assessments, the rehabilitation programme was delivered only by members of the CR team. No additional staff were required to support the delivery of the exercise sessions. The standard staff-to-patient ratio of 1:5 was maintained throughout. Previous studies into integrating stroke patients into CR exhibited a requirement to quadruple the number of staff in the exercise sessions to ensure adequate supervision (Tang et al., 2010). This extra demand on the rehabilitation programme was not required for the successful integration of IC patients into CR, therefore no extra financial pressure was placed on the service.

The number of patients included in each rehabilitation session was not required to be changed for this study. In the Tang et al. (2010), not only were more staff required to supervise patients but there was also a requirement to reduce the overall number of patients in each class. This was reduced from 100 patients per class, to only 20. This would have a massive implication on the service in terms of the number of sessions they would have to provide to ensure sufficient patient numbers could come through the service, so that patient waiting times were not increased. Previous studies into CR waiting times have shown that for every 1-day increment in waiting time, patients were 1% less likely to enrol on the programme (Russell et al., 2011). This is an essential consideration for all CRPs in the UK who have targets for reducing waiting times and improving access to CR services as part of the NHS Long term Plan (NHS, 2019).

Historically, exercise interventions for patients with IC have been involved treadmill-based walking programme (Harwood et al., 2020; Ibeggazene et al., 2022). The increase in walking capacity found in this study is similar to studies using treadmill-only programmes. A study by Gardner et al. (2001) of 31 patients with IC completing 6 months of supervised exercise showed an improvement in pain-free walking distance (PFWD) and maximal walking distance (MWD) of 134% and 77%, respectively. This current study had improvements of 108% and 60% in PFWD and MWD, respectively, in the IC treatment group. This is promising as the mode of exercise delivery was circuit-based, with minimal treadmill use, suggesting the CRP delivery method is effective. This data is also positive for wider SEP provision in the UK. A review of current SEP provision found 67% of UK-based SEPs used circuit-based delivery for their exercise sessions, and only 13% were walking-based (Harwood et al., 2021).

The education sessions during the rehabilitation programme were also delivered by CR staff without the need for specialists in PAD care to be brought in. Previous studies into integrated rehabilitation have either not delivered education to the new clinical population (Evans et al., 2010), or significant changes to the existing programme to ensure disease-specific education was included. In a study by Banzer et al. (2004) investigating the difference between cardiac patients with or without diabetes mellitus, a specialist dietician was brought into the programme to deliver weekly nutritional advice to the cardiac patients with diabetes. The requirement for specialist knowledge has been an area raised in other studies of integrated rehabilitation, with staff not feeling confident with delivering the disease-specific content for the new patient group. For example, in the CRIB study (Hubbard et al., 2016), physiotherapists delivering the exercise component felt uncomfortable delivering advice around stoma care. In a group of CR staff considering the expansion of their service to stroke patients, there was concern over the delivery of education sessions, and suggestions of separate delivery being required for both patient groups (Jeffares et al., 2021).

During this feasibility study, the practicality of incorporating IC patients into other areas of their CRP was discussed. Members of the team who provided dietary and psychological

support, through the separate 8-week Weight Management programme and 7-week Healthy Minds programme, felt that IC patients could be seamlessly integrated. They felt they could deliver the same patient-centred approach with the new patient group. For example, the approach of cognitive behavioural therapy (CBT) used in the Healthy Minds programme was also found to be suitable for IC patients. A different approach was not required. This demonstrates that the integrated programme can be delivered within the existing resources and infrastructure of the CRP, further supporting the practicality of intervention.

5.1.5 Adaptation

To fully evaluate the feasibility of the integrated programme, the extent to which the CRP is required to adapt must be established (Bowen's et al. (2008). This will help assess whether or not the new intervention resembles the original format that the cardiac patients require. It also will be a useful for guide to other CRPs interested in expanding their provision.

Emerging from the focus groups and interviews was the consensus of CR staff that the major adaptations involved in the exercise sessions. Although there was no requirement for specialist exercise equipment to be introduced, the IC patients did require a different mode of exercise than the cardiac patients. This was noticeably different from previous research into integrated rehabilitation where differences in exercise modality between groups were not facilitated (Devrome et al., 2019). There was a concern from CR staff that there was potential for IC patients to distract attention away from the cardiac patients as they required more support, especially during their initial exercise sessions. Patients required some initial support to understand the timing and rating of claudication pain on the different exercises, and often required support with the exercise record sheet. However, this adaptation to the programme was beneficial to the cardiac patients as the CR team began to use the exercise monitoring sheets with CAD patients too, which gave the patients a perceived sense of ownership of their rehabilitation.

There were other perceived benefits for the cardiac patients from adaptions required to the programme, notably the new graded exercise test used for the IC patients. The CR exercise

team began to utilise the Gardner-Skinner treadmill protocol with some cardiac patients within their service. As the GS treadmill test does not change from the 2-mph initial speed, and intensity increases only through incline, the exercise team found that some cardiac patients were able to perform better on this test, particularly those unfamiliar with treadmills, and they added it to the exercise assessment options for the standard cardiac patients.

Adaptations were also required to the education sessions, although these were minimal. Additional content around PAD is required, including a focus on the treatment options such as femoral-popliteal bypass surgery and endovascular revascularisation. However, staff felt this area of adaptation was also beneficial for the CAD patients. As they were at risk of developing PAD, adding this content to the talks made patients more aware of their risk of worsening atherosclerotic disease.

5.1.6 Integration

Successful integration of a new patient group into CRP inevitably required some to the service. In this section, the extent to which these changes impacted the CRP team and programme infrastructure are evaluated to fully establish the feasibility of the combined programme.

An element of integration introduced was the pre-screening of IC patients to establish eligibility for the programme. This was a new patient group and staff were not familiar with the IC patient screening. All of the 78 IC patients referred to the CRP within the recruitment period (August 2018 to September 2019) were screened for eligibility, with minimal assistance from the PI to clarify suitability (exact amount not recorded). The CR Specialist Nurses did not perceive this to be a burdensome task.

Another important consideration for the feasibility of successful integration was the identification of deterioration in the PAD in the new patient group. This emerged from the qualitative investigation and was not originally identified as an area of concern by the PI. The CR staff placed great importance on recognising worsening PAD during their rehabilitation journey. This was a similar requirement to cardiac patients, and lines of

communication were already in place to refer back to Cardiology for further review in the case of worsening cardiac disease. CR staff found that a similar line of communication was able to be set up with the vascular specialist teams.

Another important area that establishes the feasibility of this integrated service is the ongoing support for IC patients following the completion of their CRP. One of the core components of CR is the life-long support and continual care for patients (BACPR, 2017), and the rehabilitation journey is not limited to the 12-week SEP. After completing the SEP, cardiac patients can access community-based CR programmes (previously referred to as Phase IV CR). These ongoing, community exercise programmes were also made available to the IC patients in the integrated programme through expanding the referral pathway with the service provider (Salford Community Leisure). This shows feasible adaptations can be made to ensure similar service provision for this new patient group.

However, this was to a cardiac-specific continuation programme, and there was no record of the numbers of IC patients referred to, and those who took up and maintained this option. This is an area that needs further investigation as it needs to be established what level of adaptation is required in the ongoing community programmes, as adaptation was required in the hospital-based SEP. It cannot be assumed that the ongoing programmes can just open their doors to the new patient group.

5.1.7 Expansion

Although the efficacy of the integrated rehabilitation cannot be assessed in this feasibility and pilot study, the pilot data shows a comparable increase in IC-specific outcomes measures, such as walking ability and quality of life, between the IC treatment group and the IC control group (Table 5.3). These initial findings are promising. In addition to these quantitative outcomes, the qualitative findings from both the staff and patients show that the expansion of CR to include IC patients is an acceptable option. Indeed, participants from both patient groups in the intervention perceived the integration to be natural. Patients did not separate themselves into ‘cardiac’ and ‘PAD’ groups. They perceived each other to be people accessing support for their health condition.

The only exception to this was during the group education sessions. There were PAD patients that considered the education sessions to be very cardiac-focused and did not perceive them to be relevant covering areas such as coronary artery bypass surgery and echocardiography - all areas that IC patients might not be familiar with. A consideration for future work might explore the separate education sessions or making the link between PAD and cardiovascular diseases clearer to PAD patients.

Previous audits by the BHF have shown that PAD patients have enrolled on CRPs, albeit with a secondary diagnosis of PAD. Audit data of the 233 CRPs in the UK in 2019 showed that 6% of cardiac patients referred for rehabilitation had PAD. This is not surprising due to the strong link between PAD and cardiovascular disease such as myocardial infarction. This study shows that it is feasible for CRPs to expand their offer to patients with a primary diagnosis of PAD. It is also likely that the increased focus and tailored delivery of the rehabilitation to PAD patients will increase the outcomes of the cardiac patients who have a secondary diagnosis of PAD. Moreover, the expansion of CRPs to include primary PAD patients may have benefits for cardiac patients. Members of the CR team found that they were able to identify symptoms of PAD in patients that were referred in with CAD. They were then able to refer the patient to the vascular specialist podiatrists for IC assessment. The number of CAD patients requiring this referral was not recorded by the CR Team as part of their own audits, but one participant of this study who was enrolled on the CAD group was diagnosed with PAD via this process and was withdrawn from the study due to the newly diagnosed IC.

A study by Tam et al. (2016) screened 150 cardiac patients enrolling on a single CRP for presence of PAD. They found PAD to be present in 29 out of 150 patients. Tam et al. (2016) identified the presence of previously undiagnosed PAD in cardiac patients as a causal factor for some cardiac patients dropping out of standard CRPs as asymptomatic PAD has been found to reduce functional capacity. The authors recommend that cardiac patients should be screened for PAD as part of their rehabilitation, especially those would have dropped out of the programme due to difficulties during the exercise sessions. Screening of these patients might pose financial and logistical difficulties due to the availability of qualified

staff, equipment, and assessment time required. With the current financial demands on NHS services, and an increased need to deliver more service resources more efficiently, rather than creating new services, might make this screening process unworkable. As an alternative to this, CRP staff with experience of PAD signs and symptoms could identify cardiac patients with comorbid PAD and signpost to appropriate services for investigation, as demonstrated in this current study.

The long-term impact of this integrated CRP for IC patients has not been established, and clearly requires further investigation as a feasibility study cannot provide this. However, there is strong evidence supporting the effectiveness of CR in reducing the risk factors for CVD in patients attending their programmes (Dalal et al., 2015). There is a strong likelihood that CR can produce similar effects in the IC population as the two conditions of CAD and IC share the same risk factors for CVD. A core component of CR is lifestyle modification; therefore, CRPs might be able to reduce the risk for CVD and therefore reduce the prevalence of cardiac mortality and morbidity in the IC population. This would have an obvious impact to both the patient and the NHS, due to personal and financial costs, respectively. The NHS Long Term Plan aims to reduce the prevalence of CVD in the UK by 2029 (NHS, 2019). The BHF has stated that early detection and treatment of the risk factors for heart disease is a key preventative measure (BHF, 2019b) and will reduce the financial burden on the NHS, as well as the emotional burden to the individual and their families. Future research into the efficacy of integrated CRP for IC patients should include an assessment of the impact on individual CVD risk factor profiles. This current study included key risk factors such as BP, waist circumference, and smoking status, however, this should be expanded to include outcomes such as lipid profiling and blood glucose control in those with diabetes mellitus. The two risk factors of smoking and elevated blood glucose have been identified as they are most prevalent in patients with PAD and a key cause in developing the condition (Criqui et al., 1992; Gerhard-Herman et al., 2017; Shammas, 2007).

5.1.8 Limited-efficacy testing

This feasibility study had an embedded pilot to collect data to further support the future study design through a prior sample size testing. Although the statistical significance of this

pilot data is unreliable, due to the small sample size, there is evidence to suggest that the integrated rehabilitation could be efficacious. This potential efficacy will be demonstrated through comparison of the IC treatment group to the control group and through comparison to key studies into exercise therapy for PAD.

Following completion of the SEP, both IC patient groups had improvements in both PFWD and MWD. The level of improvement between the two groups was similar on both measures of claudication walking (see Table 5.3 for a summary, and Section 4.13.2.2 for full details). This pilot data shows that the novel treatment option performs as well as the current standard care in improving walking capacity.

Further comparison is now made between this study's pilot data and two key studies that have provided evidence for the efficacy of exercise therapy for IC patients. Many recent systematic reviews have been performed showing efficacy, however, their data is difficult to compare to this study as it is presented as weighted or standard mean differences between the exercise group and another group such as a non-exercising control or a group receiving another treatment (i.e., endovascular revascularisation), rather than a within-group pre and post-intervention change. For a direct comparison, an early meta-analysis of 21 exercise trials of IC patients undergoing exercise therapy by Gardner and Poehlman (1995), showed that PFWD and MWD increased by 179% and 122%, respectively (Table 5.3). Although the increases in MWD were only 64% in this feasibility study, the protocols used by studies in the meta-analysis by Gardner and Poehlman (1995) were 30 minute sessions, 3 x per week, for a duration of 6 months, rather than the 60 minute sessions, 1 x per week, for a duration of 12 weeks used in this study.

Table 5.3: Comparison of study data to key studies on exercise therapy for IC

	IC Control Group (current study)	IC Treatment Group (current study)	Gardner et al. (2001) 6-months, 3 x per week	Gardner et al. (1995) Systematic Review of exercise therapy for IC
Change in Walking Capacity				
PFWD % (m)	207%* (198)	108%* (190)	134%* (230)	179%* (225)
MWD % (m)	64% * (219)	60%* (284)	77%* (306)	122%* (397)
Change in WIQ				
Distance %	13*	27*	22%*	
Speed %	15*	19*	34%*	
Stairs %	10*	0	4%	
Change in Free-living activity (%)	2.2	16.2	38%*	

* Significantly different from the baseline value
PFWD – pain-free walking distance; MWD – maximal walking distance, WIQ – walking impairment questionnaire.

A study by Gardner et al. (2001) investigated the effects of supervised exercise rehabilitation on 31 patients with IC. The exercise followed the same frequency and duration that was used by Gardner and Poehlman (1995) (30 minute sessions, 3 x per week, for a duration of 6 months). The improvements in PFWD and MWD in this study (134% and 77%, respectively) are similar to those gained by the IC treatment patients in this study. There were similar improvements in WIQ between the IC treatment group and the Gardner et al. (2001) study, which is also promising. Although this is not a statistical assessment, the fact that a 1x per week programme lasting 12 weeks is successful in delivering outcomes comparable to a more intensive rehabilitation delivery shows potential efficacy.

5.1.9 Summary of Feasibility Evaluation

Using Bowen et al.'s systematic process for evaluating novel interventions, the integrated CRP for patients with IC has been shown to be feasible. The treatment is acceptable to clinicians involved in delivery, and also to those patients completing the programme. There is demand for this service, with consent rates being comparable to other integrated rehabilitation programmes. The new patient group can be integrated into the programme successfully, with minimal adaptations to the original programme, and with similar benefits achieved as more intensive disease-specific programmes.

The findings from this feasibility study are such that the decision to progress to a definitive efficacy trial can confidently be made. The remaining sections of this chapter will discuss the strengths and weaknesses of the study, and how the lessons learned during the research process will be used to guide the design of the future efficacy trial.

5.2 Strengths of the Study

This section explores the strengths of this feasibility study using the CONSORT guidance for reporting pilot trials (Sandra M. Eldridge et al., 2016).

5.2.1 Real-world Location

A key strength of this study is the two sites that were used as part of the recruitment and delivery of the rehabilitation programmes. Both research sites were NHS hospitals that delivered rehabilitation programmes so represented the 'real world' locations that would be required to offer an integrated service in future. Minimal adaptations were made to programme infrastructure, and the two centres continued to follow the NICE guidance for the delivery of IC rehabilitation (one-hour exercise session, once per week, for 12 weeks). The majority of previous studies into integrated rehabilitation have taken place in the USA and Canada utilising a more intensive programme of rehabilitation: one-hour session, 3 x per week, for a duration of 6 months (Marzolini et al., 2016; Prior et al., 2011; Regan et al., 2019; Toma et al., 2020). This study is therefore generalisable to the other CRPs with the NHS.

5.2.2 Generalisability of Study Participants

The participants in this study represented the wider population for their condition in terms of both gender and age. Participants also had similar numbers of comorbidities to patients attending rehabilitation programmes such as CR (BHF, 2019c).

5.2.3 Nature of the Control Group

A weakness of previous studies into rehabilitation for people with IC is that the comparison or 'standard care' is a non-exercise control group (Bendermacher et al., 2006; Cheetham et al., 2004; Gardner & Poehlman, 1995; Wind & Koelemay, 2007). Although the current provision of SEP for patients with IC in the UK is poor, with most patients not receiving this first-line treatment, comparing the success of an exercise-based intervention to a non-exercising population would not reflect current recommendations.

5.3 Weaknesses of the Study

The conduction of a pilot study gives the opportunity to address limitations of the study design that can be addressed prior to the definitive efficacy study. Addressing these limitations will play a key part in the development of the methodology for the future large-

scale study into the efficacy of integrating IC patients into a CRP. This is an integral part of any feasibility study (Sandra M. Eldridge et al., 2016). From these limitations and other experiences gained during the wider feasibility study, recommendations for the definitive study design will be made.

5.3.1 Differences Between Rehabilitation Programmes

The selection of the research sites was purposeful, as they had both had experience delivering their disease-specific programmes for over 15 years and were able to facilitate the research project. There were however key differences between the programmes that may influence the outcomes that need to be explored.

One distinction between the groups was the delivery of education on lifestyle modification and risk factor reduction. The CRP that provided the integrated programme provided education during the different assessments (telephone and face-to-face), as well as structured group education sessions. These group education sessions were delivered by the CRP staff and covered important topics on diet, physical activity and exercise, stress management, and cardiovascular disease. Patients enrolled on the IC-only control group received education from the rehabilitation specialists during their assessments, and during their exercise sessions, but this was more ad-hoc as no formal education sessions were offered. Although there were similar improvements between the IC control Group and IC treatment Groups, the additional educational input may have been a key element that supported the IC patients enrolled on the integrated rehabilitation programme.

The IC treatment programme also had other specialists involved in the delivery of the sessions such as dieticians, occupational therapists, and counsellors. Patients were also able to access these specialities outside of the 12-week CRP through individual or group weight management and dietary support sessions, and through individual or group stress management sessions, if required. Although the attendance of these other elements of CRP was not recorded, participants in the interview stage did report accessing these services.

5.3.2 Recruitment Bias

Due to the purposive sampling used in this study, participants were recruited from a population of patients that had agreed, at the point of diagnosis, to be referred to a supervised exercise programme (SEP). Participants might have been more likely, therefore, to adhere to the programme and might not represent the wider population of patients with IC and CAD. The study may have consisted only of patients who would have attended regardless of whether it was an integrated or a single disease rehabilitation. Patients who decided not to enrol on the study may have been influenced by the nature of the combined group. Future studies should endeavour to fully investigate the reasons for non-uptake and those who do not complete the programme through more in-depth methods such as individual interviews or focus groups.

5.3.3 Representation of Different Ethnicities in Study Participants

In this study, there was an exceptionally limited representation of participants from the Black, Asian, and minority ethnic (BAME) communities, with 98% of the study participants being White British or Irish. The figure of 2% BAME representation does not reflect the demographics of the wider UK population, with around 14% of the population coming from non-white or BAME as per the 2011 UK Census (ONS, 2011). This also does not reflect the demographics of the locations used in this study. For example, in 2009 the City of Salford had a 13.5% BAME representation, similar to the wider UK population. With evidence of the increased prevalence of PAD and IC in BAME populations compared to their White counterparts (Song, Rudan, Zhu, et al., 2019), there is a clear need to improve the involvement from BAME communities in future research.

5.3.4 Non—inclusion of Heart Failure Patients

The focus of this study was on the integration of IC patients with CAD patients. This focus was because of the shared pathophysiology of atherosclerosis and the shared risk factors for CVD between these two groups. However, this was at the exclusion of a sub-group of cardiac patients that can access CRP – those diagnosed with heart failure (HF). There are two key reasons why future studies into IC integrated CRP should include HF patients.

Firstly, the BHF aims to increase the number of patients diagnosed with HF accessing CRP. In 2021, only 15% of HF patients received a referral to CRP compared to 60% of patients following an MI with a stent, and 75% of patients following coronary artery bypass surgery (BHF, 2019a). The NHS aim to increase the offer of CR to all patients with HF in the UK (NHS, 2019), therefore, patients with HF will hopefully be more prevalent in CRPs, and the impact of the integration with this group needs to be assessed. Secondly, IC patients and HF patients have similar levels of exercise tolerance, with maximal levels being 50% less that age-matched controls (Harwood, Cayton, et al., 2016; Milani & Lavie, 2007). Therefore, patients with IC might find it easier to integrate with patients that have a similar exercise tolerance, rather than with cardiac patients who are less restricted by their condition.

5.3.5 Role of the Researcher – Influencing Responses of the Participants in the Qualitative Arm

An interesting area for consideration was the placement of the Principal Investigator (PI) within the study and the role within each rehabilitation team. Initially, it was decided that the rehabilitation staff would be responsible for the eligibility screening, and the PI would be responsible for gaining consent and conducting all pre and post-SEP assessments for participants. This was to limit any extra demands placed on the rehabilitation staff and adding to their usual workloads. Although this may have increased the consistency of pilot data collection, due to reduced inter-rater variability, this does not reflect what would happen in a truly integrated rehabilitation programme where all staff would be required complete each part of the patient's journey.

During the research process, the PI did not position himself within either of the rehabilitation teams, and he remained external. However, he did position themselves within the NHS, not solely as a doctoral student. This was due to the study being part of a Professional Doctorate studentship and the PI being employed by the NHS on an honorary contract. Participants were made aware of the PI's history of work within the NHS, specifically in the area of rehabilitation and how this has influenced the focus of the study. Initially, this was considered a strength of the study. It was decided that an independent researcher should facilitate the interviews and focus groups with patients and staff, as the PI

might have introduced some bias if they conducted them. Participants may be less likely to provide negative experiences or viewpoints and bias the results. Due to restrictions placed by COVID-19, a proportion of the interviews with IC patients in the treatment group had to be conducted over the phone as face-to-face appointments had been postponed. After discussion between the PI, University ethics representative, and CR Manager, it was decided that the PI should conduct the telephone interviews and not an independent researcher. Due to data protection restrictions, the contact details of patients could not be shared with an individual outside of the Trust. There was no scope to employ a member of the Trust's Research and Development Team (e.g., Clinical Research Nurse) to conduct the interviews as they had paused their involvement in any non-COVID related research. As the PI had an honorary contract, they were able to access the participant's contact details securely and therefore contacted participants to invite them to a telephone interview. This introduced bias to the interview process which had originally been accounted for, although this was deemed the best option due to the circumstances.

5.3.6 Non-randomised Groups

One of the benefits of conducting a feasibility or pilot study is to 'test out' the acceptability of trial processes for staff and patients to develop the methodology for future investigation such as a randomised controlled trial (RCT). Although this study did use a control group, there was no randomised allocation to groups which negatively impacts the internal validity of the study. Participants were already allocated to the control and treatment groups by geographical location. IC patients in the central Manchester area were referred to Manchester Foundation Trust (MFT) and Salford patients were referred by their Vascular Consultant to Salford Royal Foundation Trust (SRFT).

A further pilot is needed that has randomisation within each centre to access acceptability. This would, however, require a change in service delivery on both sites participating in this study if they were to be involved in a future RCT i.e., MFT would need to run an integrated CR class and SRFT to run an IC-only class. Although this was deemed outside of the scope of delivery for the current study, it would be an important consideration for future

investigations as the randomisation process might negatively impact participant uptake rates in future studies.

5.3.7 Feedback from the IC/PAD Staff

An opportunity was missed to investigate the opinions of the rehabilitation staff who supervised the control group (IC-only group). Their opinions on the suitability of integrating IC patients into CRP were not investigated. Although they did not have prior involvement in Cardiac Rehabilitation delivery, their wealth of experience in delivering treatment to IC patients may have offered an interesting and valuable insight into the particular demands or requirements of IC patients.

Chapter 6 Conclusions and Recommendations

The first part of this chapter shows how the aims of the thesis were achieved, and how a decision to progress to a definitive study of efficacy can be confidently made. The second part of the chapter covers the recommendations for a future study based on the experience gained from the feasibility and pilot study.

6.1 Conclusions

The primary aim of this thesis was to assess the feasibility of an integrated Cardiac Rehabilitation Programme (CRP) for patients with intermittent claudication (IC). During a 13-month period, 57 patients were recruited to the study. Seventeen patients with IC and twenty-one patients with coronary artery disease (CAD) were recruited to an integrated CRP consisting of 1 x 2-hour programme of exercise and education, for a duration of 12 weeks. Nineteen patients were recruited to an IC-only rehabilitation programme which acted as the control group. Using quantitative and qualitative evaluation, the feasibility of the novel intervention to both the IC and CAD patients was assessed. Feasibility of the treatment was demonstrated through high eligibility rates for the three patient groups (84.6%, 92.3%, and 81.6% for the IC control, IC treatment, and CAD group, respectively). The consent rates for the SEP across the three groups were 39.5%, 45.9%, and 25.9%, respectively. This was comparable to studies of both single-disease and integrated rehabilitation programmes. The retention rate for all three groups (78.9%, 64.7%, and 71.4%, respectively) was also high. No adverse events occurred during the study.

Acceptability of the treatment was assessed through focus groups and individual interviews of patients completing the integrated programme, with both IC and CAD patients finding the intervention appropriate. There were elements of the rehabilitation programme that were not suitable for all IC patients, mainly around the combined education sessions; however, IC patients did not feel different from the CAD patients. The CR clinicians also found the integrated service to be acceptable. Despite some adaptations to the CRP being required and the acceptance by CRP staff that IC patients were more complex than expected, they

were not deemed more complex than the standard cardiac patients referred to their programme. CRP staff found the incorporating IC patients to be a logical expansion of their service, and felt they were offering more than just an opportunity to reduce claudication symptoms but also preventing IC patients from becoming cardiac patients in the future.

Not only was the integrated treatment acceptable, but the IC treatment group also showed improvements in both walking capacity and quality of life following completion of the SEP. These improvements were similar to those achieved in the usual care group (IC control) and to larger studies into the impact of exercise therapy on IC. Although further studies are required to truly investigate efficacy, this does show limited efficacy for the novel treatment (Bowen et al. 2008). Importantly, the CAD patients in the study improved in both walking capacity and quality of life to the extent that was comparable to national averages for CRP.

The findings from this thesis have fulfilled the primary aim and have shown the integrated CRP to be both feasible and acceptable. The decision to progress to a definitive efficacy trial can confidently be made.

The secondary aims of the thesis were to investigate the feasibility and acceptability of the trial procedures to guide the definitive study into the efficacy of the integrated CRP. High return rates for all questionnaires were shown, with the lowest being for the Walking Impairment Questionnaire (WIQ), which had a 72.7% return rate from the IC treatment group. Only one participant, out of the 57 who started the study, was unable to perform the required graded exercise test (GXT); this was again in the IC treatment group. The acceptability of the accelerometers was high, and missing data was minimal, with only five monitors not recording the minimum of 4 days across the 57 baseline assessments and 41 follow-up assessments. A qualitative investigation of the trial procedures confirmed the acceptability found in the quantitative assessment, with all participants reporting a low burden.

The embedded pilot study has allowed for a version of the main efficacy study to be tested. This preparatory study has highlighted areas for development that should be implemented

to increase the efficiency of the future definitive study. These recommendations will be presented in the following section.

6.2 Recommendations for the Future Efficacy Study

6.2.1 Identifying Reasons for Not Enrolling onto Integrated Rehabilitation

A more in-depth investigation of why patients do not take up the offer of integrated rehabilitation is required. The offer of an integrated programme, rather than a disease-specific one, may itself be a barrier to attending. The future study should include focus groups and individual interviews for those patients who do not take up the integrated rehabilitation when offered.

6.2.2 Improving Representation

As shown in the participant characteristics, members of the BAME community were under-represented in this study. This needs to be improved in the future trial to improve the generalisability of the results. Comparison of the number of people from the BAME community of Salford and Manchester diagnosed with IC, referred to a SEP, and then engaged with the treatment should be made. Further investigation of reasons for declining the SEP could then be incorporated in the focus groups mentioned in the previous section.

6.2.3 Randomising the Trial

In this study, it was not possible to randomise participants to the control and intervention groups due to the control group being located at a different hospital to the intervention group. The randomisation process would reduce the risk of recruitment bias; however, the feasibility of randomisation (i.e., the acceptability of patients and staff to randomisation) will need to be investigated. It is recommended that an internal pilot be conducted with the initial participants recruited to the future efficacy trial. Using an internal pilot, if the randomisation process is deemed acceptable, data from these participants can be used in the final data analysis. That way the data from those initial participants could be included in the final analysis and reduce the overall burden of recruitment.

To ensure that the randomisation process introduces no additional barriers, the recommendation is for the control group to be offered on the same site as the intervention group i.e., by the same rehabilitation programme. Although this might require infrastructure changes (e.g., additional sessions being provided, or existing CR sessions being changed to an IC-only control session), it would not introduce the possible barrier of travel and payment for 'out of area' patients.

6.2.4 Education Delivery

Following feedback from the IC patients during the qualitative arm, there were differing opinions on whether the mixed groups were acceptable to IC patients. Some IC participants found the group sessions offered during the 12-week SEP had too much of a cardiac focus and were not relevant to their condition. However, the IC patients did find the other programmes offered to them beneficial: the Weight Management and Healthy Minds Programmes. A weakness of this study is that the attendance rates for the education sessions offered during the 12-week SEP and the number of patients accessing these two other programmes was not recorded. The future study should record the data.

The control group should also have formalised group education sessions that match the intervention group, which was not the case in this study. To ensure a more robust comparison, both the control and intervention programme structure should be as identical as possible. If both groups were facilitated using the same rehabilitation location, this would be more likely.

6.2.5 Enhanced Fidelity Measurement

During the study, fidelity to the treatment was assessed in two ways. The attendance rates of participants were recorded, and the claudication pain scale during the pre and post-SEP exercise tests were noted for IC patients. The attendance rates were high, with an average rate of 95.8%. Following the IC-specific exercise guidance provided by NICE (2012a), patients were encouraged to walk to maximal or near-maximal claudication pain, measured using an appropriate scale. The pre and post-SEP exercise tests showed that patients were able to push to these pain levels (Median pain 3 out of 4). However, to improve the measurement

of fidelity, records should be kept on the individual exercise session to investigate whether patients achieve this maximal to near-maximal pain level during each session. This will assess how closely the control and intervention groups keep to the exercise guidance as this might impact the outcomes for each group. For example, if one group exercise to maximal pain and the other to minimal pain, then the post-SEP outcomes might be affected by the different training stimuli (Parmenter et al., 2011). Measurement of the fidelity can be made through evaluation of the exercise training logs during the 12-week SEP, and activity diaries to measure the nature of exertion outside of the rehabilitation programme.

6.2.6 Full Economic Costing

Cost is an important consideration for rehabilitation programmes looking to expand their service to new clinical populations. For programmes looking at IC patients in particular, the estimated £273 provided by NICE's costing document (2012a) is not accurate. Not only is this costing nearly ten years old, but the breakdown of the costs does also not reflect the multidisciplinary nature of CRPs in the UK. NICE (2012a) state that most of the cost for providing exercise for ten patients in a class is covered by the employment of two physiotherapists and a rehabilitation technician. The CRP used in the intervention group is made up of physiotherapists, nurses, exercise physiologists, dieticians, occupational therapists, and a counsellor. This reflects the range of specialists that should be offered in a comprehensive CRP (BACPR, 2017) and would have significant cost implications that need to be considered. The future study should include a full economic evaluation to reflect the cost of integrating IC patients into a CRP comprised of a wider range of disciplines.

Moreover, it is recommended that an evaluation of the cost of providing the rehabilitation as per the format in the NICE guidance should be conducted to provide an up-to-date figure and remove the need to rely on the original estimate of £273 provided nearly a decade ago.

Another important consideration related to cost is the impact of the new intervention on quality-adjusted life years (QALYs). Evidence has shown that SEPs for IC patients cost between £711 to £1,608 per QALY gained (with 75-79% of models showing agreement) (NICE, 2012a). To fully assess the impact of the new intervention, the cost per QALY needs

to be established. This might take a period of follow-up to establish but must be considered an important element to embed into future study. To establish the impact on QALY gained, a change in the outcome measures might be required.

6.2.7 Change in Outcome Measures

Although the number of questionnaires used in this study was not deemed burdensome to patients, a requirement for change has been identified in the previous section on costings. To assess the impact of the integrated rehabilitation on QALYs, a generic quality of life measure is required, rather than a disease-specific one such as the VascuQoL (Dyer et al., 2010). One that has been used in over 150 studies of IC patients is the EuroQol EQ-5D (Dyer et al 2010). The EQ-5D is a short questionnaire consisting of five health-related questions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a visual analogue scale to assess overall health status. It is a validated tool that has been used in numerous studies to assess health-related quality of life in people with PAD (Dyer et al., 2010). Anecdotally, it is already used in the rehabilitation programme that provided the control group in this current study.

Although this is a short questionnaire, there is potential to increase the burden to the participants in completing the EQ-5D-5L in addition to the VascuQoL-25 and the HADS questionnaires. A pragmatic change to the future study's methodology would be to use the VascuQoL-6 questionnaire in place the VascuQoL-25 questionnaire. This reduced 6 question version of the original 25 question version is a validated tool that is becoming more widely used in PAD research (Larsen et al., 2017).

Another outcome that requires modification is the measure of free-living activity. In this study, the impact of completing an SEP on free-living activity was measured using mean daily step count and sedentary behaviour. There was no significant change in either measure across the three study groups. As this is a feasibility study, the significance of these results should be taken with caution (Sandra M. Eldridge et al., 2016), however, this preparatory study allows for consideration of this outcomes suitability in the IC population. A more appropriate approach may be to compare changes in walking bout length and

walking cadence. These areas have been investigated in other studies and have shown to be more sensitive to changes walking ability in the PAD population (Chaudru et al., 2019; Clarke et al., 2013; Schorr et al., 2018)

6.2.8 Rehabilitation Staff Involvement and External Research Staff

When the study protocol was being designed, a key concern was to keep the additional workload of rehabilitation staff required by the study to a minimum. Both services were running at high numbers of patient referrals and demands placed on them by their respective Trusts were great. To ensure minimal burden, the PI was involved in the pre and post-SEP data collection and consenting all participants. This created study limitations on two counts: willing patients unable to join the study and a rehabilitation process not reflecting actual practice.

Due to the PI conducting all quantitative data collection pre-SEP, there were limitations in the number of patients that could be offered an assessment within the 3-weeks from initial referral. When designing the study, it was not perceived that the amount of interest shown by patients to be involved in the study would be greater than the number of assessments the PI could offer. However, some patients displayed an interest in the study that were missed due to PI availability. A possible recommendation for the future study would be to employ someone who could dedicate their time to the data collection process, such as PhD students. As the study showed feasibility, the author, with support from their supervisory team, plans to progress to a larger scale investigation through submission of a grant application to a funding body such as the NIHR e.g., Research for Patient Benefit (RfPB). There would be scope within this grant application to include funding for a PhD student to work full-time on this project.

One concern about an individual or individuals, outside of the full-time rehabilitation staff conducting the pre-SEP again, is how this reflects the usual practice of the rehabilitation programmes. Once the research has been completed, and the researcher, or researchers, withdraw from the programmes, the rehabilitation team must then conduct all assessments for patients referred to their service – on the assumption that they continue to offer this

service once the research project has completed. A pragmatic consideration for the future efficacy trial would require rehabilitation staff to deliver all aspects of the programme with the external researcher having minimal involvement in the patient journey through the rehabilitation programme.

Further support for the reduced involvement for the PI is the impact on the study participants of the researcher being placed within the rehabilitation programme. In this feasibility study, the PI positioned themselves within the rehabilitation programmes as a doctoral student, and as someone who had experience working in Cardiac Rehabilitation. Upon reflection, this may have introduced bias into the research process. The PI's previous experience may have influenced participants in the rehabilitation setting and therefore have been less likely to provide any negative feedback about the research process. To mitigate this in the future study, research staff external to the rehabilitation setting should be used for all the qualitative interviews and focus groups.

References

AACVPR. (2013). *Guidelines for Cardiac Rehabilitation and Secondary Prevention Programs* (4th ed.). Human Kinetics

ACPICR. (2015). *Standards for Physical Activity and Exercise in the Cardiovascular Population*. Association of Chartered Physiotherapist in Cardiac Rehabilitation. https://www.acpicr.com/data/Page_Downloads/ACPICRStandards.pdf

Alsen, P., Brink, E., & Persson, L. O. (2008, Mar). Patients' illness perception four months after a myocardial infarction. *J Clin Nurs, 17*(5A), 25-33. https://doi.org/10.1111/j.1365-2702.2007.02136.x

Anderson, L., Thompson, D. R., Oldridge, N., Zwisler, A. D., Rees, K., Martin, N., & Taylor, R. S. (2016, Jan 5). Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev, 2016*(1), Cd001800. https://doi.org/10.1002/14651858.CD001800.pub3

Antoniou, G. A., Georgiadis, G. S., Antoniou, S. A., Makar, R. R., Smout, J. D., & Torella, F. (2017, Apr 3). Bypass surgery for chronic lower limb ischaemia. *Cochrane Database Syst Rev, 4*, CD002000. https://doi.org/10.1002/14651858.CD002000.pub3

BACPR. (2017). *BACPR Standards and Core Components for Cardiovascular Disease Prevention and Rehabilitation* (3rd ed.). British Association of Cardiovascular Prevention and Rehabilitation. www.bacpr.com/resources/6A7_BACR_Standards_and_Core_Components_2017.pdf

Banzer, J. A., Maguire, T. E., Kennedy, C. M., O'Malley, C. J., & Balady, G. J. (2004, Jan 1). Results of cardiac rehabilitation in patients with diabetes mellitus. *Am J Cardiol, 93*(1), 81-84. https://doi.org/10.1016/j.amjcard.2003.09.017

Bassett, D. R. (2012, Nov). Device-based monitoring in physical activity and public health research. *Physiol Meas, 33*(11), 1769-1783. https://doi.org/10.1088/0967-3334/33/11/1769

Bendermacher, B. L., Willigendael, E. M., Teijink, J. A., & Prins, M. H. (2006, Apr 19). Supervised exercise therapy versus non-supervised exercise therapy for intermittent

claudication. *Cochrane Database Syst Rev*(2), Cd005263. https://doi.org/10.1002/14651858.CD005263.pub2

Bermingham, S. L., Sparrow, K., Mullis, R., Fox, M., Shearman, C., Bradbury, A., & Michaels, J. (2013, Dec). The cost-effectiveness of supervised exercise for the treatment of intermittent claudication. *Eur J Vasc Endovasc Surg, 46*(6), 707-714. https://doi.org/10.1016/j.ejvs.2013.09.005

BHF. (2019a). *Cardiac Rehabilitation - The Big Picture*. https://www.bhf.org.uk/for-professionals/healthcare-professionals/data-and-statistics/cardiac-rehabilitation-the-big-picture

BHF. (2019b). *Early detection and diagnosis of heart & circulatory diseases*. British Heart Foundation. https://www.bhf.org.uk/what-we-do/policy-and-public-affairs/transforming-healthcare/early-detection-of-heartcirculatory-diseases

BHF. (2019c). *The National Audit of Cardiac Rehabilitation: quality and outcomes report 2019*. https://www.bhf.org.uk/informationsupport/publications/statistics/national-audit-of-cardiac-rehabilitation-quality-and-outcomes-report-2019

Billingham, S. A., Whitehead, A. L., & Julious, S. A. (2013, Aug 20). An audit of sample sizes for pilot and feasibility trials being undertaken in the United Kingdom registered in the United Kingdom Clinical Research Network database. *BMC Med Res Methodol, 13*, 104. https://doi.org/10.1186/1471-2288-13-104

Borg, G. (1998). *Borg's Perceived Exertion And Pain Scales*. Human Kinetics.

Brass, E. P., Jiao, J., & Hiatt, W. (2007, 2007/05/01). Optimal assessment of baseline treadmill walking performance in claudication clinical trials. *Vascular Medicine, 12*(2), 97-103. https://doi.org/10.1177/1358863X07078602

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology, 3*(2), 77-101. https://doi.org/10.1191/1478088706qp063oa

Buckley, J. P., Sim, J., Eston, R. G., Hession, R., & Fox, R. (2004). Reliability and validity of measures taken during the Chester step test to predict aerobic power and to prescribe aerobic exercise. *British Journal of Sports Medicine, 38*(2), 197. https://doi.org/10.1136/bjsm.2003.005389

Burns, P., Gough, S., & Bradbury, A. W. (2003, Mar 15). Management of peripheral arterial disease in primary care. *Bmj, 326*(7389), 584-588. https://doi.org/10.1136/bmj.326.7389.584

Camnitz, W. M., & Keeley, E. C. (2010, Jun). Heavily calcified coronary arteries: the bane of an interventionalist's existence. *J Interv Cardiol, 23*(3), 254-255. https://doi.org/10.1111/j.1540-8183.2010.00553.x

Care, D. o. H. a. S. (2016). *NHS Reference Costs* https://www.gov.uk/government/publications/nhs-reference-costs-2015-to-2016

Cea-Soriano, L., Fowkes, F. G. R., Johansson, S., Allum, A. M., & García Rodriguez, L. A. (2018, Jan 21). Time trends in peripheral artery disease incidence, prevalence and secondary preventive therapy: a cohort study in The Health Improvement Network in the UK. *BMJ Open, 8*(1), e018184. https://doi.org/10.1136/bmjopen-2017-018184

Chaudru, S., Jehannin, P., de Müllenheim, P. Y., Klein, H., Jaquinandi, V., Mahé, G., & Le Faucheur, A. (2019, Nov). Using wearable monitors to assess daily walking limitations induced by ischemic pain in peripheral artery disease. *Scand J Med Sci Sports, 29*(11), 1813-1826. https://doi.org/10.1111/sms.13511

Cheetham, D. R., Burgess, L., Ellis, M., Williams, A., Greenhalgh, R. M., & Davies, A. H. (2004, Jan). Does supervised exercise offer adjuvant benefit over exercise advice alone for the treatment of intermittent claudication? A randomised trial. *Eur J Vasc Endovasc Surg, 27*(1), 17-23. https://doi.org/10.1016/j.ejvs.2003.09.012

Clarke, C. L., Holdsworth, R. J., Ryan, C. G., & Granat, M. H. (2013, Feb). Free-living physical activity as a novel outcome measure in patients with intermittent claudication. *Eur J Vasc Endovasc Surg, 45*(2), 162-167. https://doi.org/10.1016/j.ejvs.2012.11.027

Conte, M. S., Bradbury, A. W., Kolh, P., White, J. V., Dick, F., Fitridge, R., Mills, J. L., Ricco, J. B., Suresh, K. R., & Murad, M. H. (2019, Jun). Global vascular guidelines on the management of chronic limb-threatening ischemia. *J Vasc Surg, 69*(6s), 3S-125S.e140. https://doi.org/10.1016/j.jvs.2019.02.016

Conte, M. S., Pomposelli, F. B., Clair, D. G., Geraghty, P. J., McKinsey, J. F., Mills, J. L., Moneta, G. L., Murad, M. H., Powell, R. J., Reed, A. B., Schanzer, A., & Sidawy, A. N. (2015, Mar). Society for Vascular Surgery practice guidelines for atherosclerotic

occlusive disease of the lower extremities: management of asymptomatic disease and claudication. *J Vasc Surg, 61*(3 Suppl), 2s-41s. https://doi.org/10.1016/j.jvs.2014.12.009

Covic, A., Kanbay, M., Voroneanu, L., Turgut, F., Serban, D. N., Serban, I. L., & Goldsmith, D. J. (2010, Apr 28). Vascular calcification in chronic kidney disease. *Clin Sci (Lond), 119*(3), 111-121. https://doi.org/10.1042/cs20090631

Cowie, A., Good, K., McKay, J., & Holt, J. (2021). Tackling multimorbidity: staff perceptions of the transition from single-condition rehabilitation to a specialist-generalist model. *International Journal of Therapy and Rehabilitation, 28*(8), 1-10. https://doi.org/10.12968/ijtr.2020.0062

Cowie, A., McKay, J., & Keenan, A. (2018, 2018/07/02). Combined generic-specialist multimorbidity rehabilitation post acute cardiac event. *British Journal of Cardiac Nursing, 13*(7), 340-347. https://doi.org/10.12968/bjca.2018.13.7.340

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: the new Medical Research Council guidance. *Bmj, 337*, a1655. https://doi.org/10.1136/bmj.a1655

Criqui, M. H., Langer, R. D., Fronek, A., Feigelson, H. S., Klauber, M. R., McCann, T. J., & Browner, D. (1992, Feb 6). Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med, 326*(6), 381-386. https://doi.org/10.1056/nejm199202063260605

Dalal, H. M., Doherty, P., & Taylor, R. S. (2015). Cardiac rehabilitation. *BMJ : British Medical Journal, 351*, h5000. https://doi.org/10.1136/bmj.h5000

Desveaux, L., Harrison, S., Lee, A., Mathur, S., Goldstein, R., & Brooks, D. (2017, Jul - Aug). "We are all there for the same purpose": Support for an integrated community exercise program for older adults with HF and COPD. *Heart Lung, 46*(4), 308-312. https://doi.org/10.1016/j.hrtlng.2017.04.008

Devrome, A. N., Aggarwal, S., McMurtry, M. S., Southern, D., Hauer, T., Lamb, B., Arena, R., Moore, R. D., Wilton, S. B., Stone, J., & Martin, B. J. (2019, Jun 15). Cardiac rehabilitation in people with peripheral arterial disease: A higher risk population that benefits from completion. *Int J Cardiol, 285*, 108-114. https://doi.org/10.1016/j.ijcard.2019.02.070

Dolan, L. B., Barry, D., Petrella, T., Davey, L., Minnes, A., Yantzi, A., Marzolini, S., & Oh, P. (2018, Jul). The Cardiac Rehabilitation Model Improves Fitness, Quality of Life, and Depression in Breast Cancer Survivors. *J Cardiopulm Rehabil Prev, 38*(4), 246-252. https://doi.org/10.1097/HCR.0000000000000256

Eaton, T., Young, P., Fergusson, W., Garrett, J. E., & Kolbe, J. (2005, 2005/04/01). The Dartmouth COOP Charts: A simple, reliable, valid and responsive quality of life tool for chronic obstructive pulmonary disease. *Quality of Life Research, 14*(3), 575-585. https://doi.org/10.1007/s11136-004-0624-2

Eldridge, S. M., Chan, C. L., Campbell, M. J., Bond, C. M., Hopewell, S., Thabane, L., & Lancaster, G. A. (2016). CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *Bmj, 355*, i5239. https://doi.org/10.1136/bmj.i5239

Eldridge, S. M., Lancaster, G. A., Campbell, M. J., Thabane, L., Hopewell, S., Coleman, C. L., & Bond, C. M. (2016). Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework. *PLOS ONE, 11*(3), e0150205. https://doi.org/10.1371/journal.pone.0150205

Evans, R. A., Singh, S. J., Collier, R., Loke, I., Steiner, M. C., & Morgan, M. D. (2010, Oct). Generic, symptom based, exercise rehabilitation; integrating patients with COPD and heart failure. *Respir Med, 104*(10), 1473-1481. https://doi.org/10.1016/j.rmed.2010.04.024

Fakhry, F., Fokkenrood, H. J. P., Spronk, S., Teijink, J. A. W., Rouwet, E. V., & Hunink, M. G. M. (2018). Endovascular revascularisation versus conservative management for intermittent claudication. *Cochrane Database of Systematic Reviews*(3). https://doi.org/10.1002/14651858.CD010512.pub2

Falk, E. (2006, Apr 18). Pathogenesis of atherosclerosis. *J Am Coll Cardiol, 47*(8 Suppl), C7-12. https://doi.org/10.1016/j.jacc.2005.09.068

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009, 2009/11/01). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods, 41*(4), 1149-1160. https://doi.org/10.3758/BRM.41.4.1149

Fowkes, G., & Gillespie, I. N. (2008). Angioplasty (versus non surgical management) for intermittent claudication. *Cochrane Database of Systematic Reviews*(4).

Frans, F. A., Bipat, S., Reekers, J. A., Legemate, D. A., & Koelemay, M. J. (2012, Jan). Systematic review of exercise training or percutaneous transluminal angioplasty for intermittent claudication. *Br J Surg, 99*(1), 16-28. https://doi.org/10.1002/bjs.7656

Gardner, A. W., & Afaq, A. (2008). Management of lower extremity peripheral arterial disease. *Journal of cardiopulmonary rehabilitation and prevention, 28*(6), 349. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2743684/pdf/nihms105289.pdf

Gardner, A. W., Katzel, L. I., Sorkin, J. D., Bradham, D. D., Hochberg, M. C., Flinn, W. R., & Goldberg, A. P. (2001, Jun). Exercise rehabilitation improves functional outcomes and peripheral circulation in patients with intermittent claudication: a randomized controlled trial. *J Am Geriatr Soc, 49*(6), 755-762. https://doi.org/10.1046/j.1532-5415.2001.49152.x

Gardner, A. W., Montgomery, P. S., & Parker, D. E. (2012, 2012/05/01/). Optimal exercise program length for patients with claudication. *Journal of vascular surgery, 55*(5), 1346-1354. https://doi.org/https://doi.org/10.1016/j.jvs.2011.11.123

Gardner, A. W., & Poehlman, E. T. (1995, Sep 27). Exercise rehabilitation programs for the treatment of claudication pain. A meta-analysis. *JAMA, 274*(12), 975-980. https://www.ncbi.nlm.nih.gov/pubmed/7674529

https://jamanetwork.com/journals/jama/article-abstract/389686

Gardner, A. W., Skinner, J. S., & Smith, L. K. (1991, Jul 1). Effects of handrail support on claudication and hemodynamic responses to single-stage and progressive treadmill protocols in peripheral vascular occlusive disease. *Am J Cardiol, 68*(1), 99-105. https://doi.org/10.1016/0002-9149(91)90719-2

Gelin, J., Jivegård, L., Taft, C., Karlsson, J., Sullivan, M., Dahllöf, A. G., Sandström, R., Arfvidsson, B., & Lundholm, K. (2001, Aug). Treatment efficacy of intermittent claudication by surgical intervention, supervised physical exercise training compared to no treatment in unselected randomised patients I: one year results of functional and physiological improvements. *Eur J Vasc Endovasc Surg, 22*(2), 107-113. https://doi.org/10.1053/ejvs.2001.1413

Gerhard-Herman, M. D., Gornik, H. L., Barrett, C., Barshes, N. R., Corriere, M. A., Drachman, D. E., Fleisher, L. A., Fowkes, F. G., Hamburg, N. M., Kinlay, S., Lookstein, R., Misra, S., Mureebe, L., Olin, J. W., Patel, R. A., Regensteiner, J. G., Schanzer, A., Shishehbor, M.

H., Stewart, K. J., Treat-Jacobson, D., & Walsh, M. E. (2017, Mar 21). 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation, 135*(12), e726-e779. https://doi.org/10.1161/CIR.0000000000000471

Greenhalgh, R. M., Belch, J. J., Brown, L. C., Gaines, P. A., Gao, L., Reise, J. A., & Thompson, S. G. (2008, Dec). The adjuvant benefit of angioplasty in patients with mild to moderate intermittent claudication (MIMIC) managed by supervised exercise, smoking cessation advice and best medical therapy: results from two randomised trials for stenotic femoropopliteal and aortoiliac arterial disease. *Eur J Vasc Endovasc Surg, 36*(6), 680-688. https://doi.org/10.1016/j.ejvs.2008.10.007

Hamburg, N. M., & Balady, G. J. (2011, Jan 4). Exercise rehabilitation in peripheral artery disease: functional impact and mechanisms of benefits. *Circulation, 123*(1), 87-97. https://doi.org/10.1161/CIRCULATIONAHA.109.881888

Hankey, G. J., Norman, P. E., & Eikelboom, J. W. (2006, Feb 1). Medical treatment of peripheral arterial disease. *JAMA, 295*(5), 547-553. https://doi.org/10.1001/jama.295.5.547

Harrison, A. S., Gaskins, N. J., Connell, L. A., & Doherty, P. (2020, Apr). Factors influencing the uptake of cardiac rehabilitation by cardiac patients with a comorbidity of stroke. *Int J Cardiol Heart Vasc, 27*, 100471. https://doi.org/10.1016/j.ijcha.2020.100471

Harwood, A. E., Caldow, E., & Cucato, G. (2022). Exercise testing in peripheral artery disease. In R. C. C. Davison, Smith, P., Hopker, J., Price, M.J., Hettinga, F., Tew, G., & Bottoms, L. (Ed.), *Sport and Exercise Physiology Testing Guidelines: Volume II - Exercise and Clinical Testing.* (pp. 267-276). Routledge.

Harwood, A. E., Cayton, T., Sarvanandan, R., Lane, R., & Chetter, I. (2016, Jan). A Review of the Potential Local Mechanisms by Which Exercise Improves Functional Outcomes in Intermittent Claudication. *Ann Vasc Surg, 30*, 312-320. https://doi.org/10.1016/j.avsg.2015.05.043

Harwood, A. E., Pymer, S., Ibeggazene, S., Ingle, L., Caldow, E., & Birkett, S. T. (2021, Aug 4). Provision of exercise services in patients with peripheral artery disease in the United Kingdom. *Vascular*, 17085381211035259. https://doi.org/10.1177/17085381211035259

Harwood, A. E., Pymer, S., Ingle, L., Doherty, P., Chetter, I. C., Parmenter, B., Askew, C. D., & Tew, G. A. (2020). Exercise training for intermittent claudication: a narrative review and summary of guidelines for practitioners. *BMJ Open Sport Exerc Med, 6*(1), e000897. https://doi.org/10.1136/bmjsem-2020-000897

Harwood, A. E., Smith, G. E., Broadbent, E., Cayton, T., Carradice, D., & Chetter, I. (2016). Access to supervised exercise services in the UK NHS for patients with peripheral vascular disease. *Annals of The Royal College of Surgeons of England*, 207-211. https://doi.org/DOI: 0.1308/rcsbull.2017.17

Harwood, A. E., Totty, J. P., Broadbent, E., Smith, G. E., & Chetter, I. C. (2017). Quality of life in patients with intermittent claudication. *Gefasschirurgie, 22*(3), 159-164. https://doi.org/10.1007/s00772-017-0269-4

Hiatt, W. R., Regensteiner, J. G., Hargarten, M. E., Wolfel, E. E., & Brass, E. P. (1990, Feb). Benefit of exercise conditioning for patients with peripheral arterial disease. *Circulation, 81*(2), 602-609. https://doi.org/10.1161/01.cir.81.2.602

Hiatt, W. R., Rogers, R. K., & Brass, E. P. (2014, Jul 1). The treadmill is a better functional test than the 6-minute walk test in therapeutic trials of patients with peripheral artery disease. *Circulation, 130*(1), 69-78. https://doi.org/10.1161/CIRCULATIONAHA.113.007003

Hiatt, W. R., Wolfel, E. E., Meier, R. H., & Regensteiner, J. G. (1994, Oct). Superiority of treadmill walking exercise versus strength training for patients with peripheral arterial disease. Implications for the mechanism of the training response. *Circulation, 90*(4), 1866-1874. https://doi.org/10.1161/01.cir.90.4.1866

Hubbard, G., Adams, R., Campbell, A., Kidd, L., Leslie, S. J., Munro, J., & Watson, A. (2016, Jan 4). Is referral of postsurgical colorectal cancer survivors to cardiac rehabilitation feasible and acceptable? A pragmatic pilot randomised controlled trial with embedded qualitative study. *BMJ Open, 6*(1), e009284. https://doi.org/10.1136/bmjopen-2015-009284

Hubbard, G., Campbell, A., Davies, Z., Munro, J., Ireland, A. V., Leslie, S., Watson, A. J., & Treweek, S. (2015). Experiences of recruiting to a pilot trial of Cardiac Rehabilitation In patients with Bowel cancer (CRIB) with an embedded process evaluation: lessons learned to improve recruitment. *Pilot Feasibility Stud, 1*, 15. https://doi.org/10.1186/s40814-015-0009-z

Hubbard, G., Munro, J., O'Carroll, R., Mutrie, N., Kidd, L., Haw, S., Adams, R., Watson, A. J. M., Leslie, S. J., Rauchhaus, P., Campbell, A., Mason, H., Manoukian, S., Sweetman, G., & Treweek, S. (2016). The use of cardiac rehabilitation services to aid the recovery of patients with bowel cancer: a pilot randomised controlled trial with embedded feasibility study. *Health Serv Deliv Res, 4*(24). https://doi.org/10.3310/hsdr04240

Hubbard, G., O'Carroll, R., Munro, J., Mutrie, N., Haw, S., Mason, H., & Treweek, S. (2016). The feasibility and acceptability of trial procedures for a pragmatic randomised controlled trial of a structured physical activity intervention for people diagnosed with colorectal cancer: findings from a pilot trial of cardiac rehabilitation versus usual care (no rehabilitation) with an embedded qualitative study. *Pilot Feasibility Stud, 2*, 51. https://doi.org/10.1186/s40814-016-0090-y

Ibeggazene, S., Moore, C., Tsakirides, C., Swainson, M., Ispoglou, T., & Birch, K. (2020). UK cardiac rehabilitation fit for purpose? A community-based observational cohort study. *BMJ Open, 10*(10), e037980. https://doi.org/10.1136/bmjopen-2020-037980

Ibeggazene, S., Pymer, S., Birkett, S. T., Caldow, E., & Harwood, A. E. (2022, Feb 7). A systematic review of exercise intervention reporting quality and dose in studies of intermittent claudication. *Vascular*, 17085381211070700. https://doi.org/10.1177/17085381211070700

JBS3. (2014). Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). *Heart, 100*(Suppl 2), ii1. https://doi.org/10.1136/heartjnl-2014-305693

Jeffares, I., Merriman, N. A., Doyle, F., Horgan, F., & Hickey, A. (2021, Feb 2). Inclusion of stroke patients in expanded cardiac rehabilitation services: a cross-national qualitative study with cardiac and stroke rehabilitation professionals. *Disabil Rehabil*, 1-13. https://doi.org/10.1080/09638288.2021.1874548

Jenkinson, C., Mayou, R., Day, A., Garratt, A., & Juszczak, E. (2002, Jun). Evaluation of the Dartmouth COOP charts in a large-scale community survey in the United Kingdom. *J Public Health Med, 24*(2), 106-111. https://doi.org/10.1093/pubmed/24.2.106

Jones, J., Buckley, J., Furze, G., & Sheppard, G. (2020). *Cardiovascular Prevention and Rehabilitation in Practice*. John Wiley & Sons.

Kieffer, E., Bahnini, A., Mouren, X., & Gamand, S. (2001, Mar). A new study demonstrates the efficacy of naftidrofuryl in the treatment of intermittent claudication. Findings of the Naftidrofuryl Clinical Ischemia Study (NCIS). *Int Angiol, 20*(1), 58-65.

Kirk, H., Kersten, P., Crawford, P., Keens, A., Ashburn, A., & Conway, J. (2014, Apr). The cardiac model of rehabilitation for reducing cardiovascular risk factors post transient ischaemic attack and stroke: a randomized controlled trial. *Clin Rehabil, 28*(4), 339-349. https://doi.org/10.1177/0269215513502211

Kowal, T. P., Chessex, C., Lee, D. S., & Grace, S. L. (2015, Mar-Apr). Integrated cardiovascular rehabilitation: how do noncardiac and polyvascular disease patients fare? *J Cardiopulm Rehabil Prev, 35*(2), 114-123. https://doi.org/10.1097/HCR.0000000000000088

Krishna, S. M., Moxon, J. V., & Golledge, J. (2015, May 18). A review of the pathophysiology and potential biomarkers for peripheral artery disease. *Int J Mol Sci, 16*(5), 11294-11322. https://doi.org/10.3390/ijms160511294

Lancaster, G. A., Dodd, S., & Williamson, P. R. (2004, May). Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract, 10*(2), 307-312. https://doi.org/10.1111/j..2002.384.doc.x

Larsen, A. S. F., Reiersen, A. T., Jacobsen, M. B., Kløw, N.-E., Nordanstig, J., Morgan, M., & Wesche, J. (2017, 2017/09/22). Validation of the Vascular quality of life questionnaire – 6 for clinical use in patients with lower limb peripheral arterial disease. *Health and Quality of Life Outcomes, 15*(1), 184. https://doi.org/10.1186/s12955-017-0760-3

Larsen, O. A., & Lassen, N. A. (1966, Nov 19). Effect of daily muscular exercise in patients with intermittent claudication. *Lancet, 2*(7473), 1093-1096. https://doi.org/10.1016/s0140-6736(66)92191-x

Layden, J., Michaels, J., Bermingham, S., Higgins, B., & Guideline Development, G. (2012, Aug 8). Diagnosis and management of lower limb peripheral arterial disease: summary of NICE guidance. *Bmj, 345*, e4947. https://doi.org/10.1136/bmj.e4947

Leon, A. C., Davis, L. L., & Kraemer, H. C. (2011, May). The role and interpretation of pilot studies in clinical research. *J Psychiatr Res, 45*(5), 626-629. https://doi.org/10.1016/j.jpsychires.2010.10.008

Liles, D. R., Kallen, M. A., Petersen, L. A., & Bush, R. L. (2006, Dec). Quality of life and peripheral arterial disease. *J Surg Res, 136*(2), 294-301. https://doi.org/10.1016/j.jss.2006.06.008

Liu, W., Zhang, Y., Yu, C. M., Ji, Q. W., Cai, M., Zhao, Y. X., & Zhou, Y. J. (2015, Nov). Current understanding of coronary artery calcification. *J Geriatr Cardiol, 12*(6), 668-675. https://doi.org/10.11909/j.issn.1671-5411.2015.06.012

Lundgren, F., Dahllöf, A. G., Lundholm, K., Scherstén, T., & Volkmann, R. (1989). Intermittent claudication--surgical reconstruction or physical training? A prospective randomized trial of treatment efficiency. *Annals of surgery, 209*(3), 346-355. https://doi.org/10.1097/00000658-198903000-00016

Mantzoukas, S. (2008, 2008/01/01). A review of evidence-based practice, nursing research and reflection: levelling the hierarchy [https://doi.org/10.1111/j.1365-2702.2006.01912.x]. *Journal of Clinical Nursing, 17*(2), 214-223. https://doi.org/https://doi.org/10.1111/j.1365-2702.2006.01912.x

Marzolini, S., Danells, C., Oh, P. I., Jagroop, D., & Brooks, D. (2016, Oct). Feasibility and Effects of Cardiac Rehabilitation for Individuals after Transient Ischemic Attack. *J Stroke Cerebrovasc Dis, 25*(10), 2453-2463. https://doi.org/10.1016/j.jstrokecerebrovasdis.2016.06.018

Marzolini, S., Tang, A., McIlroy, W., Oh, P. I., & Brooks, D. (2014, Jul). Outcomes in people after stroke attending an adapted cardiac rehabilitation exercise program: does time from stroke make a difference? *J Stroke Cerebrovasc Dis, 23*(6), 1648-1656. https://doi.org/10.1016/j.jstrokecerebrovasdis.2014.01.008

Mays, R. J., Casserly, I. P., & Regensteiner, J. G. (2013). Peripheral Artery Disease. In J. K. Ehrman, Gordon, P.M., Visich, P.S., & Keteyian, S.J. (Ed.), *Clinical Exercise Physiology* (pp. 277-295). Human Kinetics.

Mazari, F. A., Khan, J. A., Carradice, D., Samuel, N., Gohil, R., McCollum, P. T., & Chetter, I. C. (2013, Aug). Economic analysis of a randomized trial of percutaneous angioplasty, supervised exercise or combined treatment for intermittent claudication due to

femoropopliteal arterial disease. *Br J Surg, 100*(9), 1172-1179. https://doi.org/10.1002/bjs.9200

McDermott, M. M., Guralnik, J. M., Criqui, M. H., Liu, K., Kibbe, M. R., & Ferrucci, L. (2014). Six-minute walk is a better outcome measure than treadmill walking tests in therapeutic trials of patients with peripheral artery disease. *Circulation, 130*(1), 61-68. https://doi.org/10.1161/CIRCULATIONAHA.114.007002

McDermott, M. M., & Kibbe, M. R. (2017, Feb 21). Improving Lower Extremity Functioning in Peripheral Artery Disease: Exercise, Endovascular Revascularization, or Both? *JAMA, 317*(7), 689-690. https://doi.org/10.1001/jama.2016.20673

McDermott, M. M., Kibbe, M. R., Guralnik, J. M., Ferrucci, L., Criqui, M. H., Domanchuk, K., Tian, L., Zhao, L., Li, L., Patel, K., & et al. (2019). Durability of Benefits From Supervised Treadmill Exercise in People With Peripheral Artery Disease [Journal Article; Multicenter Study; Randomized Controlled Trial; Research Support, N.I.H., Extramural; Research Support, N.I.H., Intramural; Research Support, U.S. Gov't, Non-P.H.S.]. *Journal of the american heart association, 8*(1), e009380. https://doi.org/10.1161/JAHA.118.009380

McDermott., Guralnik, J. M., Criqui, M. H., Ferrucci, L., Zhao, L., Liu, K., Domanchuk, K., Spring, B., Tian, L., Kibbe, M., Liao, Y., Lloyd Jones, D., & Rejeski, W. J. (2014, May 21). Home-based walking exercise in peripheral artery disease: 12-month follow-up of the GOALS randomized trial. *J Am Heart Assoc, 3*(3), e000711. https://doi.org/10.1161/jaha.113.000711

Milani, R. V., & Lavie, C. J. (2007, Nov). The role of exercise training in peripheral arterial disease. *Vasc Med, 12*(4), 351-358. https://doi.org/10.1177/1358863X07083177

Montgomery, P. S., & Gardner, A. W. (1998, Jun). The clinical utility of a six-minute walk test in peripheral arterial occlusive disease patients. *J Am Geriatr Soc, 46*(6), 706-711. https://doi.org/10.1111/j.1532-5415.1998.tb03804.x

Morley, R. L., Sharma, A., Horsch, A. D., & Hinchliffe, R. J. . (2018). Peripheral artery disease. *British Medical Journal, 360*. https://doi.org/https://doi.org/10.1136/bmj.j5842

Mourot, L., Boussuges, A., Maunier, S., Chopra, S., Riviere, F., Debussche, X., & Blanc, P. (2010, May-Jun). Cardiovascular rehabilitation in patients with diabetes. *J*

Cardiopulm Rehabil Prev, 30(3), 157-164. https://doi.org/10.1097/HCR.0b013e3181c565fe

Müller-Bühl, U., Engeser, P., Leutgeb, R., & Szecsenyi, J. (2012, Jun). Low attendance of patients with intermittent claudication in a German community-based walking exercise program. *Int Angiol, 31*(3), 271-275.

Muller, M. D., Reed, A. B., Leuenberger, U. A., & Sinoway, L. I. (2013, Nov 1). Physiology in Medicine: Peripheral arterial disease. *Journal of Applied Physiology, 115*(9), 1219-1226. https://doi.org/10.1152/japplphysiol.00885.2013

Munro, J., Adams, R., Campbell, A., Campbell, S., Donaldson, C., Godwin, J., Haw, S., Kidd, L., Lane, C., Leslie, S. J., Mason, H., Mutrie, N., O'Carroll, R., Taylor, C., Treweek, S., Watson, A., & Hubbard, G. (2014, Feb 18). CRIB--the use of cardiac rehabilitation services to aid the recovery of patients with bowel cancer: a pilot randomised controlled trial (RCT) with embedded feasibility study. *BMJ Open, 4*(2), e004684. https://doi.org/10.1136/bmjopen-2013-004684

Murphy, T. P., Hirsch, A. T., Ricotta, J. J., Cutlip, D. E., Mohler, E., Regensteiner, J. G., Comerota, A. J., & Cohen, D. J. (2008, Jun). The Claudication: Exercise Vs. Endoluminal Revascularization (CLEVER) study: rationale and methods. *J Vasc Surg, 47*(6), 1356-1363. https://doi.org/10.1016/j.jvs.2007.12.048

NACR. (n.d.). *The National Database for Cardiac Rehabilitation - Questionnaire Masters*. http://www.cardiacrehabilitation.org.uk/nacr/dataset/Questionnaire%201.pdf

Nguyen, C. H., Marzolini, S., Oh, P., & Thomas, S. G. (2021, Feb). A Retrospective Comparison of Fitness and Exercise Progression in Patients With Coronary and Peripheral Artery Disease in Cardiac Rehabilitation. *Can J Cardiol, 37*(2), 260-268. https://doi.org/10.1016/j.cjca.2020.04.013

NHS. (2019). *The NHS Long Term Plan*. https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf

NICE. (2012a). *Lower limb peripheral arterial disease - Methods, evidence and recommendations*. https://www.nice.org.uk/guidance/cg147

NICE. (2012b). *Lower Limb Peripheral Artery Disease: diagnosis and management. NICE Clinical Guidance (147)*. https://www.nice.org.uk/guidance/cg147/chapter/recommendations

NICE. (2013). *National Institute for Health and Care Excellence: Peripheral Arterial Disease - Briefing paper* https://www.nice.org.uk/guidance/qs52/documents/peripheral-arterial-disease-briefing-paper2

Nicolaï, S. P., Kruidenier, L. M., Rouwet, E. V., Graffius, K., Prins, M. H., & Teijink, J. A. (2009, Jul). The walking impairment questionnaire: an effective tool to assess the effect of treatment in patients with intermittent claudication. *J Vasc Surg, 50*(1), 89-94. https://doi.org/10.1016/j.jvs.2008.12.073

Nicolaï, S. P., Viechtbauer, W., Kruidenier, L. M., Candel, M. J., Prins, M. H., & Teijink, J. A. (2009, Aug). Reliability of treadmill testing in peripheral arterial disease: a meta-regression analysis. *J Vasc Surg, 50*(2), 322-329. https://doi.org/10.1016/j.jvs.2009.01.042

Nordanstig, J., Broeren, M., Hensäter, M., Perlander, A., Österberg, K., & Jivegård, L. (2014, 2014/08/01/). Six-minute walk test closely correlates to "real-life" outdoor walking capacity and quality of life in patients with intermittent claudication. *Journal of vascular surgery, 60*(2), 404-409. https://doi.org/https://doi.org/10.1016/j.jvs.2014.03.003

Norgren, L., Hiatt, W. R., Dormandy, J. A., Nehler, M. R., Harris, K. A., & Fowkes, F. G. (2007, Jan). Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg, 45 Suppl S*, S5-67. https://doi.org/10.1016/j.jvs.2006.12.037

ONS. (2011). *2011 UK Census*. https://www.nomisweb.co.uk/sources/census_2011

Parmenter, B. J., Raymond, J., Dinnen, P., & Singh, M. A. (2011, Sep). A systematic review of randomized controlled trials: Walking versus alternative exercise prescription as treatment for intermittent claudication. *Atherosclerosis, 218*(1), 1-12. https://doi.org/10.1016/j.atherosclerosis.2011.04.024

Patterson, R. B., Pinto, B., Marcus, B., Colucci, A., Braun, T., & Roberts, M. (1997, Feb). Value of a supervised exercise program for the therapy of arterial claudication. *J Vasc Surg, 25*(2), 312-318; discussion 318-319. https://doi.org/10.1016/s0741-5214(97)70352-5

Peach, G., Griffin, M., Jones, K. G., Thompson, M. M., & Hinchliffe, R. J. (2012, Aug 14). Diagnosis and management of peripheral arterial disease. *Bmj, 345*, e5208. https://doi.org/10.1136/bmj.e5208

Popplewell, M. A., & Bradbury, A. W. (2014, Dec). Why do health systems not fund supervised exercise programmes for intermittent claudication? *Eur J Vasc Endovasc Surg, 48*(6), 608-610. https://doi.org/10.1016/j.ejvs.2014.07.008

Prior, P. L., Hachinski, V., Unsworth, K., Chan, R., Mytka, S., O'Callaghan, C., & Suskin, N. (2011, Nov). Comprehensive cardiac rehabilitation for secondary prevention after transient ischemic attack or mild stroke: I: feasibility and risk factors. *Stroke, 42*(11), 3207-3213. https://doi.org/10.1161/STROKEAHA.111.620187

Regan, E. W., Handlery, R., Beets, M. W., & Fritz, S. L. (2019, Aug 20). Are Aerobic Programs Similar in Design to Cardiac Rehabilitation Beneficial for Survivors of Stroke? A Systematic Review and Meta-Analysis. *J Am Heart Assoc, 8*(16), e012761. https://doi.org/10.1161/JAHA.119.012761

Reiner, Z., De Sutter, J., Ryden, L., Mirrakhimov, E., Pogosova, N., Dolzhenko, M., Fras, Z., Kotseva, K., Wood, D., & De Bacquer, D. (2021, Jan 1). Peripheral arterial disease and intermittent claudication in coronary heart disease patients. *Int J Cardiol, 322*, 227-232. https://doi.org/10.1016/j.ijcard.2020.09.004

Russell, K. L., Holloway, T. M., Brum, M., Caruso, V., Chessex, C., & Grace, S. L. (2011, Nov-Dec). Cardiac rehabilitation wait times: effect on enrollment. *J Cardiopulm Rehabil Prev, 31*(6), 373-377. https://doi.org/10.1097/HCR.0b013e318228a32f

Sagar, S. P., Brown, P. M., Zelt, D. T., Pickett, W. L., & Tranmer, J. E. (2012). Further clinical validation of the walking impairment questionnaire for classification of walking performance in patients with peripheral artery disease. *Int J Vasc Med, 2012*, 190641. https://doi.org/10.1155/2012/190641

Sami, F., Ranka, S., Lippmann, M., Weiford, B., Hance, K., Whitman, B., Wright, L., Donaldson, S., Boyer, B., & Gupta, K. (2021, Jun). Cardiac rehabilitation in patients with peripheral arterial disease after revascularization. *Vascular, 29*(3), 350-354. https://doi.org/10.1177/1708538120945530

Schorr, E., Whipple, M., & Treat-Jacobson, D. (2018). Effects of supervised exercise therapy on free-living physical activity among patients with symptomatic peripheral artery disease [Journal: Conference Abstract]. *Circulation, 138*. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01935858/full

Shalhoub, J., Hamish, M., & Davies, A. H. (2009, Sep). Supervised exercise for intermittent claudication - an under-utilised tool. *Ann R Coll Surg Engl, 91*(6), 473-476. https://doi.org/10.1308/003588409X432149

Shammas, N. W. (2007). Epidemiology, classification, and modifiable risk factors of peripheral arterial disease. *Vasc Health Risk Manag, 3*(2), 229-234. https://doi.org/10.2147/vhrm.2007.3.2.229

Singh, S. (2014, 2014/11/01). Physical activity and pulmonary rehabilitation – A competing agenda? *Chronic Respiratory Disease, 11*(4), 187-189. https://doi.org/10.1177/1479972314552999

Singh, S. J., Morgan, M. D., Scott, S., Walters, D., & Hardman, A. E. (1992, Dec). Development of a shuttle walking test of disability in patients with chronic airways obstruction. *Thorax, 47*(12), 1019-1024. https://doi.org/10.1136/thx.47.12.1019

Skinner, J. S., & Strandness, D. E., Jr. (1967, Jul). Exercise and intermittent claudication. I. Effect of repetition and intensity of exercise. *Circulation, 36*(1), 15-22. https://doi.org/10.1161/01.cir.36.1.15

Song, P., Rudan, D., Wang, M., Chang, X., & Rudan, I. (2019, Jun). National and subnational estimation of the prevalence of peripheral artery disease (PAD) in China: a systematic review and meta-analysis. *J Glob Health, 9*(1), 010601. https://doi.org/10.7189/jogh.09.010601

Song, P., Rudan, D., Zhu, Y., Fowkes, F. J. I., Rahimi, K., Fowkes, F. G. R., & Rudan, I. (2019, Aug). Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis. *Lancet Glob Health, 7*(8), e1020-e1030. https://doi.org/10.1016/S2214-109X(19)30255-4

Stone, J. E., Dukelow, S., & Stone, J. A. (2020, Jul). Stroke Rehabilitation and Cardiac Rehabilitation: Siblings or Strangers? *CJC Open, 2*(4), 189-191. https://doi.org/10.1016/j.cjco.2020.05.003

Tam, M. C., Longenecker, C. T., Chow, C., Vest, M., Sukeena, R., Madan Mohan, S. K., Carman, T., Parikh, S. A., & Josephson, R. A. (2016, Apr). Occult peripheral artery disease is common and limits the benefit achieved in cardiac rehabilitation. *Vasc Med, 21*(2), 130-136. https://doi.org/10.1177/1358863x15625370

Tang, A., Marzolini, S., Oh, P., McIlroy, W. E., & Brooks, D. (2010, Jun 9). Feasibility and effects of adapted cardiac rehabilitation after stroke: a prospective trial. *BMC Neurol, 10*, 40. https://doi.org/10.1186/1471-2377-10-40

Thabane, L., Ma, J., Chu, R., Cheng, J., Ismaila, A., Rios, L. P., Robson, R., Thabane, M., Giangregorio, L., & Goldsmith, C. H. (2010, 2010/01/06). A tutorial on pilot studies: the what, why and how. *BMC Medical Research Methodology, 10*(1), 1. https://doi.org/10.1186/1471-2288-10-1

Tisi, P., & Shearman, C. (1997). The impact of treatment of intermittent claudication on subjective health of the patient. *Health trends 1998/99, 30*, 109-114. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-00601733/full

Toma, J., Hammond, B., Chan, V., Peacocke, A., Salehi, B., Jhingan, P., Brooks, D., Hebert, A. A., & Marzolini, S. (2020, Jul). Inclusion of People Poststroke in Cardiac Rehabilitation Programs in Canada: A Missed Opportunity for Referral. *CJC Open, 2*(4), 195-206. https://doi.org/10.1016/j.cjco.2020.01.007

Verges, B., Patois-Verges, B., Cohen, M., Lucas, B., Galland-Jos, C., & Casillas, J. M. (2004, Aug). Effects of cardiac rehabilitation on exercise capacity in Type 2 diabetic patients with coronary artery disease. *Diabet Med, 21*(8), 889-895. https://doi.org/10.1111/j.1464-5491.2004.01262.x

Wasserman, K., Hansen, J. E., Sue, D. Y., Stringer, W. W., Sietsema, K. E., Sun, X., & J., W. B. (2011). *Principles of Exercise Testing and Interpretation: Including Pathophysiology and Clinical Applications* (5th ed.).

Lippincott Williams & Wilkins.

Watson, L., Ellis, B., & Leng, G. C. (2008). Exercise for intermittent claudication. *Cochrane Database of Systematic Reviews*(4). https://doi.org/10.1002/14651858.CD000990.pub2

West, R. R., Jones, D. A., & Henderson, A. H. (2012, Apr). Rehabilitation after myocardial infarction trial (RAMIT): multi-centre randomised controlled trial of comprehensive cardiac rehabilitation in patients following acute myocardial infarction. *Heart, 98*(8), 637-644. https://doi.org/10.1136/heartjnl-2011-300302

Whitehead, A. L., Sully, B. G., & Campbell, M. J. (2014, May). Pilot and feasibility studies: is there a difference from each other and from a randomised controlled trial? *Contemp Clin Trials, 38*(1), 130-133. https://doi.org/10.1016/j.cct.2014.04.001

Whorlton-Jones, E. R., Seed, S. A., Waddell, A., Caldow, E., Harwood, A. E., & Birkett, S. T. (2022). Does the level of encouragement affect 6-minute walk test performance in patients with intermittent claudication? A protocol for a randomised multicentre controlled trial. *J.Vasc.Soc.G.B.Irel.*(Online Ahead of Publication). http://doi.org/10.54522/jvsgbi.2022.028

Wind, J., & Koelemay, M. J. (2007, Jul). Exercise therapy and the additional effect of supervision on exercise therapy in patients with intermittent claudication. Systematic review of randomised controlled trials. *Eur J Vasc Endovasc Surg, 34*(1), 1-9. https://doi.org/10.1016/j.ejvs.2006.12.030

Appendices

Appendix 1 – Literature review – Search Strategy

1. Rehabilitation ab, All Fields, kwd, mh, ti.
2. physical therapy modalities ab, All Fields, kwd, mh, ti.
3. exercise ab, All Fields, kwd, mh, ti.
4. “exercise therapy” ab, All Fields, kwd, mh, ti.
5. therapy ab, All Fields, kwd, mh, ti.
6. “supervised exercise programme” ab, All Fields, kwd, mh, ti.
7. 1 OR 2 OR 3 OR 4 OR 5 OR 6
8. comorbid* ab, All Fields, kwd, mh, ti.
9. multimorbid* ab, All Fields, kwd, mh, ti.
10. combined ab, All Fields, kwd, mh, ti.
11. integrated ab, All Fields, kwd, majr, subheading, MeSH Terms, Text Word, ti.
12. incorporate* ab, All Fields, kwd, mh, ti.
13. 8 OR 9 OR 10 OR 11 OR 12
14. 7 AND 13
15. education ab, All Fields, kwd, mh, ti.
16. “education only” ab, All Fields, kwd, mh, ti.
17. Pharmacotherapy ab, All Fields, kwd, mh, ti.
18. musculoskeletal ab, All Fields, kwd, mh, ti.
19. 14 OR 15 OR 16 OR 17
20. 14 NOT 19

Legend:
ab – includes all words and numbers in the abstract of an article
All Fields – includes all searchable PubMed Central (PMC) fields
kwd – key terms in the body of an article except abstract and references
mh – includes all National Library of Medicine (NLM) Medical Subject Headings (MeSh) terms
ti – Title (words and numbers included in the title of the article

Appendix 2 - University of Salford Ethics Approval

Research, Enterprise and Engagement
Ethical Approval Panel

Research Centres Support Team
G0.3 Joule House
University of Salford
M5 4WT

T +44(0)161 295 2280

www.salford.ac.uk/

19 December 2017

Dear Edward,

RE: ETHICS APPLICATION HSR1617-184 – 'An investigation into the feasibility of incorporating an exercise rehabilitation programme for people with peripheral artery disease into an already established Cardiac Rehabilitation service.'

Based on the information that you have you provided, I am pleased to inform you that your application HSR1617-184 has been approved to go forward to NRES.

Once you have received it, please submit a copy of the NRES approval letter to Health-ResearchEthics@salford.ac.uk so that it can be placed on your application file.

If there are any changes to the project and/or its methodology, then please inform the Health Research Ethics Support team as soon as possible.

Yours sincerely,

Sue McAndrew

Chair of the Research Ethics Panel

Appendix 3 - NHS Ethical Approval letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Mr Edward Caldow
C718 Allerton Building
Frederick Road Campus University of Salford
M6 6PU

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

13th June 2018

Dear Mr Caldow

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**An investigation into the feasibility of incorporating an exercise rehabilitation programme for people with intermittent claudication into an already established Cardiac Rehabilitation service.**
IRAS project ID:	**230391**
Protocol number:	**HSR1617**
REC reference:	**18/NW/0375**
Sponsor	**University of Salford**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales? You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).
It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed **here**.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.
If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.
Please see **IRAS Help** for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non- NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?
The document "After Ethical Review – guidance for sponsors and investigators", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Mr Edward Caldow Tel: 0161 295 8118
Email: e.j.caldow@salford.ac.uk

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below. Your IRAS project ID is **230391**. Please quote this on all correspondence.

Yours sincerely,

Steph Blacklock Senior Assessor

Email: hra.approval@nhs.net

Copy to: *Mr Brian Boag, Sponsor Contact*
Katie Doyle, Salford Royal NHS Foundation Trust, Lead R&D Contact

Appendix 4 - Patient Information Sheet (PIS)

Participant Information Sheet

Study title

An investigation into the feasibility of incorporating an exercise rehabilitation programme for people with intermittent claudication into an already established Cardiac Rehabilitation service

You are being invited to take part in a research project to help investigate the use of supervised exercise programmes for the treatment of peripheral artery disease. Before you decide, it is important for you to understand why the research is being done and what it will involve. This document will explain the purpose of the study as well as any risks or benefits of you being involved. Please take the time to read the following information carefully. If you have any questions then feel free to contact the lead researcher **Eddie Caldow**, whose details are at the end of this document. Take time to decide whether or not you wish to take part in this study.

Background to the study

Supervised exercise programmes for people with peripheral artery disease have been shown to reduce the symptoms of pain and discomfort when walking (which is also known as intermittent claudication). Also, supervised exercise programmes have been shown to improve the quality of life for people with peripheral artery disease. Due to how strong the evidence is for this, the National Institute for Health and Care Excellence (NICE) has recommended exercise programmes should be offered as the first treatment for people diagnosed with peripheral artery disease, before any surgery is considered. Although an exercise programme is available for you, nationally there is a shortage of exercise programmes in the UK that vascular specialists can refer patients to. It has been suggested that Cardiac Rehabilitation departments within the UK could provide for this group of patients, as they already have facilities and staff in place. However, there has been no investigations to date on whether this would be successful. This research project would investigate if Cardiac Rehabilitation programmes could provide the same benefits as stand-alone rehabilitation programmes for people with peripheral artery disease. The study would investigate the possible impact on both peripheral artery disease patients and Cardiac Rehabilitation patient in attending a combined rehabilitation programme of exercise and education.

What will happen if I take part in this study?

The study will be looking at the effect of you attending the supervised exercise programme at your local hospital. If you agree to join in the study then there will only be a couple of extra things asked of you that do not normally take place during your programme. These are listed below:

What will I do?

a. Wear an activity monitor for one week at the start and end of your exercise programme (2 weeks in total). This is worn on the thigh and kept in place by a water-proof medical dressing
b. Continue with your normal daily routine for those 2 weeks.
c. Complete an activity diary for those 2 weeks
d. Complete one extra questionnaire than is normally required during your exercise programme (completed at the start and end of your programme)
e. Once you have completed the exercise programme you will be invited to a group interview where you be asked about your experience and views on the programme itself

Am I able to participate?

To participate:

- You must have been recently diagnosed with either peripheral artery disease or coronary artery disease
- You must NOT have an existing skin condition such as psoriasis or eczema that would be affected by the application of a medical dressing or a medical adhesive dressing
- You must be able to participate in the 12-week exercise programme based at your local hospital

Risks and potential benefits of the study

What risk are involved in participating in the study?

This study is being conducted around the 12-week exercise programme you will be attending so will therefore have no extra risk to you. Some participants may experience some mild skin irritation from the hydrogel stickie pad and/or medical grade dressing used to attach the activity monitor. The activPAL monitor has been used for many years in a number of studies involving thousands of users, hence the risks of using these are minimal.

What are the benefits involved in participating in the study?

Although there will be no direct benefit for you taking part in the study, the information we collect will be used to improve our knowledge of exercise rehabilitation and may improve services for future patients.

If I participate in this study, can I also participate in other studies?

As the supervised exercise programme lasts for 12 weeks some other studies may interfere with our study, particularly if it involves a change in medication that is specific for your condition (either adding new medication, or increasing the dosage or stopping current medication). If you are taking part in other research, or would like to do so, please contact the lead researcher (contact details at the end of this document).

What if something goes wrong?

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you have grounds for legal action but you may have to pay for it. If you have a concern about any aspect of this study, you should ask to speak to the lead researcher who will do their best to answer your questions

(contact details of researcher). However, if you remain unhappy and wish to complain formally you can do this by contacting Dr Susan McAndrew**,** Chair of the Health Research Ethics Panel, Room MS1.91, Mary Seacole Building, Frederick Road Campus, University of Salford, Salford, M6 6PU. Tel: 0161 295 2778. E: s.mcandrew@salford.ac.uk

You can also contact the Research and Development teams at either Central Manchester University Hospital or Salford Royal Hospital NHS Trust using the following information:

Central Manchester University Hospital: Elizabeth Mainwaring (Phone: 01612763340; Email: R&D.application@cmft.nhs.uk)

Salford Royal NHS Foundation Trust: Katie Doyle (Phone: 01612064734; Email: Katie.doyle@srft.nhs.uk)

Ending the study

What if I want to leave the study early?

There is no problem if you wish to leave the study early. You can withdraw from this study at any time and continue to participate in the rehabilitation programme if you wish. Your current treatment or any future treatment within the Vascular or Cardiovascular Service will not be affected in any way. If you wish to leave the study you only need inform one of the rehabilitation team members. Or alternatively you can contact the lead researcher Eddie Caldow (details at the end of this document). If you withdraw from the study after participating in the group interviews, data collected up to this point will remain as part of the study.

Financial information

Who is organising and funding the research?

The University of Salford is funding this research as part of a student's professional doctorate.

Will I be paid for participating?

Unfortunately, financial reward will not come from taking part in this research. However, you will be participating in a study with a novel idea that could have a positive impact on exercise rehabilitation for both people with peripheral artery disease and coronary artery disease.

Confidentiality of participant records

Will my taking part in this study be kept confidential?

Yes. We take great care to protect the confidentiality of the information we are given, and we take careful steps to ensure that all data is kept secure at all times. The information collected is used for research purposes only and is dealt with according to the General Data Protection Regulation and Data Protection Act 2018 for health and care research. With your permission, we would like to inform your GP about you taking part in this study, however you do not have to consent to this. If you take part in the focus group discussions we cannot guarantee that other participants will not share your comments outside the group.

How will my data be used?

The University of Salford is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Anonymised research data will be archived in the University of Salford data repository computer system. This data will be made available for future research studies, however, no information collected and recorded can be used to identify individuals in the dataset (such as names of date of births).

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting our Data Protection Officer Andrew Hartley on 01612956428, or via a.hartley2@salford.ac.uk.

Salford Royal NHS Foundation Trust and Central Manchester University Hospital will keep your name, NHS number and contact details confidential and will not pass this information to the University of Salford. Salford Royal NHS Foundation Trust and Central Manchester University Hospital will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from University of Salford and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The University of Salford will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Salford Royal NHS Foundation Trust and Central Manchester University Hospital will keep identifiable information about you from this study for 5 years after the study has finished.

What will happen to the results of the study?

A summary of the research findings will be sent to everyone who is participating in the research. Significant findings may be published in clinical journals.

Contact information

If you require more information about the study, you want to participate, or if you are already participating and want to withdraw, please contact the lead researcher or supervisor:

Lead Researcher
Eddie Caldow
Email: e.j.caldow@salford.ac.uk
Telephone: 016129558118
Address:
Room C718
Allerton Building
Frederick Road Campus
School of Health Sciences
University of Salford
Salford
M6 6PU

Supervisor:

Professor Malcolm Granat

Email: M.H.Granat@salford.ac.uk

Telephone: 01612952568

Address:

Room PQ28a

Record of information provided

You will receive a copy of the information sheet and a signed consent form to keep for your personal records.

Thank you very much for taking the time to read this document!

We appreciate your interest in this study.

Appendix 5 – Consent Form (Patients)

Informed Consent (Version 3 Date: 27th October 2017)

The University of Salford attaches high priority to the ethical conduct of research. We therefore ask you to consider the following points before signing this form. Your signature confirms you are happy to participate in the study.

I, the undersigned, confirm that (please initial each box as appropriate):

1.	I have read and understood the information about the project, as provided in the Patient Information Sheet dated 24th October 2017.	
2.	I have been given the opportunity to ask questions about the project and my participation.	
3.	I voluntarily agree to participate in the project.	
4.	I understand I can withdraw at any time without giving reasons and that I will not be penalised for withdrawing nor will I be questioned on why I have withdrawn. I also understand that if I withdraw after the group interview stage, the data I have given up to that point will remain part of the study.	
5.	The procedures regarding confidentiality have been clearly explained (e.g. use of names, pseudonyms, anonymisation of data, etc.) to me.	
6.	If applicable, separate terms of consent for interviews, audio, video or other forms of data collection have been explained and provided to me.	
7.	The use of the data in research, publications, sharing and archiving has been explained to me.	
8.	I agree to keep what is discussed in the group interviews confidential	
9.	I understand that other researchers will have access to this data only if they agree to preserve the confidentiality of the data and if they agree to the terms I have specified in this form.	
10.	Select only **one** of the following: • I would like my name used and understand what I have said or written as part of this study will be used in reports, publications and other research outputs so that anything I have contributed to this project can be recognised. • I do not want my name used in this project.	
11.	I, along with the Researcher, agree to sign and date this informed consent form.	

Participant:

_____ _____ _____

Name of Participant Signature Date

Researcher:

_____ _____ _____

Name of Researcher Signature Date

Appendix 6 – Consent From (Staff)

Participant ID Number:

Informed Consent

Study Title: An investigation into the feasibility of incorporating an exercise rehabilitation programme for people with intermittent claudication into an already established Cardiac Rehabilitation service

The University of Salford attaches high priority to the ethical conduct of research. We therefore ask you to consider the following points before signing this form. **Your signature confirms you are happy to participate in the study**.

I, the undersigned, confirm that (please initial each box as appropriate):

1.	I have read and understood the information about the project, as provided in the Participant Information Sheet dated 16th June 2021	
2.	I have been given the opportunity to ask questions about the project and my participation	
3.	I agree to the interviews being recorded for data collection and analysis purposes, and that the audio recordings will not be made available to the public. Only the research team (lead researcher and supervisory team) will have access to the recordings.	
4.	The procedures regarding confidentiality have been clearly explained (e.g. use of names, pseudonyms, anonymisation of data, etc.) to me	
5.	I agree to keep what is discussed in the group interviews confidential	
6.	I understand that other researchers will have access to this data only if they agree to preserve the confidentiality of the data and if they agree to the terms specified in this form	
7.	The use of the data in research, publications, sharing and archiving has been explained to me, and that only anonymised quotes will be included in publications	

Participant:

_____ _____ _____

Name of Participant Signature Date

Researcher:

_____ _____ _____

Name of Researcher Signature Date

Appendix 7 – GP Information Letter

Dr _____

GP Surgery Address

_____

_____

_____

XXXX
Lead Researcher
School of Health Sciences
Room XXXC
Allerton Building
University of Salford
Salford
M6 6PU
Email: XXXX
Telephone: XXXX

Date: INSERT DATE

Dear Dr **INSERT NAME**

Re: **INSERT PATIENT NAME**

Date of birth: **INSERT DOB**

Study Title: *An investigation into the feasibility of incorporating an exercise rehabilitation programme for people with intermittent claudication into an already established Cardiac Rehabilitation service*

The University of Salford is currently running a study to assess the feasibility of combining exercise rehabilitation for patients with peripheral artery disease (PAD) with patients diagnosed with coronary artery disease (CAD).

Your patient, **INSERT PATIENT NAME**, has agreed to take part in the study which will take place during their 12 week supervised exercise programme at **INSERT NAME OF HOPITAL.**

In addition to the receiving the usual treatment as part of the exercise programme, their physical activity levels will be recorded using an accelerometer, and they will complete an additional questionnaire which assesses their disease-specific quality of life (VascuQoL questionnaire). Upon completion of the exercise programme they will be invited to a focus group to get their thoughts and experiences of the programme.

If you would like any further information about this project, please contact me using the details above.

Yours sincerely

XXXX

Doctoral Student

University of Salford

Appendix 8 – Case Report From

Research ID:		Initial Assessment:	
Date:			
Resting BP:		Resting HR:	
Height:		Weight:	
Waist:		BMI:	
Treadmill:			
Initial Claudication Distance:		Maximal Claudication Distance:	
Peak HR:		Peak Pain:	
Questionnaires:			
VASCQOL:		HADS:	
Walking Impairment Questionnaire:			
Activity			
activPAL given:		activPAL received back:	
Home Exercise Sheet given:	**Y/N**		
Comments:			

Appendix 9 – Participant Daily Activity Record Sheet

Patient ID Number:

Daily Activity Log

Day and Date	Time woke up	Time got out of bed	Did you remove your monitor for >10 mins today?	If removed, record time of removal and reason why	Time got into bed	Time went to sleep	Other comments
Day 1 17/12/2013	*07:00am*	*07:15am*	*Yes* *No*	*Time off: 18:00pm Time on:18:45pm Reason: Swimming in the sea*	*21:45pm*	*22:10pm*	*Slight irritation on right leg so put monitor on left leg*
Day 1 Date:			Yes No				
Day 2 Date:			Yes No				
Day 3 Date:			Yes No				
Day 4 Date:			Yes No				
Day 5 Date:			Yes No				
Day 6 Date:			Yes No				
Day 7 Date:			Yes No				

Appendix 10 – Accelerometer & Diary Guidance for Participants

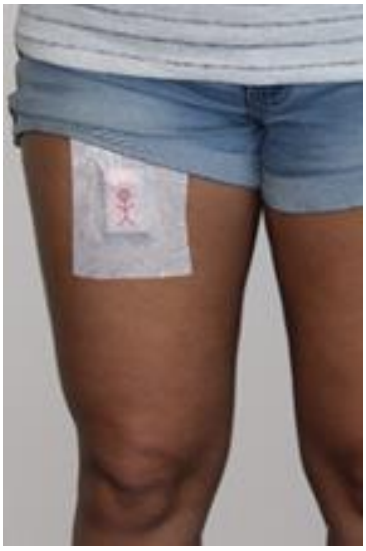
Integrated Rehabilitation Study

Patient ID Number: _____

activPAL serial # __ __ __ __ __ __ __

Return Appointment: _____ am/pm on _____/_____/_____

Activity Monitor & Daily Log Instructions



- The Activity Monitor is attached directly onto the skin and positioned on the front of the thigh, roughly 1/3 of the way between hip and knee with the stick man standing up (see picture right).
- Please wear the monitor every day for 7 days removing it on the morning of day 8.
- Please wear the Activity Monitor continuously (24 hours/day)
- The Activity Monitor can be worn during sleep and is water resistant (to 1m) so you can wear it whilst showering and bathing but please do not wear it in the swimming pool in case it falls off.
- The adhesive patch that sticks the Activity Monitor to your skin may last up to 7 days but to avoid skin irritation to may want to change the adhesive patch. Use the Micropore tape or adhesive dressings to secure device (provided in Activity Monitor Pack)

It may be easier to attach the Activity Monitor whilst sitting down (see picture below)

For a useful video to show how to put the Activity Monitor on please follow this link:

https://www.youtube.com/watch?v=CHCCX2GW3DM

How do I change the adhesive patch?

- Remove the Activity Monitor from your thigh (note that this may cause some slight discomfort) and peel the adhesive patch off the Activity Monitor. The monitor is covered in a waterproof sleeve and wrapped in one adhesive patch—please make sure that these remain on the monitor when you do this.
- With an alcohol prep pad provided in your Activity Monitor Pack, thoroughly wipe down the monitor and the area of your leg where the Activity Monitor was attached.
- Position the Activity Monitor in the same spot as previously on your thigh (or on the other thigh if you have had a slight irritation), ensuring that the stick man on the front of the Activity Monitor is standing up (head facing upwards).
- Peel the backing off an adhesive patch and place it over the Activity Monitor. Press the patch onto your skin, peel back the top layer of the patch and smooth out the air bubbles and wrinkles as much as possible to ensure that the Activity Monitor is firmly secured to your thigh. Use the Micropore tape or adhesive dressings to secure device (provided in Activity Monitor Pack)
- If you require assistance re-attaching your Activity Monitor, or if you experience any skin irritation whilst wearing it, please call the lead researcher Eddie Caldow on 01612958118.

What else do I need to do?

- It is important that you fill in the **Daily Log** on the following pages every day for the 7 days while you are wearing the monitor.
- This helps us to look specifically at the data from when you were awake.

How do I fill in the daily activity log?

- The log is divided into 7 days. Please complete each question for all of the 7 days. Please try and be as accurate as possible—record the exact times if you can, or at least to the nearest 5 minutes of your estimated times.
- Start by writing the date in the top row.
- Then record the time that you woke up and the time that you actually got out of bed (these times may be the same for some days). We ask for these two times because people sometimes spend time in bed before going to sleep or getting up and we are interested in distinguishing between actual sleeping time and time in bed before sleep or once awake, for example going to bed and watching TV for an hour before going to sleep.
- If you remove the device for longer than 10minutes during the day please note

down the time that you removed the device, the time that you re-attached it and the reason why you removed the device. This is particularly important as we cannot tell from the data if you are you are lying down or whether you have removed the device and are just not wearing it (the data looks the same when we look at it).

- Then record what time you got into bed to go to sleep and the time that you actually went to sleep time. (i.e., the estimated time that you fell to sleep not the time that you got into bed). This is important as the monitor cannot tell the difference between asleep and awake times, and we are only interested in your activity while you are awake
- Please record your sleep time first thing in the morning when you wake up along with your wake time.
- There is also a space for you to make comments. It is useful for us to know if you have had any skin irritations, accidentally worn the monitor upside down or any other information that you think we should know.

How can I be sure the monitor is working?

The Activity Monitor will emit a green flash every 6 seconds. This is an indication that it is working and recording data.

Returning your Activity Monitor and Daily Log

After you have worn your Activity Monitor for 7 days, please just bring it back with you on your next visit to the hospital for your exercise programme

If you are having difficulty attending the exercise programme and cannot return the monitor please contact **Eddie Caldow** on **01612958118** or via email at **e.j.caldow@salford.ac.uk**.