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DEVELOPMENT & EVALUATION OF AN MHEALTH PLATFORM
FOR REMOTELY DELIVERED EXERCISE-BASED CARDIAC
REHABILITATION

Jonathan Charles Rawstorn

ABSTRACT

**Background:** Exercise-based cardiac rehabilitation (exCR) has multifactorial secondary prevention benefits for people with coronary heart disease (CHD). However, utilisation of traditionally supervised, centre-based programmes is limited by numerous barriers, including several factors that limit programme accessibility. Information and telecommunication technologies (i.e. telehealth), and mobile technologies in particular, could overcome access-related participation barriers and have demonstrated promising early health benefits, but exercise-specific interventions are limited.

**Aim:** To develop and evaluate a mobile health (mHealth) exCR delivery model that combines clinical exercise specialists’ expertise with enhanced access.

**Methods:** Four phases of research were undertaken: A systematic review and meta-analysis assessed current evidence in telehealth exCR, and identified opportunities to enhance programme delivery. A novel mHealth platform was designed to connect exCR participants with clinical exercise specialists from any location. Platform features enable evidence- and theory-based real-time remote exercise monitoring and coaching, behaviour change, and social support. A laboratory experiment evaluated platform feasibility and validity. A non-inferiority randomised controlled pilot trial (RCT) was designed and conducted to compare the effectiveness of remote and centre-based exCR programmes.

**Results:** Existing telehealth exCR health benefits are similar to centre-based exCR; however, innovation is lacking and recent technological advances could enable more responsive, flexible, individualised and interactive interventions. A custom mHealth platform and complementary intervention content were developed to provide real-time remote exercise monitoring and coaching, theory-based behaviour change education, and social support. The platform demonstrated acceptable validity, and pilot RCT results show real-time remotely monitored exCR increased maximal aerobic exercise capacity, physical activity energy expenditure, and exercise self-confidence. Benefits were comparable to centre-based exCR, and intervention acceptability was highly rated.

**Conclusion:** An mHealth platform can bring near universal accessibility to clinically supervised, evidence- and theory-based exCR, and health benefits compare favourably with gold standard centre-based programmes. Remotely monitored exCR could complement existing services by overcoming common access barriers, and may meet the needs of individuals who do not current access exCR.
ACKNOWLEDGEMENTS

With great pleasure I would like to thank a number of people, without whom this thesis would not have become what it had.

Firstly, my sincere thanks to my supervisory team Professor Ralph Maddison and Dr Nick Gant. Your wisdom, guidance, encouragement and patience have been invaluable throughout this research, and undoubtedly enabled me to achieve this goal.

I would also like to thank Dr Ian Warren and Dr Andrew Meads, without your technical expertise my ideas would not have been brought to life. I am proud of what we have achieved, and incredibly grateful to have had the opportunity to work with both of you.

Thank to my co-authors, who are too numerous to name here. Your advice was appreciated every step of the way, and it was a pleasure working with you.

I must give a special thank you to Dr Luke Gemming. From my first day you were there to discuss ideas, ponder issues, overcome challenges, and most importantly, to have a laugh. Now we are both finished it must be time to settle the tab! My heartfelt thanks also to the NIHI PhD crew, Vaughan Roberts, Samantha Marsh, Leila Pfaeffli, Artur Direito and Rosie Dobson; you were an integral part of this process and the encouragement, support and advice you provided along the way to helped enormously.

To my family and friends, and in particular to my parents Robyn and Neville, and brother Brad. This has been a longer time coming than initially planned and your constant support helped to keep me happy, healthy and on track throughout. A special thanks also to my wife, Melissa. It took longer to fulfil my vow than I had anticipated, but you were there with me every step of the way and I am pleased to finally keep my word. Your contribution to the latter stages of this research has been invaluable, and your love, reassurance, and wisdom not only helped me to reach this point but made sure I had a great time doing it.

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Professor Ralph Maddison and Doctor Nicholas Gant supervised this thesis, and provided guidance throughout. Dr Ian Warren was an advisor, and provided subject-specific support.

Chapter 1-2: The candidate wrote these chapters with supervisory support.

Chapter 3: The candidate primarily contributed to the design, selection of studies, data extraction, analysis, and interpretation of the systematic review and meta-analysis, and wrote the manuscript. Co-authors provided assistance with independent selection of studies, data extraction, interpretation of the results, and contributed to editing of the manuscript.

Chapter 4: The candidate was responsible for conceiving and designing the software components of a custom mobile health platform, created all graphical works, contributed to platform user testing, and wrote the manuscript. Co-authors provided technical development expertise, and contributed to editing of the manuscript.

Chapter 5: The candidate was responsible for the design, ethical approval, implementation, analysis, and interpretation of the validation and feasibility study, and wrote the manuscript. Co-authors assisted with interpretation of results and editing of the manuscript.

Chapter 6: The candidate contributed substantially to drafting the full study protocol and manual of procedures. Co-authors provided editorial support, and contributed to abbreviation of the full study protocol in preparation for publication.

Chapter 7: The candidate was responsible for ethical approval, study management, delivery of the mobile health intervention, and baseline assessment of the primary outcome for a pilot trial nested within the study described in Chapter 6. The candidate also analysed and interpreted the pilot trial results, and wrote a draft manuscript that will be updated and submitted for publication when final results from the main trial are available. The candidate substantially contributed to the successful funding grant application that supported this trial.

Chapter 8: The candidate wrote this chapter with supervisory support.
PUBLICATIONS, PRESENTATIONS, REPORTS, & AWARDS

PUBLICATIONS


1 Where the candidate is listed as the primary author his contribution comprised full responsibility for writing, submission, and revision of the manuscript. Where the candidate is listed as a co-author he prepared the full study protocol, and co-authors assisted with reformatting (i.e. abbreviating) for publication.
CONFERENCE PRESENTATIONS


OTHER PRESENTATIONS


REPORTS

AWARDS DURING CANDIDATURE

2015

University of Auckland Annual School of Population Health Showcase
- Runner-up, best post graduate presentation
- People’s choice poster award
Breaking cardiac rehabilitation barriers: development and on-going evaluation of remotely delivered exercise-based cardiac rehabilitation

University of Auckland Annual Exposure Conference
- Top 20 student poster
Breaking cardiac rehabilitation barriers: development and on-going evaluation of remotely delivered exercise-based cardiac rehabilitation

HealthEx Annual Conference
- Runner-up, best doctoral poster
Breaking cardiac rehabilitation barriers: development and on-going evaluation of remotely delivered exercise-based cardiac rehabilitation

2014

Australasian Epidemiology Association Annual Conference
- Student conference award
Development and evaluation of a mHealth cardiac rehabilitation system

2013

University of Auckland SPARK $100k Entrepreneurial Challenge
- Runner up entrepreneurial venture
Avatar Anonymous - Global leader in virtual reality healthcare solutions
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GLOSSARY

GENERAL
AF Atrial fibrillation
App Software application (commonly smartphone or web-based)
BMI Body mass index
CABG Coronary artery bypass graft
Centre-based exCR delivered in clinical settings (hospitals, rehabilitation centres)
CHD Coronary heart disease
Comprehensive CR CR that includes several/all recommended core components
CR Cardiac rehabilitation
CVD Cardiovascular disease
DBP Diastolic blood pressure
ECG Electrocardiogram
EQ-5D EuroQol 5 dimensional HRQoL instrument
exCR Exercise-based CR
GPS Global positioning system
HbA1C Glycated haemoglobin
HDL-C High density lipoprotein cholesterol
Home-based exCR exCR delivered in the home setting
HRQoL Health-related quality of life
HRR Heart rate reserve (maximal – resting heart rate)
ICT Information and communication technologies
LDL-C Low density lipoprotein cholesterol
MB Megabyte
MeSH Medical Subject Heading
mHealth Health delivery via mobile ICT
MI Myocardial infarction
NZD New Zealand dollar
PCI Percutaneous coronary intervention
QUALY Quality adjusted life years
RCT Randomised controlled trial
REMOTE-CR Remote Exercise Monitoring Trial for Exercise-based CR
RPE Rating of perceived exertion
SBP Systolic blood pressure
SF-36 Medical outcomes study 36-item short form health survey
SMS Mobile phone short message service
Telehealth Health delivery via ICT
Total-C Total cholesterol
USD United States dollar
VO₂max Oxygen consumption (maximal)
VO₂peak Oxygen consumption (peak)
Wi-Fi Wireless local area network

MEASUREMENT
b·min⁻¹ Beats per minute (heart rate)
br·min⁻¹ Breaths per minute (respiratory rate)
Cm Centimetres
cm² Centimetres squared
Hz Hertz
kg Kilogram
kg·m⁻² Unit for BMI, kilograms per metre squared
L·min\(^{-1}\)  Litres per minute
lb  Pounds
m  Metre
MET  Metabolic equivalents (1 MET ≈ 3.5 ml·kg\(^{-1}\)·min\(^{-1}\))
mg·kgFFM\(^{-1}\)·min\(^{-1}\)  Milligrams per kilogram of fat free body mass per minute
mg·dl\(^{-1}\)  Milligrams per decilitre
min  Minutes
ml·kg\(^{-1}\)·min\(^{-1}\)  Millilitres per kilogram of body mass per minute
mm Hg  Millimetres of mercury
mmol·L\(^{-1}\)  Millimoles per litre
n  Number (usually refers to participants)
s  Seconds
W  Watts
y  Years
μIU·mL\(^{-1}\)  Micro international units per millilitre

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Chapter 3. Telehealth exercise-based cardiac rehabilitation: A systematic review & meta-analysis.

| Nature of contribution by PhD candidate | Developed research methods, undertook literature search and independently verified screening/data extraction. Completed analyses, and wrote the manuscript. |
| Extent of contribution by PhD candidate (%) | 90 |

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<td>Artur Direito</td>
<td>Assisted with article screen and selection</td>
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<tr>
<td>Christina Beckman</td>
<td>Assisted with article screening, selection and data extraction</td>
</tr>
<tr>
<td>Ralph Maddison</td>
<td>Assisted with development of the study design, provided editorial support, and assisted with interpretation of the findings</td>
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**Certification by Co-Authors**

The undersigned hereby certify that:

- the above statement correctly reflects the nature and extent of the PhD candidate’s contribution to this work, and the nature of the contribution of each of the co-authors; and

- in cases where the PhD candidate was the lead author of the work that the candidate wrote the text.

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Chapter 4. Design and development of an mHealth model for remotely delivered exercise-based cardiac rehabilitation: the REMOTE-CR platform.

Nature of contribution by PhD candidate
Designed the smartphone and web-based application feature sets, created a design specification to inform technical development, oversaw technical development, conducted usability testing, and wrote the manuscript.

Extent of contribution by PhD candidate (%)
85

CO-AUTHORS

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Name | Signature | Date
---|----------|----
Nicholas Gant |  | 22/12/2015
Andrew Meads |  | 23/12/2015
Ian Warren |  | 6/01/2016
Ralph Addison |  | 22/12/2015

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Chapter 5. Measurement and data transmission validity of a multi-biosensor system for real-time remote exercise monitoring among cardiac patients

| Nature of contribution by PhD candidate | Developed research methods, wrote the ethics application, completed all study procedures for data collection and analysis, and wrote the manuscript. |
| Extent of contribution by PhD candidate (%) | 90 |

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Chapter 6. The Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation: A randomised controlled trial protocol

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**CO-AUTHORS**

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<tr>
<td>Jocelyne Benatar</td>
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**Certification by Co-Authors**

The undersigned hereby certify that:

- the above statement correctly reflects the nature and extent of the PhD candidate's contribution to this work, and the nature of the contribution of each of the co-authors; and
- in cases where the PhD candidate was the lead author of the work that the candidate wrote the text.

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Last updated: 25 March 2013
The problem is not so much to see what nobody has yet seen,  
As to think what nobody has yet thought,  
Concerning that which everybody sees

Arthur Schopenhauer

Innovation is hard because “solving problems people didn’t know they had”
& “building something no one needs” look identical at first.

Aaron Levie
CHAPTER 1. THESIS INTRODUCTION

Among people with diagnosed coronary heart disease exercise training can improve several physiological and psychological cardiovascular risk factors, and clinical events. However, access barriers limit participation in exercise programmes delivered via clinical settings such as hospitals and rehabilitation centres. Alternatives delivery models have been developed, but the opportunity cost of accessibility has been supervision and support from clinical exercise specialists, and there remains a substantial need for innovative new alternatives that can bridge this gap.

The overall goal of this thesis is, therefore, to determine what is already known in this area, identify gaps in the existing knowledge base, conduct research to address these identified gaps, and synthesise past and emerging findings in order to inform innovative solutions to cardiac rehabilitation accessibility, and guide new directions for future research.

1.1. THESIS AIMS

This thesis has three primary aims:

1. Increase understanding of the effectiveness of alternative, technology-assisted exercise-based cardiac rehabilitation.

2. Develop a novel exercise-based cardiac rehabilitation delivery model that can combine the expertise of clinical exercise specialists with enhanced flexibility and accessibility.

3. Determine the effectiveness of the novel delivery model for augmenting sub-optimal utilisation of exercise-based cardiac rehabilitation.
1.2. THESIS OBJECTIVES

The objectives of this thesis are

1. Assess what is already known about traditional and emerging technology-assisted exercise-based cardiac rehabilitation interventions, and identify gaps in the literature (Chapters 2 and 3)

2. Design and develop an alternative model for delivering exercise-based cardiac rehabilitation that addresses emerging opportunities (Chapter 4)

3. Assess the validity and feasibility of an alternative exercise-based rehabilitation delivery model (Chapter 5)

4. To rigorously evaluate the effectiveness and acceptability of an alternative exercise-based rehabilitation delivery model by comparing it with existing gold standard, supervised exercise-based cardiac rehabilitation (Chapters 6 and 7)

5. To synthesise findings from the extant literature with the research presented in Chapters 3 to 7, in order to: identify implications for clinical practice, identify opportunities for further development, and identify new directions for technology-assisted exercise-based cardiac rehabilitation research that could enhance intervention delivery and utilisation (Chapter 8)

1.3. THESIS STRUCTURE

This thesis comprises four main experimental phases reported in six chapters:

Chapter 2: Provides a comprehensive overview of background literature relevant to coronary heart disease secondary prevention, in order to place the subsequent chapters in context. The chapter outlines cardiovascular and coronary heart disease burden, reviews current cardiac rehabilitation guidelines, and identifies the critical role of exercise training in cardiovascular risk management. Evidence for the efficacy of exercise training in coronary heart disease is presented, and factors limiting utilisation are described to identify research opportunities. Finally, the chapter briefly introduces the emerging field of telehealth CR and highlights potential to overcome existing challenges.

Chapter 3: Describes the methods and reports the findings from a systematic review and meta-analysis designed to evaluate the effectiveness of technology-assisted exercise-based cardiac rehabilitation, in comparison to traditional cardiac rehabilitation and usual care.
Chapter 4: Describes the development of a technology platform and intervention content designed for remote delivery of exercise-based cardiac rehabilitation, including underlying theoretical and evidential tenets of the intervention.

Chapter 5: Describes the methods and reports the findings of a laboratory study designed to determine the validity and feasibility of the remote monitoring platform during a range of exercise intensity levels and activities.

Chapter 6: Describes the design of a non-inferiority randomised controlled pilot trial that was designed to evaluate the effectiveness of remotely delivered exercise-based cardiac rehabilitation in comparison to the current gold standard, traditional supervised exercise-based cardiac rehabilitation.

Chapter 7: Describes the findings of the pilot trial described in Chapter 6

Chapter 8: Reviews the key findings from the thesis and gives a critical account of how the research makes a coherent and significant contribution to the cardiac rehabilitation literature. Implications of the findings are discussed, and the chapter concludes by making recommendations for future research and identifying future opportunities for development within the field of technology-assisted exercise-based cardiac rehabilitation.
CHAPTER 2. CORONARY HEART DISEASE: BURDEN & PREVENTION

2.1. CORONARY HEART DISEASE BURDEN

Cardiovascular disease (CVD) encompasses a range of diseases including rheumatic fever and subsequent chronic rheumatic heart disease, hypertension, coronary and pulmonary disease, cerebrovascular disease, and vascular disease.[1] CVD is the leading cause of death worldwide; approximately one third of annual global deaths (≈17 million) are attributed to CVD and this is predicted to increase to around 25 million by 2030.[2, 3] The global cost of CVD was estimated to be USD 863 billion in 2010, and is estimated to rise to USD 1044 billion by 2030.[4]

Coronary heart disease (CHD; angina pectoris, acute and recurrent myocardial infarction, other acute ischaemic heart disease, and chronic ischaemic heart disease)[1] accounts for the largest proportion of all CVD deaths; approximately 7% of deaths in the United States are attributed to CHD.[5] CHD prevalence is estimated to be 6% among adults in the United States, and is expected to increase 18% by 2030. Moreover, prevalence is disproportionately high among men and older aged individuals, although evidence of ethnic disparities appears mixed.[3, 5, 6] The cost of CHD was estimated to be approximately USD 204 billion in 2010.[5]

Although CVD and CHD prevalence are increasing, the rate of death attributable to these conditions has been declining for several decades.[3, 7] The reduction in case fatality has been attributed to enhanced coronary care and improvements in cardiovascular risk factors such as cholesterol, systolic blood pressure, smoking prevalence, and physical activity; coronary care and risk factor modification are estimated to account for similar proportions of the total improvement in case fatality at ≈47% and ≈44%, respectively.[5]

While improving event survival is positive, this emphasises a need for secondary prevention interventions that reduce recurrent coronary event risk and optimise health outcomes for individuals with established CHD. Indeed, within five years of a first myocardial infarction it is estimated ≈15% to 22% of individuals will experience a recurrent event or CHD fatality.[5] Further, more than 40% of all CHD events, more
than 35% of non-fatal myocardial infarction, and more than 50% of fatal coronary events have been attributed to individuals with existing CHD.[8]

2.1.1 Coronary Heart Disease Burden In New Zealand

The burden of CVD and CHD in New Zealand are comparable with global data. Approximately 30% of all deaths in New Zealand are attributed to CVD, and 6% to CHD.[7] The prevalence of CHD is estimated to be 5% among New Zealand adults, and is disproportionately high among men, older aged, Māori (indigenous) and Pacific ethnicities, and socioeconomically disadvantaged population groups.[9] In New Zealand, CHD accounts for nearly twice the health loss of the second ranked condition anxiety and depression (9.3% vs. 5.3% disability adjusted life years).[5, 10] These data indicate CHD and secondary prevention are key health issues in New Zealand, and this is reflected by both Governmental and non-Governmental policy targets.[11, 12]

2.2. CARDIOVASCULAR RISK FACTORS: KEY SECONDARY PREVENTION TARGETS

Given that a large proportion of the improvement in CHD case fatality is associated with improved cardiovascular risk factor profile, these factors appear to be a critical target for secondary prevention strategies. Alongside non-modifiable risk factors such as genetics and familial history of CHD, several modifiable factors have been identified to be associated with CHD. Modifiable risk factors include hypertension, dyslipidaemia, insulin resistance, overweight and obesity, tobacco use, unhealthy diet and physical inactivity. Collectively these modifiable risk factors have been estimated to account for 90% of the global population attributable risk of myocardial infarction, and these associations were consistent among men and women, young and old, and in all regions of the world.[13] Aerobic exercise capacity is also an independent cardiovascular risk factor; in comparison to individuals with low aerobic exercise capacity, moderate and high exercise capacity reduces the risk of mortality by 46% (HR = 0.54, 95% CI 0.42 to 0.69 ) and 68% (HR = 0.32, 95% CI = 0.24 to 0.44), respectively. [14] Furthermore, traditional risk factors such as hypertension, insulin resistance, and overweight and obesity are more prevalent among individuals with low aerobic exercise capacity.[14] This suggests multifactorial secondary prevention interventions that can successfully target traditional modifiable cardiovascular risk factors and aerobic exercise capacity could substantially reduce the risk of recurrent coronary events and the associated burden of chronic CHD.
2.3. CARDIAC REHABILITATION

Cardiac rehabilitation (CR) is an essential component of contemporary CHD management that aims to optimise cardiovascular risk reduction, facilitate adoption and adherence to healthy behaviours, reduce disability, and promote an active lifestyle.\[15\] International guidelines recommend a comprehensive approach with input from a multidisciplinary team that may include physicians (cardiologist, general practitioner), nurse specialists, physiotherapists, dieticians, psychologists, occupational therapists, and exercise specialists (e.g. clinical exercise physiologists).\[15, 16\] CR should aim to address all cardiovascular risk factors, and a number of essential core components have been identified. Terminology varies globally but core CR components remain fundamentally similar in multiple guidelines, and include audit/evaluation, cardioprotective therapies, psychosocial management, health behaviour change and education, management of medical and lifestyle risk factors, and long term management. A brief outline of core CR components is provided below; United States \[15\] and United Kingdom \[17\] guidelines have been integrated. Initial, ongoing, and follow-up assessment is critical for all components, and CR specialists should be appropriately trained and qualified for each component they manage.\[15, 17\]

**Audit And Evaluation**

CR programmes should be formally audited, including evaluation of individual clinical outcomes, service performance, and patient satisfaction. Opportunities to contribute data to national policy initiatives, and compare data against comparable alternative and standards should be undertaken.

**Cardioprotective Therapies**

Cardioprotective therapies include medication and implantable devices. Medication should be uptitrated to achieve evidence-based dosages, and patients’ medication beliefs should be assessed as these can influence medication use. Key cardioprotective medications include antiplatelet and lipid-lowering therapies, beta-adrenergic receptor blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers/aldosterone antagonists, calcium channel blockers, anticoagulants, and diuretics. Implantable devices may include defibrillators and/or resynchronisation therapy, and require specialist management.
Psychosocial Management
A comprehensive, holistic, valid assessment of anxiety and depression, illness perceptions, stress, health behaviour change self-efficacy, social support, and health-related quality of life (HRQoL) should be conducted upon entry to CR. Clinical anxiety or depression, or signs of severe/enduring mental illness should be referred to appropriately qualified practitioners. Patients should be assisted to develop stress management skills.

Health Behaviour Change And Education
Health behaviour change and education are integral to all the other core CR components. Evidence-based approaches should be used to increase risk factor knowledge, restore confidence and promote perceived personal control. Education should help patients to make informed choices that meet individual needs. Education should be delivered via dedicated education sessions, and be embedded throughout CR. Content should be tailored to suit individuals’ assessed needs, and misconceptions that impair progress should be addressed.

Educational topics may include pathophysiology/symptoms, lifestyle/medical risk factors, psychological self-management, social/vocational factors, sexual dysfunction, medications, surgical interventions, and cardiopulmonary resuscitation.

Medical Risk Factor Management
Blood pressure, lipids and glucose should be assessed upon entry into CR and regularly throughout, to inform medication use and assist achievement of risk factor targets (see [17] for review). Achieving medical risk factor targets is also important for safe exercise.

Lifestyle Risk Factor Management
Physical activity, exercise (i.e. planned, structured, regular physical activity), a healthy diet, weight management, and smoking cessation should be promoted via individualised, evidence-based health behaviour change strategies. Exercise should include a progressive programme of aerobic and strength training that is individualised based on initial and ongoing assessment of risk stratification, functional capacity, clinical status, comorbidities, and goals.[15] A choice of setting should be provided (home, community, or hospital).

Dietary habits weight, body mass index and waist circumference should be assessed upon entry to CR. Individualised advice should focus on making healthy dietary changes, correcting misconceptions, and avoidance of weight cycling to help achieve
and adhere to a cardioprotective diet. Weight management could include weight gain, maintenance or loss, as to meet individualised needs. Weight loss requires a combination of increased physical activity and reduced energy intake, with possible support via pharmacotherapy.

Smoking status, including previous tobacco use and quit attempts, should be assessed and monitored. For current smokers, frequency, quantity of tobacco use, quit readiness and nicotine dependence should also be assessed. Smoking cessation and relapse prevention support should be provided, including individualised advice, access to smoking cessation services and pharmacological support.

**Long Term Management**

Before concluding CR, patients and significant supporting others should be assisted to set long term management goals for preceding components and be encouraged to utilise community support groups and health services when appropriate, as identified via individual assessment.

**2.3.1 Cardiac Rehabilitation In New Zealand**

In New Zealand, CR comprises three distinct phases.[18] Phase one inpatient rehabilitation is delivered prior to hospital discharge and typically includes early mobilisation and education for patients and significant supporting others that promotes physical and psychological recovery, risk factors modification, and patients’ sense of control. The scope of inpatient rehabilitation is increasingly limited by decreasing length of hospital stay.

Phase two outpatient rehabilitation comprises six to twelve week supervised programmes that are tailored to patient and significant supporting others’ needs, and is initiated soon after hospital discharge or referral. Outpatient CR includes core components of CR outlined above, and many are delivered via face-to-face outpatient clinics and group seminars. Exercise-based CR (exCR) is commonly provided in clinical settings (hospitals and rehabilitations clinics (centre-based exCR), although home- and community-based programmes are available in some locations. Programme content varies regionally due to differing resources, staff expertise, and population density. Many areas of New Zealand are sparsely populated. In total 22% of the population live in rural areas (11%) and small towns (11%) with little or no reliance on major metropolitan centres,[19] and this is likely to influence both the types of CR service available, and accessibility to CR. These proportions are even
greater in the South Island, where 34% of the population live in rural areas (16%) and small towns (18%).[19]

Phase three long-term maintenance relates to sustaining skills and behaviour change learned during in and outpatient CR, and is primarily achieved via a network of independent community-based support groups that are affiliated with the National Heart Foundation of New Zealand.

2.4. EXERCISE AS A MULTIFACTORIAL SECONDARY PREVENTION INTERVENTION

As outlined above, international guidelines recommend CR should address all risk factors, and should not be limited to exCR alone; however, exCR remains a central component and has substantial potential for CHD secondary prevention as it is a multifactorial intervention in and of itself. Physical inactivity has been estimated to account for around 30% of CHD burden [20] and has been labelled an actual cause of death. [21] Among the general population physical activity and increased cardiorespiratory fitness reduce the risk of CHD, all-cause and cardiac mortality;[22-25] this indicates physiological adaptations to physical activity and exercise promote favourable cardiovascular and metabolic health outcomes.

Exercise training is associated with many adaptations that improve functional capacity and CHD risk factor profile. These adaptations include enhanced maximal and submaximal exercise capacity, increased cardiac output and stroke volume, reduced heart rate and myocardial work at sub-maximal exercise intensities, increased cardiac and skeletal muscle capillarisation, improved endothelial function and blood pressure regulation, enhanced glucose and lipid metabolism, increased oxidative metabolic capacity, improved blood lipid profile, improved glucose tolerance and insulin sensitivity, and enhanced body composition.[22, 26-28] These physiological adaptations directly align with many of the objectives set forth in CR guidelines,[15, 17] and highlight the potential of exCR as a multifactorial risk management intervention.
2.5. CENTRE-BASED EXERCISE PROGRAMMES

International guidelines consistently identify exCR as a critical component of CHD secondary prevention [15, 17, 29, 30] and, unsurprisingly, the literature assessing its effectiveness is large. In New Zealand, exCR has commonly been delivered in hospitals and rehabilitation clinics (i.e. centre-based exCR) and focuses on exercise training and physical activity behaviour; additional core components such as nutritional counselling, risk factor education, and psychosocial counselling [15] are delivered via outpatient clinics and group education seminars. Alternative delivery models including home- and community-based options are available in some locations, and some of these programmes include additional core CR components. An overview of research that has assessed exCR effectiveness is presented below.

2.5.1 Effect On Mortality

There is substantial evidence that exCR reduces all-cause and cardiac mortality. Four meta-analyses report reduced mortality following CR interventions comprising an exercise component, either alone or as part of a more complex multi-factorial programme (comprehensive CR).[31-34] Results of these meta-analyses are briefly summarised below.

Taylor and colleagues reported exercise-inclusive CR reduced all-cause and cardiac mortality by 20% (odds ratio [OR] = 0.80, 95% confidence interval [CI] 0.68 to 0.93) and 26% (OR = 0.74, 95% CI 0.61 to 0.96), respectively.[34] Similarly, Clark and colleagues reported a 17% (risk ratio [RR] = 0.83, 95% CI 0.72 to 0.96) reduction in all-cause mortality following exercise-inclusive CR.[33] Lawler and colleagues reported exercise-inclusive CR reduces all-cause and cardiac mortality by 26% (OR = 0.74, 95% CI 0.58 to 0.95) and 36% (OR = 0.64, 95% CI 0.46 to 0.88), respectively. Moreover, cardiovascular mortality (death due to cardiac, cerebrovascular or peripheral vascular diseases) was reduced by 39% (OR = 0.61, 95% CI 0.40 to 0.91).[31] Heran and colleagues report exCR interventions with > 12 months follow-up durations reduce all-cause mortality by 13% (RR = 0.87, 95% CI 0.75 to 0.99); the effect of interventions with ≤ 12 months follow-up was not statistically significant (RR = 0.82, 95% CI 0.67 to 1.01), although substantial mortality benefits may be unlikely to be realised in the short term.[32] Moreover, interventions with > 12 month follow-up duration reduced cardiovascular mortality by 26% (RR = 0.74, 95% CI 0.63 to 0.87).
Standalone exCR programmes appear to confer similar protective benefits when compared with comprehensive CR; two meta-analyses reported no statistically significant differences for effects of all-cause mortality between exercise-only (OR = 0.76, 95% CI 0.59 to 0.98;[34] RR = 0.72, 95% CI 0.54 to 0.95)[33] or comprehensive CR (OR = 0.84, 95% CI 0.72 to 0.99;[34] RR = 0.88, 95% CI 0.74 to 1.04).[33]

The cardioprotective effects of exCR appear to follow a dose-response relationship. Among 30 000 participants, completion of all (n = 36) CR sessions yielded 47%, 22% and 14% reductions in all-cause mortality compared with completion of 1, 12 or 24 sessions, respectively.[35] Finally, exCR appears to be more cost-effective for reducing premature death than most common pharmacological and surgical interventions.[36]

In summary, current evidence strongly supports the efficacy of exCR for reducing all-cause, cardiac, and cardiovascular mortality among those with established CHD; supplementary CR components (i.e. comprehensive CR) do not appear to augment efficacy.

### 2.5.2 Effect On Recurrent Cardiac Events

Evidence regarding effects on recurrent cardiac events is less conclusive. Meta-analyses have reported 27% (RR = 0.73, 95% CI 0.60 to 0.89)[33] and 46% (OR = 0.54, 95% CI 0.38 to 0.76)[31] reductions in recurrent myocardial infarction (MI) following exercise-inclusive CR. Similar to effects on all-cause mortality, effects on recurrent MI risk appear to be comparable between exCR (RR = 0.76, 95% CI 0.57 to 1.01) and comprehensive CR (RR = 0.62, 95% CI 0.44 to 0.87).[33] However, Taylor and colleagues reported no statistically significant reductions in recurrent MI (OR = 0.79, 95% CI 0.59 to 1.09), coronary artery bypass grafts (CABG; OR = 0.87, 95% CI 0.65 to 1.06) or percutaneous coronary intervention (PCI; OR = 0.81, 95% CI 0.49 to 1.34) following exCR.[34] A more recent review also reported no statistically significant reductions in recurrent fatal or non-fatal MI (≤ 12 months follow-up RR = 0.92, 95% CI 0.70 to 1.22; > 12 months follow-up RR = 0.97, 95% CI 0.82 to 1.15), CABG (≤ 12 months follow-up RR = 0.91, 95% CI 0.67 to 1.24; > 12 months follow-up RR = 0.93, 95% CI 0.68 to 1.27) or PCI (≤ 12 months follow-up RR = 1.02, 95% CI 0.69 to 1.50; > 12 months follow-up RR = 0.89, 95% CI 0.66 to 1.19).[32]

Similar to mortality, recurrent cardiac event risk reduction may be dose-responsive; among 30 000 participants completion of all (36) exCR sessions yielded 31%, 23% and 12% reductions in recurrent MI risk compared with completion of 1, 12, or 24
sessions, respectively.[35] Furthermore, stratified meta-analyses indicate recurrent MI risk is reduced to a greater extent following exercise interventions lasting more than three months (OR = 0.40, 95% CI 0.24 to 0.66) than those lasting fewer than three months (OR = 0.69, 95% CI 0.43 to 1.11).[31]

In summary, evidence demonstrating beneficial effects of exCR on recurrent cardiac event risk remains equivocal. However, greater effects may be realised by exposure to larger doses of exercise over longer periods of time. Once again, it appears the additional complexity of comprehensive CR may not augment the cardioprotective effects of exCR.

### 2.5.3 Effect On Exercise Capacity

A comparison of moderate intensity/frequency exCR and sedentary control resulted in a statistically significantly greater change in maximal oxygen consumption ($\dot{V}O_2\text{max}$) following exCR (5.1 ml·kg$^{-1}$·min$^{-1}$, 27.4%) compared with control (-1.1 ml·kg$^{-1}$·min$^{-1}$, -5.4%).[37] Ades and colleagues compared high energy expenditure and standard exCR programmes among obese adults with established CHD and reported identical statistically significant increases in $\dot{V}O_2\text{max}$ after both programmes (both 2 ml·kg$^{-1}$·min$^{-1}$, 9.1%).[38]

Comparison of a twelve month exCR programme with no-exercise control demonstrated statistically significant increases in $\dot{V}O_2\text{max}$ and $V_O2$ at the ventilatory threshold (which indicates enhanced aerobic metabolic capability) after exCR (0.25 ± 0.4 L·min$^{-1}$ and 0.08 ± 0.2 L·min$^{-1}$, respectively).[39] Both outcomes decreased statistically significantly in the control group (-0.01 ± 0.50 L·min$^{-1}$ and -0.09 ± 0.30 L·min$^{-1}$, respectively). Similarly, a statistically significant increase in exercise time during a graded maximal exercise test following exCR (71 ± 96 s) but not control (17 ± 52 s) indicated an increase in functional capacity following exCR. Finally, mean weekly energy expenditure was moderately, yet statistically significantly, correlated with the change in $\dot{V}O_2\text{max}$ ($r = 0.62$). This correlation supports a dose-response relationship between exercise and adaptive health outcomes.

Statistically significant improvements in $\dot{V}O_2\text{max}$ (5.0 ml·kg$^{-1}$·min$^{-1}$, 35.2%) and $V_O2$ at the anaerobic threshold (2.7 ml·kg$^{-1}$·min$^{-1}$, 30.7%) have also been reported among people who have undergone CABG following six months of exCR. Conclusions were not definitive as this study employed an uncontrolled experimental design; however, it seems unlikely a no-exercise control group would attain improvements of similar relative magnitude.[40]
An evaluation of high- (10 sessions·week⁻¹) and low-frequency (2 sessions·week⁻¹) exCR demonstrated statistically significant improvements in VO₂max for both groups (high = 3.3 ml·kg⁻¹·min⁻¹; low = 2.7 ml·kg⁻¹·min⁻¹).[41] Moreover, both groups improved exercise time (high = 2.3 min; low = 1.6 min) and peak power output (high = 25 W; low = 18 W) during a graded maximal exercise test. Change in VO₂max did not differ between groups, but improvements in exercise test duration and peak power output were both statistically significantly greater in the high frequency group. These data likely indicate superior sub-maximal exercise capacity following higher frequency exCR and support dose-responsive exercise adaptations.

Finally, a recent meta-analysis of 31 studies (n = 3 827) demonstrated an average improvement of 1.55 metabolic equivalents (MET; 95% CI 1.21 to 1.89).[42] Improvements in aerobic exercise capacity did not vary between exercise-alone or comprehensive CR programmes, shorter and longer programmes (< 12 weeks vs ≥ 12 weeks), or between high and low baseline exercise capacity (< 6.6 MET vs ≥ 6.6 MET). Unsurprisingly, programmes including aerobic training (alone or mixed mode) improved aerobic fitness capacity more than strength-only training programmes. Improvements were much larger for programmes with more than 36 scheduled sessions, but the difference did not reach statistical significance. Moreover, improvements were larger in male and younger participants.

In summary exCR is consistently associated with improved exercise capacity and the magnitude of change is likely mediated by intervention characteristics that determine the exercise dose, such as exercise frequency and level of intensity. These beneficial effects are particularly encouraging because aerobic exercise capacity is a strong independent predictor of mortality among men and women with CHD; improvements of 1 ml·kg⁻¹·min⁻¹ and 1 MET (=3.5 ml·kg⁻¹·min⁻¹) have been associated with 10% and 25% improvements in cardiac and all-cause mortality, respectively.[14, 43-45]

### 2.5.4 Effect On Blood Pressure

Belardinelli and colleagues reported improved systolic blood pressure (SBP) following exCR (-6 mm Hg) but not a no-exercise control group (6 mm Hg). Diastolic blood pressure (DBP) was not reported.[37] A similar mean change in SBP (-6 mm Hg) was reported following another six month exCR programme, but did not reach statistical significance.[40] This discrepancy may be attributed to substantial differences in exCR group sample size (n = 59 [37] vs n = 32 [40]), as pre- and post-intervention variability was lower in this second study;[40] a larger sample size and
resulting reduction standard error may have produced a more favourable statistical test result for this 6 mm Hg improvement. Statistically significant reductions in SBP have been reported following high energy expenditure (-8 mm Hg) and standard exCR (-10 mm Hg), and these effects were comparable between groups. High energy expenditure exCR also improved DBP (-7 mm Hg); the effect of standard exCR did not reach statistical significance (-4 mm Hg).[38]

Meta-analytical findings also demonstrate improvements in blood pressure following exCR. Taylor and colleagues reported a statistically significantly greater improvement in SBP (WMD = -3.2 mm Hg, 95% CI -5.4 to -0.9) but not DBP (WMD = -1.2 mm Hg, 95% CI -2.7 to 0.3) following exCR.[34] Once again, Lawler and colleagues did not subject risk factors to meta-analysis, but reported more favourable changes in SBP and DBP for exCR than control.[31]

In summary exCR is regularly associated with improved SBP; however, effects on DBP are less clear.

### 2.5.5 Effect On Blood Lipid Profile

Moderate intensity and frequency exCR has been reported to improve total (-0.59 mmol·L⁻¹), low (LDL-C; -0.44 mmol·L⁻¹) and high density lipoprotein cholesterol (HDL-C; 0.13 mmol·L⁻¹), and triglyceride concentrations (-0.26 mmol·L⁻¹).[37] These changes were statistically significantly greater than a no-exercise control group, whose blood lipid profile worsened over six months (Total-C = 0.78 mmol·L⁻¹; LDL-C = 0.26 mmol·L⁻¹; HDL-C = -0.10 mmol·L⁻¹; triglyceride = 0.09 mmol·L⁻¹).

High energy expenditure exCR has been associated with statistically significant improvements in HDL-C (0.08 mmol·L⁻¹) triglyceride (-0.35 mmol·L⁻¹) concentrations and the total-C-to-HDL-C ratio (-0.50), but not total-C (-0.18 mmol·L⁻¹) or LDL-C concentration (-0.13 mmol·L⁻¹). A lower energy expenditure standard exCR intervention did not improve blood lipid profile.[38] Hambrecht and colleagues reported exCR resulted in statistically significant improvements in total-C (-0.56 ± 0.72 mmol·L⁻¹), LDL-C (-0.36 ± 0.54 mmol·L⁻¹) and triglyceride concentrations (-0.41 ± 0.54 mmol·L⁻¹) and the total-C-to-HDL-C ratio (-0.02 ± 0.02 mmol·L⁻¹), but not HDL-C (0.02 ± 0.13 mmol·L⁻¹); among no-exercise controls only triglycerides improved (-0.34 ± 0.76 mmol·L⁻¹).[39] High- and low-frequency exCR were reported to improve total-C (high = -0.47 mmol·L⁻¹; low = -0.43 mmol·L⁻¹) and LDL-C concentrations (high = -0.40 mmol·L⁻¹; low = -0.47 mmol·L⁻¹), but not HDL-C or triglyceride concentrations; an absence of between-group differences confounds other evidence demonstrating
dose-responsive risk factor modification.[41] A six month exCR programme yielded statistically significant improvements in total-C (−0.44 mmol·L⁻¹) and LDL-C concentrations (−0.28 mmol·L⁻¹), but not HDL-C or triglycerides.[40]

Meta-analytical findings also support beneficial effects of exCR on blood lipid profile. Taylor and colleagues reported statistically significantly greater improvements in total-C (weighted mean difference [WMD] = -0.37 mmol·L⁻¹, 95% CI -0.63 to -0.11) and triglyceride concentrations (WMD = -0.23 mmol·L⁻¹, 95% CI -0.39 to -0.07), but not LDL-C (WMD = -0.20 mmol·L⁻¹, 95% CI -0.53 to 0.12) or HDL-C concentrations (WMD = 0.05 mmol·L⁻¹, 95% CI -0.03 to 0.14) following exCR, compared with no-exercise control.[34] While Lawler and colleagues did not subject cardiovascular risk factors to meta-analysis, trends toward reductions in total-C were identified in the intervention arms of several randomised controlled trials (RCT).[31]

Despite considerable variability between studies exCR has been regularly associated with favourable effects on blood lipid profile. Some evidence indicates a minimum dose threshold may exist.[38] Variability in blood lipid outcomes may be partly accounted for by differences in exercise prescription characteristics (i.e. frequency, intensity level and duration).

### 2.5.6 Effect On Glucose Metabolism

High energy expenditure exCR is associated with statistically significant improvements in fasting blood glucose (−0.39 mmol·L⁻¹) and insulin concentrations (−6 μIU·mL⁻¹), and insulin-stimulated blood glucose disposal (1.80 mg·kg fat free mass [FFM]⁻¹·min⁻¹).[38] Insulin-stimulated glucose disposal (1.00 mg·kgFFM⁻¹·min⁻¹) and insulin concentration (−3 μIU·mL⁻¹) were the only statistically significant changes following standard exCR. Further, the improvement in insulin-stimulated glucose disposal was statistically significantly larger following high energy exCR compared with standard CR. Conversely, Onishi and colleagues reported no statistically significant change in fasting blood glucose or glycated haemoglobin (HbA1c) following six months of exCR.[40]

Literature assessing the effect of exercise on glucose metabolism is limited within the CR domain, but more common among diabetic, overweight/obese and metabolic syndrome populations. Experiments examining these populations are likely relevant as the incidence of co-morbid insulin resistance/diabetes, overweight/obesity and metabolic syndrome are high among people with CHD, and results are summarised below.
A meta-analysis evaluating the effect of exercise training on HbA1c among adults with type 2 diabetes mellitus demonstrated a statistically significantly lower HbA1c concentration following exercise training compared to no-exercise control (WMD = -0.66%, 95% CI -0.98 to -0.34).[46] Similar effects were reported for aerobic (WMD = -0.67%, 95% CI -1.04 to -0.30), and strength training (WMD = -0.64%, 95% CI -1.29 to 0.01), and interventions combining exercise with dietary modification (WMD = -0.76%, 95% CI -1.32, -0.20). The absence of an additive effect of dietary modification suggests exercise-induced metabolic adaptations may play a greater role in regulating glucose than dietary intake.

Cochrane systematic reviews of exercise for type 2 diabetes mellitus [47] and overweight/obesity [48] provide mixed evidence for the effect of exercise on glucose metabolism. Thomas and colleagues reported statistically significantly lower HbA1c concentration after an exercise intervention compared with controls (WMD = -0.62%, 95% CI -0.91 to -0.33); however fasting plasma glucose and insulin did not differ between groups.[47] Conversely, Shaw and colleagues reported a statistically significantly greater improvement in fasting serum glucose after exercise training compared with no-exercise control (WMD = -0.17 mmol·L⁻¹, 95% CI -0.30 to -0.05).[48] Furthermore, high-intensity exercise yielded a larger improvement than low-intensity exercise (WMD = -0.31 mmol·L⁻¹, 95% CI -0.45 to -0.16). Importantly, it was also noted that beneficial effects of exercise on blood glucose control were evident even in the absence of weight loss. Finally, a review of exercise and insulin sensitivity indicated acute effects of exercise on insulin sensitivity are greater in trained compared with untrained individuals.[49]

In summary, evidence describing the effects of exercise on glucose metabolism is mixed. However, it appears effects may be dose-dependent, and regular exercise may be required to optimise effects on insulin sensitivity. Similar to other risk factors, it is possible differences in exercise intervention characteristics may account for some variability in treatment effects.

### 2.5.7 Effect On Body Composition

High energy expenditure exCR has been associated with statistically significant improvements in body mass (-8.2 kg), BMI (-2.8 kg·m²), fat mass (-5.90 kg), waist circumference (-7.0 cm), total abdominal fat (-120 cm²) and intra-abdominal fat (-63 cm²).[38] Standard exCR also improved body mass (-3.7 kg), BMI (-1.3 kg·m²), fat mass (-2.80 kg), waist circumference (-5 cm), total abdominal fat (-52 cm²) and intra-
abdominal fat (-23 cm²). Effects of high energy expenditure exCR were statistically significantly greater than standard exCR. Similarly Onishi and colleagues reported statistically significant improvements in body mass (-1.9 kg), fat mass (-1.3 kg), lean body mass (0.9 kg), percentage of body fat (-1.9%), and waist circumference (-3.1 cm) following a six month aerobic and strength training exCR intervention.[40] Hambrecht and colleagues reported statistically significantly lower BMI following exCR (-1.2 ± 2.1 kg·m⁻²), and this improvement was statistically significantly better than a no-exercise control group (-0.1 ± 2.0 kg·m⁻²).[39] 

Cochrane systematic reviews of exercise for type 2 diabetes mellitus [47] and overweight/obesity [48] provide further support for the beneficial effect of exercise on body composition. Thomas and colleagues reported statistically significantly lower visceral adipose tissue (-45.54 cm²; 95% CI -63.76, -27.31 cm²), but not body mass or BMI following exercise training.[47] Changes in fat mass and fat free mass were not directly assessed, but reduced visceral adiposity is indicative of reduced fat mass. Further, as total body mass remained stable, a decrease in fat mass likely also indicates favourable changes in fat free body mass (i.e. lean tissue), thereby further improving body composition. Meta-analytical evidence also supports statistically significantly greater improvements in body mass (WMD = -2.03 kg, 95% CI -2.82 to -1.23 kg) and BMI (WMD = -0.73 kg·m⁻², 95% CI -0.99 to -0.46) following exercise training, compared with no-exercise control, and high intensity exercise had a greater effect than low intensity exercise (WMD = -1.47 kg, 95% CI -2.28 to -0.66).[48] 

In summary exCR is consistently associated with favourable changes in body composition, and effects are consistent in populations with co-morbidities common among people with CHD. Similar to other cardiovascular risk factors, effects on body composition also appear to be dose-dependent.

2.5.8 Effect On Psychosocial Risk Factors

Psychological factors such as depression, anxiety, hostility, chronic stress, social isolation, and a lack of sense of purpose are strongly associated with cardiovascular risk,[50] and targeted evaluation and treatment is recommended for people with CHD by the American Heart Association.[51] The literature describing effects of exercise on psychosocial factors such as anxiety, depression, and quality of life is broad, particularly outside the exCR domain, and a brief review is presented here. A recent meta-analysis of 35 trials (n = 1 356) demonstrated a reduction in depression symptoms after exercise training compared with no treatment or control treatment.
(standardised mean difference [SMD] = -0.62, 95% CI -0.81 to -0.42).\[52\] However, removing less rigorous trial designs reduced the effect (SMD = -0.18, 95% CI -0.47 to 0.11). Further, the effect of exercise did not differ compared with psychological (seven trials, n = 189, SMD = -0.03, 95% CI -0.32 to 0.26) or pharmacological therapies (four trials, n = 300, SMD = -0.11, 95% CI -0.34 to 0.12). These results are consistent with an earlier review which also indicated exercise-induced improvements may be larger among clinical populations, including after MI. However, it was noted people with depression secondary to other conditions may differ from people with primary depression.\[53\] Similar to physiological risk factors, higher energy expenditure exercise training also appears to be more effective than lower energy expenditure training, irrespective of exercise frequency.\[54\] Within exCR, cohort studies have demonstrated promising effects of exCR on depression, anxiety, hostility, and suggest these effects also improve prognosis.\[55, 56\]

A Cochrane review comparing exCR with usual care sought to assess effects on HRQoL.\[32\] Heterogeneity of measurement instruments and reporting precluded meta-analysis, but seven of ten trials that used validated measurement instruments reported significantly higher HRQoL following exCR compared with usual care. These beneficial effects of exCR on HRQoL are supported by an additional systematic review.\[57\]

In summary, exercise appears to have multifactorial benefits for psychosocial wellbeing, and these effects may be dose-responsive.

### 2.5.9 Summary Of Evidence For exCR

Despite some inconsistency, exCR is generally associated with multifactorial improvements in cardiovascular risk profile and mortality. Larger exercise doses appear to increase the magnitude of improvement for many risk factors, and effects are likely mediated by intervention-specific characteristics and adherence to prescribed exercise. Numerous beneficial physiological and psychological adaptations to exercise training enable exCR to simultaneously target multiple risk factors, reinforcing its crucial role as a multifactorial CHD secondary prevention intervention.
2.6. UTILISATION

Despite the documented benefits, global provision of centre-based CR is inadequate.[58] Many eligible individuals are not offered CR and uptake is low among those invited to participate.[36, 58-61] Cost is a barrier in locations where CR operates as a user-pays service; however, uptake is low even where access is free.[62, 63] Estimates of centre-based exCR utilisation vary globally, but are almost universally below 50%, sometimes even below 20%. CR utilisation is affected by a diverse range of factors including system/service, psychological, and physical barriers, and these can vary by ethnicity and sex.[64] System/service barriers include poor recall or understanding of CR information presented in hospital, contradictory information presented in hospital, variable inpatient CR support, a lack of referral to CR, and insufficient or negative recommendations from physicians. Psychological participation barriers include misconceptions about CR, ambivalence about the benefits of participation, distress arising from the diagnosis and/or cardiac event, a lack of perceived control or risk factors and prognosis, embarrassment, and negative perceptions about individuals who participate in CR. Physical participation barriers include limited availability of centre-based CR programmes, transport restrictions, geographic isolation, inconvenient programme scheduling, lack of parking, and domestic or occupational responsibilities.[64-67] Overcoming participation barriers should be prioritised as non-attendance is associated with poorer risk factor knowledge and risk profile.[68] A range of approaches will be required to address all barriers, particularly psychological factors which are likely to vary substantially between individuals. Common physical barriers indicate accessibility is an important factor that limits utilisation of traditional centre-based exCR programmes, and these may be easier to overcome than psychological and system/service barriers.

Among those who undertake centre-based exCR, short term adherence to prescribed exercise is poor [39, 69] and long term adherence is even worse, with up to 50% dropping out of regular exercise within six months of programme completion.[28, 70, 71] Failure to adopt exCR precludes exercise-induced physiological adaptations that facilitate beneficial CHD risk factor modification. While more favourable than non- adoption, sub-optimal adherence to prescribed exercise training reduces the exercise dose participants are exposed to, thereby limiting the potential magnitude of physiological adaptation and CHD risk factor modification. It is clear Current exCR delivery methods are inadequate; innovation is required to improve exCR adoption and adherence, and subsequent health outcomes.
Utilisation In New Zealand

Utilisation of exCR in New Zealand is similar to other countries. Adoption (44%) and completion (19%) of outpatient programmes are low, and participation is limited by sub-optimal referral, programme availability, coordination and continuity. [72-74] It is clear that current exCR services do not meet the needs of many people, and innovation is required to develop more responsive and accessible delivery models.

2.7. HOME-BASED EXERCISE PROGRAMMES

Home-based exCR programmes have been introduced to broaden access and participation.[75] A meta-analysis that compared home- and centre-based exCR across twelve studies (n = 1 938) reported no differences (either statistically and/or clinically significant) in treatment effects on mortality (RR = 1.31, 95% CI 0.65 to 2.66), exercise capacity, SBP (WMD = -0.58 mmHg, 95% CI -3.29 to 4.44), DBP (WMD = 1.85 nm Hg; 95%CI 0.74 to 2.96), total-C (WMD = 0.13 mmol·L⁻¹, 95% CI -0.05 to 0.31), HDL-C (WMD = -0.06 mmol·L⁻¹, 95% CI -0.11 to -0.02), LDL-C (WMD = 0.15 mmol·L⁻¹, 95% CI -0.01 to 0.31), or triglyceride concentrations (WMD = 0.15 mmol·L⁻¹, 95% CI -0.11 to 0.41). Heterogeneity of measurement instruments precluded meta-analysis of HRQoL, but most individual studies reported no differences between home- and centre-based exCR.[76, 77] A very recent update of this review confirmed most of these effects in a larger pooled sample (17 studies, n = 2 172); however, small effects in favour of centre-based exCR were reported for HDL-C (WMD = -0.07 mmol·L⁻¹, 95% CI -0.11 to -0.03) and triglyceride concentrations (WMD = -0.18 mmol·L⁻¹, 95% CI -0.34 to -0.02), and DBP (WMD = -1.86 mm Hg, 95% CI -0.76 to -2.95). Conversely, programme adherence (not pooled) and completion (RR = 1.04, 95% CI 1.01 to 1.07) favoured home-based exCR.[78]

Home-based exCR overcomes several participation barriers that limit centre-based programme accessibility and comparable treatment effects are encouraging. However, many home-based programmes are unable to include exercise supervision from clinical exercise specialists in a manner consistent with centre-based exCR. In addition to concerns about safety, this lack of supervision and monitoring of physiological responses to exercise restricts opportunities to individualise and optimally manage exercise prescription. Given that the beneficial effects of several cardiovascular risk factors are dose dependent [35, 38, 79] this may limit improvements in modifiable cardiovascular risk factors and functional capacity.[18,
38] Addressing this shortcoming may help participants in home-based exCR to achieve recommended exercise training loads, and improve health outcomes.

2.8. TELEHEALTH CARDIAC REHABILITATION

Telehealth, alternately referred to as telemedicine, telecare, telerehabilitation or telemonitoring,[65, 80, 81] refers to the use of information and communication technologies (ICT) to deliver health services. Within CR, telehealth refers to the use of ICT to augment home-based CR programmes, and can enable provision of additional feedback, education and counselling from CR specialists. By definition telehealth technologies could provide near universal accessibility to CR by connecting specialists with participants outside of traditional clinical environments. Therefore, telehealth holds great potential to improve not only the characteristics of home-based CR, but also overall CR utilisation.

An early systematic review of telehealth CR (11 studies, n = 3 145) reported that compared to usual care controls telehealth CR can improve total-C (WMD = 0.37 mmol·L⁻¹, 95% CI 0.19 to 0.56), HDL-C (WMD = 0.05 mmol·L⁻¹, 95% CI 0.01 to 0.09), LDL-C (WMD = 0.41 mmol·L⁻¹, 95% CI 0.36 to 0.56), and SBP (WMD = 4.69 mm Hg, 95% CI 2.91 to 6.47). Physical activity outcomes were not subjected to meta-analysis, but five of seven studies that included physical activity outcomes reported greater physical activity for telehealth CR. Some evidence also suggests telehealth CR can enhance physical HRQoL and reduce programme costs.[82]

A more recent review identified several models of telehealth CR including multifactorial, internet-based, exercise-focused (i.e. exCR), and recovery-focused programmes.[83] Multifactorial programmes were suggested to be effective when they addressed multiple risk factors in line with clinical guidelines. An internet-based programme demonstrated improvements in risk factor profile, but due to a very small sample size (n = 15) effects were not statistically significant compared to control. ExCR programmes comprised transtelephonic electrocardiogram (ECG) monitoring during exercise, some with concurrent telephone contact with a health professional, and some evidence indicated physical activity was higher after telehealth exCR compared with control. Telehealth recovery interventions focused mainly on surgical recovery, provided little CHD secondary prevention information, and fall outside the scope of this thesis.

A third very recent (2015) systematic review synthesised studies that provided telemonitoring (sensor data collection/analysis), telecoaching, and social
networking.[84] Most interventions were reported to include few core CR components, and predominantly focused on physical activity. Meta-analyses of adverse events, cardiac rehospitalisation, and adherence to physical activity guidelines favoured telehealth programmes, although numeric data were not presented.

These reviews provide promising early evidence for telehealth CR utilisation but few studies have been able to deliver or monitor structured, individualised, prescriptive exercise training in a manner similar to centre-based exCR. Telehealth programmes have most commonly used fixed-line telephone, email and mobile phone short message service (SMS) to deliver motivational support, behavioural change counselling, and feedback about goal achievement or exercise adherence. While these tools augment standard home-based CR they limit programme flexibility, and cannot emulate gold standard evidence-based exercise supervision and coaching that is common to centre-based exCR. Physiological monitoring has recently been identified as a particularly important direction for future development [85] but solutions have remained elusive. Telehealth must now move beyond traditional communication tools to encompass rapidly advancing technologies that allow more responsive, individualised, interactive interventions, including remote physiological exercise monitoring.

2.9. MOBILE HEALTH CARDIAC REHABILITATION

Powerful mobile technologies offer enhanced capability to deliver and monitor exCR outside the home and clinical environments, and could provide substantially more flexible and immersive interventions. Use of mobile technologies for health service delivery has been termed mobile health (mHealth).[86] The integration of advanced physiological sensor and mobile communication technologies into exCR delivery has yet to be fully explored; however, this approach may have numerous benefits. The flexibility offered by wireless devices enables intervention delivery to a broader range of environments than most previous telehealth CR programmes. True mobility could extend the reach of exCR even beyond that of home-based programmes, and near-universal accessibility has potential to substantially increase exCR utilisation.

Recent advances in wearable sensing technologies have provided devices that are capable of quantifying an array of exercise-related metrics that extend beyond traditional heart rate monitoring. Sensors can now track respiration, skin conductance, skin temperature, body movement, and posture to name just a few.[87]
Mobile and smartphone market penetration continues to grow rapidly worldwide. Smartphone ownership has reached \( \approx 75\% \) in many countries.[88] Further, mobile broadband coverage (70% and 90% of the total and urban global population, respectively) and subscriptions (80% in developed countries) are nearing ubiquity.[88-90] This unprecedented level of mobile connectedness suggests the time is right to introduce more sophisticated telehealth exCR platforms that can optimise programme flexibility, accessibility, responsiveness, and individualisation.

These technologies could enable development of physiological monitoring platforms that connect participants with exCR specialists in real-time, from almost any location, to provide real-time remote exercise monitoring and coaching. Real-time remotely monitored exCR could help to provide more responsive tailoring of exercise prescription and enhance safety during home-or community-based exercise, and this could help to ensure individuals accrue recommended exercise doses to achieve beneficial health outcomes. Moreover, mobile communications technologies could enable provision of immersion tailored education, feedback, and social support. Remote monitoring could also enable high resolution quantification of physiological responses throughout exercise in free-living environments that have not previously been possible, and this could help to enhance understanding of the relationship between exercise dose and CHD risk factor modification. There have already been calls in the literature for exCR to embrace modern technologies in exCR,[85, 91] but the call has remained largely unanswered.

The feasibility of a real-time remote monitoring platform was demonstrated among a small (\( n = 6 \)) cohort of people with CHD.[67] The platform comprised a smartphone and heart monitor that enabled real-time, remote transmission of ECG, heart rate, speed, distance and geographic position data to a remotely located secure web server. Remote monitoring enabled exCR specialists to make periodic modifications to exercise prescription based on individual exercise responses, although real-time communication between specialists and participants was largely limited to phone calls if technical problems or clinically significant ECG changes were observed. The six week (frequency = three sessions·week\(^{-1}\)) remotely monitored walking programme resulted in statistically significant improvements in functional capacity (which was noted as comparable to centre-based exCR), cardiac depression, and physical HRQoL; however interpretation of these results was limited given the uncontrolled experimental design. Participants rated the usability of the remote monitoring platform favourably, and the results are able to demonstrate that real-time remote exercise monitoring is feasible and could help to augment exCR utilisation.
2.10. SUMMARY

An extensive body of literature demonstrates dose-dependent beneficial effects of exercise on physiological and psychological cardiovascular risk factors, and clinical events among individuals with established CHD. These data show the benefits of exercise extend well beyond improvements in physical activity level alone and suggest that, rather than being narrowly focused, exCR is a multifactorial risk factor modification strategy. This reinforces the critical role of exCR in CHD secondary prevention.

Unfortunately, numerous barriers substantially limit utilisation of centre-based exCR programmes, and urgent innovation is needed to address this. New exCR delivery models are necessary, and should strive to close the gap between the gold standard practices of centre-based exCR and widespread accessibility of home-based programmes.

Telehealth and mHealth in particular, offer exciting opportunities to overcome a number of factors that limit programme accessibility by delivering the expertise of exCR specialists to participants in almost any location. This could not only enhance exCR utilisation, but could also enable collection of previously unobtainable exercise data that could help determine how different types of exercise prescription, carried out in free-living environments, contribute to cardiovascular risk factor modification.

This thesis aims to address a two part problem that affects exCR clinical practice. The first part of the problem is not that exCR lacks efficacy; a substantial body of literature provides evidence to the contrary. The first part of the problem is that many people are unable to access exCR programmes in traditional clinical settings. As a result, individuals who may otherwise choose to participate in exCR are unable to do so. The second part of the problem is not that research has failed to address factors that limit access to exCR; home-based programmes have been available in some regions for many years. The second part of the problem is that home-based programmes, including recent technology-assisted telehealth interventions, have overcome access-related participation barriers at the opportunity cost of clinical expertise and oversight. While this has not precluded beneficial health outcomes, it suggests more could be done for people who cannot attend centre-based exCR. In summary then, this thesis aims to create an intervention delivery model that combines the clinical expertise and oversight of centre-based exercise specialists with the near universal accessibility of home-based programmes. Very little research has
attempted to combine the best attributes of centre- and home-based programmes, and this will be one of the first attempts to mobilise gold standard secondary prevention practices.
CHAPTER 3. TELEHEALTH EXERCISE-BASED CARDIAC REHABILITATION: A SYSTEMATIC REVIEW & META-ANALYSIS

3.1. INTRODUCTION TO PUBLICATION

This chapter includes content from a manuscript entitled “Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis”, which was published in Heart Journal, 102(15), 1183-1192.

A substantial body of literature supports the effectiveness of exCR for CHD secondary prevention, yet utilisation remains poor in almost all countries. Telehealth technologies have demonstrated encouraging potential for delivering the core components of CR, but little is known about the use of telehealth technologies to deliver and/or monitor structured, individualised, prescriptive exercise.

This chapter presents a systematic review and meta-analysis of experimental studies that evaluated the effectiveness of telehealth exCR for modifying cardiovascular risk factor profile, in comparison to either traditional centre-based programmes or usual care.

This piece of research was undertaken to address Objective 1, which was to assess what is known about emerging technology-assisted exCR interventions, and identify gaps in the literature.

3.2. AUTHOR CONTRIBUTION

Jonathan Rawstorn developed the research question, conducted the search, selected the studies, extracted the data for the review, conducted the meta-analyses, interpreted the findings and wrote the manuscript. Co-authors contributed to study selection, data extraction, and provided editorial support for the manuscript.
Telehealth exercise-based cardiac rehabilitation: A systematic review & meta-analysis.

1,2 Rawstorn JC, 2 Gant N, 1 Direito A, 3 Beckmann C, 1 Maddison R.

1 National Institute for Health Innovation, 2 Department of Exercise Sciences, The University of Auckland, Auckland, New Zealand.

3 Department for Prevention, Rehabilitation and Sports Medicine. Technische Universität München, Munich, Germany.

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Email addresses: j.rawstorn@auckland.ac.nz, n.gant@auckland.ac.nz, a.direito@auckland.ac.nz, christina.m.beckmann@gmail.com, r.maddison@auckland.ac.nz
3.3. ABSTRACT

Objective

Despite proven effectiveness, participation in traditional supervised exercise-based cardiac rehabilitation (exCR) remains low. Telehealth interventions that use information and communication technologies to enable remote exCR programme delivery can overcome common access barriers while preserving clinical supervision and individualised exercise prescription. This meta-analysis aimed to determine the benefits of telehealth exCR on exercise capacity and other modifiable cardiovascular risk factors compared with traditional exCR and usual care, among patients with coronary heart disease (CHD).

Methods

CINAHL, The Cochrane Library, Embase, MEDLINE, PubMed, and PsycINFO were searched from inception through May 31 2015 for randomised controlled trials comparing telehealth exCR with centre-based exCR or usual care among patients with CHD. Outcomes included maximal aerobic exercise capacity, modifiable cardiovascular risk factors, and exercise adherence.

Results

11 trials (n = 1 189) met eligibility criteria and were included in the review. Physical activity level was higher following telehealth exCR than after usual care. Compared to centre-based exCR, telehealth exCR was more effective for enhancing physical activity level, exercise adherence, diastolic blood pressure, and LDL cholesterol. Telehealth and centre-based exCR were comparably effective for improving maximal aerobic exercise capacity and modifiable cardiovascular risk factors.

Conclusions

Telehealth exCR appears to be at least as effective as centre-based exCR for improving modifiable cardiovascular risk factors and functional capacity, and could substantially enhance exCR utilisation by providing additional options for patients who cannot attend centre-based exCR. Telehealth exCR must now capitalise on technological advances to provide more comprehensive, responsive and interactive interventions.
3.4. INTRODUCTION

Cardiac rehabilitation (CR) is an essential part of contemporary coronary heart disease (CHD) management that aims to optimise cardiovascular risk reduction, facilitate adoption and adherence to healthy behaviours, reduce disability, and promote an active lifestyle.[15] International guidelines recommend a multidisciplinary approach that includes patient evaluation, medical and lifestyle risk factor management, cardioprotective therapies, psychosocial management, exercise training, and health behaviour change education.[15, 16] While programmes comprising exercise training alone are not considered CR, exercise training remains a central component.[15] Exercise-based cardiac rehabilitation (exCR) is traditionally delivered in clinical or community settings by physicians, nurse specialists, physiotherapists or clinical exercise specialists,[77] and should include individualised and progressive aerobic and strength training. ExCR reduces mortality,[15, 32] can concurrently improve several modifiable cardiovascular risk factors,[14, 34, 47, 48] and is more cost-effective for increasing life expectancy than common pharmacotherapies and surgical interventions.[36]

Despite these benefits, referral and uptake of supervised centre-based exCR are inadequate.[58, 60] Common participation barriers include limited programme availability, transport restrictions, inconvenient programme scheduling, and domestic or occupational responsibilities.[64, 67] Among those who undertake centre-based exCR short and long term adherence are poor.[69, 92] Traditional centre-based exCR does not meet the needs of many eligible patients, and innovation is required to enhance utilisation.

Home-based programmes overcome traditional participation barriers [64] and provide comparable effects on mortality, recurrent coronary event risk and cardiovascular risk factors,[76] but do not provide supervision during exercise or optimally individualised exercise prescription.

Use of information and communication technologies (ICT) to augment home-based programmes, termed telehealth CR, enables provision of additional feedback, education and counselling. Systematic reviews indicate telehealth CR improves cardiovascular risk factors, health related quality of life, adverse events and cost-effectiveness;[82-84] however, few studies have used telehealth to deliver or monitor structured, individualised, prescriptive exercise training in a manner similar to centre-based exCR.
A recent meta-analysis that compared centre-based exCR with telehealth interventions that included exercise components reported comparable effects on mortality, cardiovascular events, cholesterol, blood pressure, body mass, and exercise capacity.[93] While promising, telehealth exercise components were predominantly limited to periodic assessment of exercise adherence and high level exercise prescription, and lacked delivery or monitoring of structured individualised exercise prescription.

Telehealth can combine the accessibility of home-based exCR with the specialist monitoring, interaction and support of centre-based programmes, but the effectiveness of telehealth-exCR is not well established. Therefore, the aim of this systematic review and meta-analysis was to determine the effectiveness and safety of structured telehealth exCR on maximal aerobic exercise capacity and modifiable cardiovascular risk factors, compared with traditional centre-based exCR and usual care.

3.5. METHODS

Criteria for identifying and selecting study reports, outcomes of interest, methods of data extraction, methods for assessing risk of bias, and methods for statistical analysis were pre-specified (a protocol was not published).

3.5.1 Eligibility Criteria and Search Methods

Eligible studies were randomised controlled trials (RCT) comparing secondary prevention outpatient (home- or community-based) telehealth exCR with usual care or non-telehealth centre-based exCR, among adults (≥ 18 years) with diagnosed CHD (atherosclerosis, angina pectoris, myocardial infarction or coronary revascularisation). Telehealth exCR interventions used ICT (e.g. telephone, mobile/smartphone, mobile application [app], portable computer, Internet, biosensors) to deliver or monitor structured exercise training that included prescriptive components such as frequency, level of intensity, and duration. Telehealth and centre-based exercise could be delivered alone or as part of comprehensive CR. Usual care could include standard medical care but not structured, prescriptive exercise training.

Outcomes of interest included maximal aerobic exercise capacity, modifiable cardiovascular risk factors, exercise adherence, mortality, and clinical events.
Electronic databases (CINAHL, The Cochrane Library, Embase, MEDLINE, PubMed, and PsycINFO) were searched from inception to 31/05/2015 for studies combining three subject areas, telehealth, CHD, and exercise. A search strategy was developed for MEDLINE and adapted for other databases (see Appendix 1). Searches were limited to human studies published in English. Conference abstracts and dissertations were ineligible, but authors were contacted to request full-text peer-reviewed manuscripts. Reference lists of included studies and relevant systematic reviews, meta-analyses and conference proceedings identified by the search strategy were hand searched to identify additional studies.

### 3.5.2 Data Extraction and Analysis

Search results were assessed by independent reviewers (JR, AD), and underwent full-text review if the title or abstract identified the specified population and intervention components. Data describing eligibility, study design, participant characteristics, treatment characteristics, outcome variables, results, risk of bias and sources of funding were extracted by independent reviewers (JR, AD, CB) using a standardised form. Differences in eligibility assessment or outcome data were resolved by discussion.

Where multiple reports of a single study were included relevant data were extracted from all reports. Authors were contacted to request information not presented in study reports. When possible, continuous outcomes were transformed onto uniform measurement scales. Metabolic equivalent of task (MET) was transformed to oxygen consumption (1 MET = 3.50 ml·kg⁻¹·min⁻¹). Cholesterol, triglyceride and glucose concentrations were transformed to mmol·L⁻¹ (1 mg·dl⁻¹ = 0.02586 mmol·L⁻¹, 1 mg·dl⁻¹ = 0.01129 mmol·L⁻¹, and 1 mg·dl⁻¹ = 0.05556 mmol·L⁻¹, respectively). Body mass was transformed to kg (1 lb = 0.45359 kg).

Risk of bias was evaluated (JR, CB) using the Cochrane Collaboration’s recommended tool that assesses the risk of selection, detection, attrition, and reporting biases. Performance bias was not assessed as participants and treatment delivery personnel could not be blinded to treatment allocation. Published study protocols and clinical trial registry data were sought and, when available, informed risk of bias assessment.[94] Blinding and incomplete data handling were assessed at the outcome level if required; remaining domains were assessed at the study level. Risk was judged as high, low, or unclear if data were insufficient or uncertain. The number of included studies was insufficient to detect publication bias via funnel plot.
asymmetry,[94] or the influence of risk of bias on pooled outcomes. Heterogeneity was explored qualitatively by comparing study characteristics, and quantitatively using the $\chi^2$ test and the $I^2$ statistic.

Data synthesis and analyses were conducted using Review Manager (v5.3.5, The Nordic Cochrane Centre, Copenhagen) in accordance with the Cochrane handbook.[94] Outcome data were sought at post-intervention and long-term follow-up time points. When appropriate, results were pooled across studies using a fixed effect meta-analysis model to yield overall estimates of treatment effects comparing telehealth exCR and usual care, and comparing telehealth and centre-based exCR. Differences between means and 95% confidence intervals (CI) were calculated for continuous outcomes. Outcomes that could occur more than once per participant (i.e. counts) were treated as continuous outcomes.

Differences between standardised means were calculated when pooling outcomes with non-uniform measurement scales. A random effects model was used if statistically significant heterogeneity was identified. This review includes several small trials, which can be over-weighted by a random effects model.[32] Therefore, if effect estimates remained statistically significant using a random effects model, the fixed effect estimate was reported.

Meta-analyses were stratified by type of comparison group to differentiate effects between actively and passively controlled studies. The threshold for statistical significance was set at $\alpha < .05$. Where meta-analysis was inappropriate, individual study findings are summarised narratively. If required, data describing statistical comparisons were calculated manually following accepted methods.[94]

One multi-report study[95] re-consented participants for extended follow-up. Due to attrition, subsequent study reports [96, 97] describe sub-sets of the original sample. This review includes data from the earliest possible report to include the largest proportion of the original sample. The risk of introducing selection bias was low as randomised allocation was maintained throughout, and number and reasons for attrition were balanced.
3.6. RESULTS

3.6.1 Description of Studies

Database searches identified 1555 study reports. Eleven additional reports were identified by hand searching identified systematic reviews and bibliographies of included studies, and correspondence regarding abstracts and dissertations. After removing duplicates, 102 reports underwent full review; 13 reports,[95-107] describing 11 studies (n = 1189), met the eligibility criteria and were included in the review and meta-analysis (Figure 1). Characteristics of included studies and reasons for exclusions are presented in Appendix 1.

Telehealth exCR was compared against usual care in six studies,[100, 102-105, 107] and centre-based exCR in five studies.[95, 98, 99, 101, 106]. Nine studies used a two arm, parallel RCT design.[95, 98, 100-106] Zutz and colleagues included parallel telehealth exCR and usual care arms, plus a matched historic centre-based exCR arm.[107] The non-randomised arm did not meet eligibility criteria and was excluded. Gordon and colleagues included centre-based exCR, physician-supervised nurse-case managed, and community-based arms.[99] The latter arm did not meet telehealth exCR eligibility criteria and was excluded.

Studies were conducted in Canada,[95, 104, 107] Australia,[106] Belgium,[98] Brazil,[105] France,[100] Korea,[102] the Netherlands,[101] New Zealand,[103] and the United States,[99] and published between 2002 and 2014. Sample sizes varied from 15[107] to 242.[95] Mean participant age was 58 y (range = 53 to 63 y), and most were male (75%). Participants were recruited via CR programmes,[95, 98, 101, 107] hospitals/medical centres,[102-106] and previous exCR studies.[100] Study enrolment occurred 1-2[95, 98, 106] or 3-24[103] months after admission for acute coronary syndrome or revascularisation, or after completing a CR programme.[100] Six studies did not specify post-event enrolment duration.[99, 101, 102, 104, 105, 107] Median treatment duration was 3 months (range = 1.5 to 12 months). Only two studies reported longer-term follow-up data at 6 months,[106] or 1.5 and 7.2 years post-randomisation;[95] these data are presented narratively.

Commonly used telehealth technologies were fixed-line telephone,[95, 99-102, 105, 106] biosensors (accelerometry,[98, 100, 106] heart rate)[101, 102, 107] and websites.[98, 101, 103, 104, 106, 107] Biosensor data were asynchronously uploaded to websites for review by doctors or clinical exercise specialists. Four
interventions used computers [98, 100, 101, 107] and mobile or smartphones,[98, 102, 103, 106] respectively. One intervention used mobile apps.[106]

Seven telehealth exCR interventions delivered exercise prescription and monitored exercise performance or adherence,[95, 98, 100-102, 104, 107] two delivered exercise prescription only,[99, 103] and two monitored exercise adherence only.[105, 106] Among studies that described exercise prescription parameters,[95, 99, 101, 102, 105, 106] telehealth interventions comprised ≥2 to ≥5 sessions per week, lasting 30 to 60 minutes per session. Exercise intensity level typically increased from moderate (40% to 60% peak capacity) to vigorous (70% to 85% peak capacity) throughout telehealth exCR programmes, and the predominant exercise mode was walking.

In addition, all telehealth exCR interventions included feedback, education, psychosocial support and/or behaviour change components delivered via fixed-line telephone, short message service (SMS), email, website, online tutorial or online chat. Two telehealth interventions were explicitly designed to emulate traditional models of comprehensive CR,[106, 107] Six interventions included face-to-face consultations before [98] or during [95, 99, 101, 102, 105] the programme.

Centre-based exCR programmes comprised 2 to 3 supervised sessions per week, lasting 30 to 60 minutes per session, at light (rating of perceived exertion [RPE] = 6 to 10) to moderate (RPE = 11 to 13; 60% to 85% peak capacity) levels of intensity. Centre-based exCR programmes were predominantly aerobic in nature; only one study explicitly reported a strength training component.[106]

Description of usual care varied but typically included encouragement to be physically active without participation in supervised exCR, self-initiated access to CR education classes, and psychosocial support.

3.6.2 Assessment of Risk of Bias

Limited methodological reporting impaired risk of bias assessment in several studies. Five studies were registered in a clinical trials registry [98, 101, 103, 104, 106] and two referred to peer-reviewed protocols.[101, 103] Judgements about risks of bias are presented in Appendix 1.

Six studies described methods for generating and concealing the allocation sequence.[95, 101, 103-106] Two studies reported blinded outcome assessors,[103, 104] one reported an unblinded design,[106] and remaining studies provided
Loss to follow-up varied considerably (0% to 60%). Two studies included 100% follow-up,[100, 105] two conducted intention-to-treat [103, 104] or modified intention-to-treat analyses,[98, 106] four analysed complete cases,[99, 101, 102, 107] and one multi-report study specified intention-to-treat analyses but only described missing data handling procedures in the final study report.[95] Missing data handling procedures included multiple imputation after confirming data were missing at random,[104] imputation of primary outcome data only,[95, 103, 106] and imputation for participants who were lost to follow-up but not those who withdrew.[98]

Four studies reported all specified outcomes,[99, 102, 105, 107] six did not report all specified outcomes;[98, 100, 101, 103, 104, 106] two did not report all outcomes at all specified time points,[104, 106] and one reported unspecified outcomes.[95]

Additional risks of bias included progressive attrition throughout longer-term follow-up,[95] not reporting the primary outcome specified in the study protocol,[101] altering a secondary outcome measurement instrument,[101] and altering the primary outcome.[106]

### 3.6.3 Effects of Interventions

#### 3.6.3.1. Maximal Aerobic Exercise Capacity

Seven studies reported maximal aerobic exercise capacity as maximal oxygen consumption (\( \dot{V}O_2 \max \)) or MET. Telehealth exCR was compared with centre-based exCR in four studies,[95, 98, 99, 101] and usual care in three studies.[103, 105, 107]

\( \dot{V}O_2 \max \) did not differ between telehealth and centre-based exCR (random effects weighted mean difference [WMD] = 0.85 ml·kg\(^{-1}\)·min\(^{-1}\), 95% CI -1.36 to 3.05, Figure 2), or usual care (random effects WMD = 3.72, ml·kg\(^{-1}\)·min\(^{-1}\), 95% CI -1.96 to 9.39, Figure 2). There was evidence of statistically significant heterogeneity in the centre-based (\( I^2 = 78\% \), Chi\(^2 = 13.87, \) d.f. = 3, \( P < 0.01 \)) and usual care analyses (\( I^2 = 76\% \), Chi\(^2 = 8.27, \) d.f. = 2, \( P = 0.02 \)).

Over the longer term \( \dot{V}O_2 \max \) was statistically significantly higher 1.5 and 7.2 years after randomisation to telehealth exCR compared with centre-based exCR.[95]

#### 3.6.3.2. Physical Activity Level

Five studies reported objective (daily step count,[98, 104] weekly energy expenditure)[100] or self-reported physical activity level.[103, 107] Telehealth exCR
was compared with centre-based exCR in one study,[98] and usual care in four studies.[100, 103, 104, 107]

Physical activity level was statistically significantly higher following telehealth exCR compared with centre-based exCR (fixed effect standardised mean difference [SMD] = 9.84, 95% CI 8.05 to 11.64, Figure 3) and usual care (fixed effect SMD = 0.29, 95% CI 0.07 to 0.50, Figure 3). There was evidence of statistically significant heterogeneity in the usual care comparison (I² = 79%, Chi² = 14.42, d.f. = 3, P < 0.01) but the difference remained in a random effects model.

At longer term follow-up physical activity level was statistically significantly higher 1.5 years but not 7.2 years after randomisation to telehealth exCR compared with centre-based exCR.[95]

### 3.6.3.3. Exercise Adherence

Three studies reported exercise adherence as mean weekly exercise session completion,[95] the proportion of participants completing ≥8/12 scheduled exercise sessions,[106] and the number of exercise sessions completed.[101] All studies compared telehealth and centre-based exCR.[95, 101, 106]

Exercise adherence was statistically significantly higher following telehealth exCR (fixed effect SMD = 0.75, 95% CI 0.52 to 0.98, Figure 4). There was no evidence of heterogeneity (I² = 0%; Chi² = 1.16, d.f. = 2, P = .56).

Over the longer term exercise adherence did not differ between telehealth and centre-based exCR 7.2 years post-randomisation.[95]

### 3.6.3.4. Blood Pressure

Seven studies reported systolic and diastolic blood pressure. Telehealth exCR was compared with centre-based exCR in three studies,[98, 99, 106] and usual care in four studies.[102, 103, 105, 107]

Systolic blood pressure did not differ between telehealth and centre-based exCR (random effects WMD = -0.25 mm Hg, 95% CI -3.63 to 3.13, Figure 5), or usual care (random effects WMD = -1.97 mm Hg, 95% CI -11.03 to 7.09, Figure 5). There was evidence of heterogeneity in the usual care analysis only (I² = 75% Chi² = 12.14, d.f. = 3, P = 0.01).

Diastolic blood pressure was statistically significantly lower following telehealth exCR compared with centre-based exCR (fixed effect WMD = -4.59 mm Hg, 95% CI -6.91
to -2.27, Figure 5) but not usual care (fixed effect WMD = -1.08 mm Hg, 95% CI -3.32 to 1.17, Figure 5). There was evidence of moderate heterogeneity in the usual care analysis only ($I^2 = 56\%$; $Chi^2 = 6.80$, d.f. = 3, $P = .08$).

At longer term follow-up blood pressure did not differ between telehealth and centre-based exCR 6 months post-randomisation.[106]

### 3.6.3.5. Blood Lipids

Four studies reported total (total-C), high (HDL-C) and low density lipoprotein (LDL-C) cholesterol, and triglyceride concentrations in millimoles per litre (mmol·L$^{-1}$) or milligrams per decilitre (mg·dl$^{-1}$). Telehealth exCR was compared with centre-based exCR in three studies,[98, 99, 106] and usual care in one study.[107]

When comparing telehealth and centre-based exCR there were no differences in total-C (fixed effects WMD = 0.03 mmol·L$^{-1}$, 95% CI -0.16 to 0.22, Figure 6), HDL-C (fixed effects WMD = -0.00 mmol·L$^{-1}$, 95% CI -0.08 to 0.07, Figure 6), or triglyceride concentrations (fixed effects WMD = -0.03 mmol·L$^{-1}$, 95% CI -0.14 to 0.21, Figure 6). There was no evidence of heterogeneity for these analyses. LDL-C concentration was statistically significantly lower following telehealth exCR compared with centre-based exCR (fixed effects WMD = -0.15 mmol·L$^{-1}$, 95% CI -0.29 to -0.01, Figure 6); there was evidence of heterogeneity ($I^2 = 68\%$; $Chi^2 = 6.21$, d.f. = 2, $P = .04$).

When comparing telehealth exCR and usual care there were no differences in total-C (fixed effects WMD = -0.49 mmol·L$^{-1}$, 95% CI -1.00 to 0.02, Figure 6), HDL-C (fixed effects WMD = 0.07 mmol·L$^{-1}$, 95% CI -0.30 to 0.44, Figure 6), LDL-C (fixed effects WMD -0.38 mmol·L$^{-1}$, 95% CI -0.81 to 0.05, Figure 6), or triglyceride concentrations (fixed effects WMD = -0.53 mmol·L$^{-1}$, 95% CI -1.27 to 0.21, Figure 6).

In the longer term blood lipid concentrations did not differ between telehealth and centre-based exCR 6 months post-randomisation.[106]

### 3.6.3.6. Body Composition

Six studies reported body composition as body mass index (BMI), body mass, waist and hip circumferences and waist-to-hip ratio. Telehealth exCR was compared with centre-based exCR in four studies,[95, 98, 99, 106] and usual care in two studies.[103, 107] BMI and body mass were pooled, with BMI in preference to body mass as it is the preferred indicator of cardiovascular risk.[108] Additional body composition data are presented in Appendix 1. One study [99] reporting changes
from baseline could not be included in the pooled analysis of standardised mean differences.[94]

Body composition did not differ between telehealth and centre-based exCR (random effects SMD = 0.15, 95% CI -0.47 to 0.76, Figure 7), or usual care (random effects SMD = -0.05, 95% CI -0.34 to 0.41, Figure 7). There was evidence of heterogeneity in the centre-based analysis only ($I^2 = 86\%$; $Chi^2 = 14.22$, d.f. = 2, $P < .001$).

Two studies compared body composition between telehealth and centre-based exCR at longer-term follow-up; Arthur and colleagues reported statistically significantly lower body composition 1.5 but not 7.2 years post-randomisation to telehealth exCR;[95] Varnfield and colleagues reported no differences between groups 6 months post-randomisation.[106]

3.6.3.7. **Blood Glucose**

Only one study compared blood glucose and glycated haemoglobin (HbA1c) concentrations between telehealth and centre-based exCR.[98] There were no differences in between groups (see Appendix 1).

3.6.3.8. **Clinical Events**

Six studies reported clinical events including mortality,[104] coronary events,[105] cardiac events,[103] revascularisation,[103, 104, 106] rehospitalisation,[98, 103, 104] and total adverse events.[101]. Telehealth exCR was compared with centre-based exCR in three studies,[98, 101, 106] and usual care in three studies.[103-105] Given the heterogeneity of outcomes a meta-analysis across all studies was not appropriate; individual study data are summarised in Appendix 1; conclusions about treatment effects were not drawn due to the small numbers of events in each study.
Figure 1 Summary of the study selection process

Figure 2 Forest plot for maximal aerobic exercise capacity

TexCR and CBexCR = telehealth and centre-based exercise-based cardiac rehabilitation, respectively
Figure 3 Forest plot for physical activity level

TexCR and CBexCR = telehealth and centre-based exercise-based cardiac rehabilitation, respectively

Figure 4 Forest plot for exercise adherence

TexCR and CBexCR = telehealth and centre-based exercise-based cardiac rehabilitation, respectively
Figure 5 Forest plots for systolic (A) and diastolic (B) blood pressure

**TexCR and CBexCR = telehealth and centre-based exercise-based cardiac rehabilitation, respectively**
Figure 6 Forest plots for total cholesterol (A), high density lipoprotein cholesterol (B), triglyceride (C), and low density lipoprotein cholesterol (D) concentrations

TexCR and CBexCR = telehealth and centre-based exercise-based cardiac rehabilitation, respectively
Figure 7 Forest plot for body composition

TexCR and CBexCR = telehealth and centre-based exercise-based cardiac rehabilitation, respectively
3.7. DISCUSSION

To our knowledge this is the first systematic review and meta-analysis to examine the use of telehealth specifically for delivering and monitoring structured, individualised, prescriptive exercise in a CHD population. Eleven RCTs (n = 1 189) were included in the review. The main findings were that telehealth exCR appears to be at least as effective, and in some cases more effective, for improving cardiovascular risk factors and functional capacity, although there was some evidence of heterogeneity between studies. Characteristics of the telehealth platforms likely influence the intensity of telehealth exCR interventions and may contribute to the variability; the influence of telehealth platform characteristics on intervention delivery and effectiveness warrants further consideration.

3.7.1 Telehealth exCR vs Usual Care

Compared to usual care, telehealth exCR appears more effective for improving physical activity level, but no differences were observed for other outcomes. As beneficial effects of exCR on exercise capacity, blood pressure, blood lipid concentrations, and body composition are well documented [33, 34, 109] these null meta-analytical effects were unexpected, though not without precedent in the literature.[110] The unexpected findings may be partly accounted for by the small number of usual care-controlled studies, and characteristics that influence the intensity of telehealth exCR interventions. The small number of included studies may have been insufficient to detect intervention effects. Further, exercise-induced physiological adaptations are dose-dependent [38] and intervention intensity is likely affected by study-specific characteristics such as exercise prescription, choice and implementation of different telehealth technologies, and intervention engagement or appeal. Characteristics of telehealth exCR interventions in usual care-controlled studies may have provided insufficient intervention intensity to augment the beneficial effects of medicines that are routinely prescribed to CHD patients.

3.7.2 Telehealth exCR vs Centre-based exCR

Compared to centre-based programmes, telehealth exCR appears more effective for improving physical activity level, exercise adherence, diastolic blood pressure, and LDL cholesterol concentration. No statistically significant differences were observed for other outcomes. These findings are largely consistent with previous comparisons of telehealth CR[93] and home-based exCR[77, 110, 111] against centre-based exCR, and provide promising early evidence that telehealth exCR may be a suitable
and effective alternative option for patients who are unable or unwilling to attend centre-based programmes.

Higher physical activity and exercise adherence reinforce the potential for telehealth to transform exCR accessibility and promote positive lifestyle behaviour change. Structured, individualised, prescriptive exercise training has traditionally been provided by exercise specialists via centralised clinical facilities; telehealth exCR reverses this paradigm by distributing specialists’ expertise from clinical centres to any location with fixed and/or mobile communications. This simultaneously overcomes common participation barriers, provides opportunities to augment existing home-based interventions, and enables scaling of programme availability to meet the needs of many more patients. This is particularly important for rural and remote regions that have limited access to exCR,[112] but will also benefit metropolitan areas by reducing or eliminating travel requirements and allowing more flexible delivery of programme content. Centralised programme delivery may also have economic benefits, but this yet to be examined.

While the results of this review at times favour telehealth exCR it is important to note telehealth should be viewed as a compliment to existing home and centre-based exCR, rather than as a replacement. Researchers have questioned whether telehealth should become the new standard [85] but there remains demand for centre-based programmes.[75] Telehealth exCR is best viewed as an additional option for patients whose needs are not met by existing services. As a complimentary option telehealth exCR can augment home-based programmes, help to broaden the reach of exCR, and may also assist patients' transition from supervised centre-based exCR into sustainable, independent exercise.

### 3.7.3 Opportunities for Future Development

By shifting exCR out of clinical settings telehealth exCR faces substantial challenges to provide monitoring and support that align with international exCR guidelines. Technological advances can enable more comprehensive, responsive and interactive telehealth exCR programme delivery[85, 91] yet characteristics of the studies included in this review suggest there has been little technological innovation since an early review of telehealth CR in 2009.[82] Most interventions were based on telephone counselling, with some use of SMS and email. The utility of biosensors was constrained by asynchronous data uploading that prevented timely monitoring and feedback from exCR specialists. Asynchronous monitoring augments early
models of home-based exCR, but technological advances that align with centre-based exCR monitoring practices, enhance safety and guide optimal individualisation of exercise prescription have yet to be capitalised on. Mobile sensor and communication (e.g. smartphones) technologies enable real-time remote monitoring of physiological responses and provision of instantaneous feedback during exercise. The capability for exCR specialists to measure exercise parameters and prompt modification of exercise behaviour while participants are exercising would provide substantially greater opportunity to individualise exercise prescription, optimise intervention intensity and enhance dose-dependent health outcomes. Further, patients’ knowledge they were being monitored in real-time by exCR specialists may provide reassurance, enhance exercise self-efficacy, and enhance social support; this may be particularly beneficial for individuals with low exercise self-efficacy or anxiety about returning to exercise after a cardiac event.

Some latency can be expected between technological advances, deployment in intervention studies, and appearance in the published literature. Several studies have demonstrated the feasibility of real-time remote monitoring technologies for telehealth exCR,[67, 113, 114] but effectiveness, usability and safety have yet to be assessed in intervention studies. Evaluation studies are currently in progress,[115] but realising the potential of existing and emerging technologies remains a priority for the future development of telehealth exCR.

3.7.4 Limitations

Interpretation of the review findings is limited by the small number of included studies, small sample sizes in several studies, and methodological limitations of the included studies. Telehealth is a young and rapidly evolving field and the number of studies evaluating telehealth exCR interventions is likely to increase as technology platforms mature; at least three trials are currently in progress,[115-117] although not all include real-time remote exercise monitoring or feedback. Emerging research will help to clarify the promising findings of this review.

Study methods were often not well described. Several studies were judged to have high risks of bias, although some flaws were unlikely to affect outcomes of interest in this review. Only English language studies were included; however, language-restriction does not bias estimates of intervention effectiveness.[118] Several meta-analyses were affected by statistical heterogeneity, possibly due to varying intervention length, frequency, and intensity, and telehealth technology utilisation.
Few studies reported longer term follow-up data and the sustainability of telehealth exCR effects remains unclear; however, promising results from individual studies indicate telehealth exCR is at least as effective for sustaining several outcomes of interest. As participants were predominantly male, low-to-moderate risk, and relatively young; generalisability to female, higher risk, and older aged individuals is limited.

### 3.7.5 Conclusions

Telehealth exCR appears to be at least as effective as centre-based exCR for supporting improvements in factors that contribute to cardiovascular risk and functional capacity, and simultaneously overcomes common barriers that limit participation in centre-based programmes. Telehealth exCR could substantially enhance exCR utilisation by providing additional options for patients whose needs are not met by existing services. The challenge is now to capitalise on advances in mobile sensor and communication technologies that enable more comprehensive, responsive and interactive intervention delivery.
3.8. COMPETING INTERESTS

RM and JR are co-authors on one included study.[103] Decisions regarding eligibility for inclusion, risk of bias, and data extraction were verified independently by AD and CB. The authors have no other competing interests to declare. No specific funding was received to support the preparation of this review.

3.9. CONTRIBUTORSHIP STATEMENT

JR, NG and RM designed the review. JR, AD and CB screened articles and extracted the data. JR analysed the data. All authors contributed to the interpretation of results, manuscript preparation, and final aproval. We (authors) accept accountability for all aspects of the work.

3.10. DATA SHARING STATEMENT

This review summarises results from previously published research. Individual study data can be extracted from original publications; some unpublished data were obtained from study authors. There are no unpublished original data available for this review.

3.11. PERMISSION TO PUBLISH

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or nonexclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article (if accepted) to be published in HEART editions and any other BMJPGL products to exploit all subsidiary rights.
CHAPTER 4. TELEHEALTH PLATFORM DESIGN & DEVELOPMENT

4.1. INTRODUCTION TO PUBLICATION

This chapter includes a content from a manuscript entitled “Remotely delivered exercise-based cardiac rehabilitation: design and content development of a novel mHealth platform”, which was published in the Journal of Medical Internet Research: mHealth and uHealth, 4(2):e57.

The small number of eligible studies identified in the meta-analysis (Chapter 3) demonstrated telehealth exCR research is in its infancy. Yet promising early findings demonstrate beneficial effects on cardiovascular risk factors that appear to be at least as good as traditional centre-based programmes. The paucity of research highlights the need for innovative telehealth approaches. Further, there are substantial opportunities to enhance intervention quality by moving beyond traditional telecommunication tools, and capitalising on recent advances in wearable sensor and mobile communication technologies.

This chapter describes the development of a novel real-time exercise monitoring platform and intervention content, including the scientific rationale, which was custom designed for remotely delivered exCR.

This piece of research was undertaken to address Objective 2, which was to design and develop an alternative model for delivering exCR that addresses emerging opportunities.

4.2. AUTHOR CONTRIBUTION

Jonathan Rawstorn was responsible for the design specification of the remote monitoring platform, and development of the intervention content. Co-authors contributed to technical platform development and testing, and provided editorial support for the manuscript.
Remotely delivered exercise-based cardiac rehabilitation: design and content development of a novel mHealth platform.

1,2Rawstorn JC, 2Gant N, 3Meads A, 3Warren I, 1Maddison R

1National Institute for Health Innovation, 2Department of Exercise Sciences, 3Department of Computer Science, The University of Auckland, Auckland, New Zealand.

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Email addresses: j.rawstorn@auckland.ac.nz, n.gant@auckland.ac.nz, andrew.meads@auckland.ac.nz, i.warren@auckland.ac.nz, r.maddison@auckland.ac.nz
4.3. ABSTRACT

Introduction

Participation in traditional supervised, centre-based exercise cardiac rehabilitation is limited by numerous barriers, including factors related to programme accessibility. Mobile health (mHealth) technologies can overcome common access barriers while preserving critical attributes of centre-based exCR, exercise monitoring and coaching, but these opportunities have not yet been capitalised on. This paper outlines the development of an evidence- and theory-based mHealth exCR platform (REMOTE-CR) that provides real-time remote exercise monitoring and coaching, behaviour change education, and social support in almost any location.

Design

The REMOTE-CR platform comprises a commercially available smartphone and wearable sensor, custom smartphone and web-based applications (apps), and a custom middleware. The platform allows exCR specialists to monitor participants’ exercise and provide individualised coaching in real-time, and provide behaviour change education and social support. Intervention content incorporates Social Cognitive Theory, Self-determination Theory, and a taxonomy of behaviour change techniques. Exercise components are based on guidelines for clinical exercise prescription.

Discussion

The REMOTE-CR platform extends the capabilities of previous telehealth exCR platforms and narrows the gap between existing centre- and home-based exCR services. REMOTE-CR can complement centre-based exCR by providing an alternative option for people whose needs are not currently being met. Remotely monitored exCR may be more cost-effective than establishing additional centre-based programmes.
4.4. INTRODUCTION

Coronary heart disease (CHD) is a leading cause of mortality and morbidity worldwide. CHD accounts for 1 in 7 deaths in the United States, approximately 1 in 20 adults have diagnosed CHD, and prevalence is expected to increase ≈18% by 2030.[5] Further, people with CHD account for more than 40% of all CHD events, more than 35% of non-fatal myocardial infarction, and more than 50% of fatal coronary events.[8] This emphasises a need for effective secondary prevention programmes that target modifiable cardiovascular risk factors in order to reduce the risk of recurrent cardiac events and mortality.

Cardiac rehabilitation (CR) is an essential component of contemporary cardiac care, and exercise training is consistently identified as a central element in international guidelines.[15, 29, 30] Exercise-based cardiac rehabilitation (exCR) is commonly delivered in hospitals and rehabilitation clinics (centre-based exCR) and should include a progressive programme of aerobic and strength training that is individualised based on clinical status, risk stratification, comorbidities, and goals.[15] ExCR improves all-cause and cardiac mortality, recurrent cardiac event risk, several modifiable cardiovascular risk factors and exercise capacity,[14, 30, 32, 34, 47, 48] and is more cost-effective for reducing premature death than most common pharmacological and surgical interventions.[36] However, referral rates and uptake of exCR are low,[36, 60, 119] and participation is commonly limited by programme availability, transport restrictions, inconvenient programme scheduling, and domestic or occupational responsibilities.[64, 67] These barriers suggest accessibility is a primary factor limiting utilisation of traditional centre-based exCR programmes and overcoming participation barriers should be prioritised as non-attendance is associated with poorer risk factor knowledge and risk profile.[68]

Home-based exCR programmes enhance accessibility[76] and provide comparable health benefits,[77] but cannot deliver the supervision, feedback and individualised coaching provided by exCR specialists during centre-based exCR. These limitations preclude optimal individualisation of exercise prescription and may limit improvements in modifiable cardiovascular risk factors and functional capacity.[18, 38]

Information and communication technologies (ICT) offer opportunities to augment home-based exCR by connecting exCR specialists with participants outside the traditional clinical environment. These telehealth-assisted programmes have
commonly utilised fixed-line telephones, email and mobile phone short message service (SMS) to deliver motivational support, behavioural change counselling, and feedback about goal achievement or exercise adherence.[95, 98-107] Additional telehealth interaction between participants and exCR specialists augments early home-based exCR programmes, and secondary prevention effects appear promising. However, constraints of the telehealth technologies have limited programme flexibility and been unable to emulate the exercise supervision, coaching, and individualisation that is typical of centre-based exCR. Some telehealth exCR platforms have enabled participants to upload accelerometer or heart rate data to web-based portals for review by exCR specialists.[98, 100-102, 106, 107] However, asynchronous uploading of data has limited the utility of these platforms to high level review of physical activity, and adherence.

To date telehealth exCR has been unable to provide exercise monitoring, feedback, coaching and individualised exercise prescription in a manner consistent with best-practice or international CR guidelines; however, rapid advances in mobile sensor and communication technologies can help to bridge this gap. Increasingly powerful smartphones, rapid mobile broadband connection speeds, and interoperable wearable sensors mean the technological capability for real-time remote exercise monitoring and coaching is now readily available. Smartphones are appealing for health intervention delivery as they enable provision of individualised and timely intervention content.[119] Moreover, rapid growth in smartphone ownership (≈75% in many countries), mobile broadband subscriptions (80% in developed countries), and coverage (70% and 90% of the total and urban global population, respectively) [88-90] suggest the time is right to introduce more sophisticated telehealth exCR platforms that can optimise programme flexibility, accessibility, responsiveness, and individualisation. This is supported by results from several studies that indicate telehealth exCR has beneficial effects on modifiable cardiovascular risk factors,[95, 98-107] but intervention characteristics are likely constrained by telehealth platforms that don’t enable sufficient individualisation of exercise prescription or monitoring of exercise performance.[103] Further, predominant reliance on fixed-line telephone communications in previous telehealth exCR interventions constrains people within the home environment, and limits programme flexibility.

The feasibility of more advanced mobile health (mHealth) exCR platforms comprising wearable sensors, smartphones and real-time remote data transmission has been demonstrated, [67, 114] but only one evaluation study has been published. Real-time remotely monitored exercise appears to improve sub-maximal aerobic exercise
capacity and health-related quality of life (HRQoL); [102] however, real-time monitoring was only sustained for two weeks and it was unclear whether exCR specialists used the data to inform real-time individualised feedback or coaching. One of these platforms is currently being evaluated in a non-inferiority randomised controlled trial comparing mHealth and centre-based exCR.[115]

Embracing advances in wearable sensor and mobile communications technologies can enable mHealth exCR to combine the universal accessibility of home-based exCR with the clinical expertise, supervision, and coaching that has traditionally been limited to centre-based exCR. To date these opportunities have not been capitalised on; addressing these opportunities could substantially increase the reach of exCR by providing more flexible, responsive, and interactive alternatives to existing centre- and home-based programmes. This paper describes the development of an mHealth exCR platform designed to address these limitations. The paper begins by defining the main platform design objectives and describing how components of an mHealth CR development framework were integrated into the design process. Subsequent sections outline the platform design, including the technology components and intervention content development.

4.5. DESIGN OBJECTIVES

The primary purpose of the mHealth exCR platform was to overcome accessibility barriers that limit centre-based exCR participation while retaining the clinical expertise provided by exCR specialists during centre-based programmes. As such the major platform design objectives were to provide universal access to real-time exercise monitoring, coaching and feedback, and theory-based behaviour change strategies. In achieving these objectives we aimed to develop an alternative option for the large number of people with CHD whose needs are not currently being met by centre-based exCR programmes.

We developed an mHealth exCR platform, named REMOTE-CR, that integrates smartphones, wearable sensors and custom smartphone and web-based apps to provide real-time remote exercise monitoring, evidence-based exercise prescription and coaching, theory-based behaviour change education, and social support to CHD outpatients in almost any location. REMOTE-CR was designed to align with evidence-based exCR guidelines, optimise ease of use and allow rapid scalability, as these characteristics will likely facilitate transition into practice.[120]
4.6. DEVELOPMENT FRAMEWORK

A recently proposed mHealth CR development and evaluation framework suggests CR interventions should address the core components of CR, apply behaviour change theory, enable individual tailoring of features, demonstrate high usability, and be evaluated in a randomised controlled trial that assesses patient-centred outcomes.[121] The design, development and subsequent evaluation of REMOTE-CR were based on this framework, with appropriate adaptations to suit the intended design objectives.

4.6.1 Core Components Of Cardiac Rehabilitation

Core components of CR include patient evaluation, medical and lifestyle risk factor management, cardioprotective therapies, psychosocial management, exercise training, and health behaviour change education.[15, 16] Many traditional centre-based exCR programmes focus on exercise training and physical activity counselling, while other core components may be delivered via alternative channels such as outpatient clinics and group seminars. As REMOTE-CR is intended to provide an alternative to traditional centre-based exCR programmes, platform features are also focused on exercise training and physical activity behaviour change. By aligning REMOTE-CR with the format of centre-based exCR we aimed to increase the likelihood of transition into practice, an approach that has previously been recommended for the development of health behaviour change interventions.[120] Although REMOTE-CR does not currently include additional core CR components the platform architecture was designed to enable modular expansion in future iterations. An initial focus on exercise training and physical activity behaviour change was also intended to facilitate robust evaluation of remotely delivered exCR in comparison to centre-based programmes.

4.6.2 Behaviour Change Theory

Theory based interventions are considered more effective than those without theoretical underpinning, and integrating principles from behaviour change theories into mHealth intervention design may significantly increase the likelihood of success.[122, 123] Development of the REMOTE-CR platform and intervention content were informed by behaviour change theories including Social Cognitive Theory and it’s key component self-efficacy,[124] Self-determination Theory,[125, 126] and a taxonomy of behaviour change techniques.[127]
Self-efficacy refers to individuals’ perceptions they can control their health behaviours;[128] higher levels of self-efficacy are expected to facilitate behaviours that help to maintain self-regulated motivation such as setting goals, creating incentives, and seeking social support.[129] Sources of self-efficacy information include performance accomplishment, vicarious experience, verbal persuasion, and physiological cues. Self-efficacy influences exercise initiation and maintenance,[130, 131] physical activity level [132] and clinical outcomes,[133] is one of the most commonly examined psychological variables in the cardiac setting, and is a recommended interventional component in New Zealand CR guidelines.[18]

Self-determination Theory proposes motivational orientation lies on a continuum anchored by intrinsic and extrinsic motivation, where individuals’ orientation is determined by effects of environmental and individual factors on the satisfaction of three basic psychological needs: autonomy, competence, and relatedness.[125, 126, 134] Briefly, intrinsic motivation refers to the pursuit of internal outcomes such as accomplishment, development, and satisfaction; conversely, extrinsic motivation refers to the pursuit of external outcomes such as tangible or social rewards.[134] Autonomy refers to a sense of regulating one’s own behaviour, competence refers to a sense one’s actions are effective, and relatedness refers to a sense of connection with others in a specific setting.[125, 126] Competence shares fundamental similarities with self-efficacy as both constructs reference perceived confidence in task-specific success, and are informed by performance accomplishment. Perceptions of autonomy, competence and relatedness are influenced by physical and social environmental factors, individuals’ motives for undertaking exercise, and their propensity to pursue intrinsic or extrinsic directives.[134] A comprehensive meta-analysis examining the influence of self-determination on exercise behaviour associated more self-determined motivational orientations with superior exercise adoption and long term adherence.[134] Further, some evidence suggests self-determined motivation has a greater effect on exercise adherence than self-efficacy.[131]

While Social Cognitive Theory and Self-determination Theory served as the theoretical constructs underlying design and development of REMOTE-CR, they do not provide tangible or identifiable intervention components, per se. A taxonomy of behaviour change techniques has been developed to identify, define and categorise active intervention components that are designed to alter processes that underlie behaviour regulation.[127] The taxonomy defines 93 behaviour change techniques across 16 categories. Behaviour change techniques that support REMOTE-CR’s
underlying theoretical constructs (i.e. self-efficacy and self-determination) were adapted as required to suit the technological requirements of the REMOTE-CR platform. In total REMOTE-CR includes 24 behaviour change techniques from 10 categories (Table 1). Behaviour change techniques were integrated throughout the REMOTE-CR platform, including the intervention content and features of the participant-facing smartphone app and exCR specialist-facing web-based app.

4.6.3 Individualisation And Usability

A review of mHealth behaviour change suggests individualised interventions are more effective at changing behaviour, although few interventions have implemented tailored components.[135] The accessibility of mobile platforms may encourage greater use of tailored features,[121] and the REMOTE-CR was designed to include several individualised components including exercise prescription, exercise performance feedback, exercise coaching, goal setting and achievement feedback, and social support. Further details about platform features are provided in the following section.

People with CHD are typically older aged, and use of smartphones and wearable sensors presents substantial usability challenges that may impact on adoption and adherence. Factors that facilitate mHealth exCR usability are not well defined;[121] however, features such as automated and/or wireless data entry promote ease of use.[136] REMOTE-CR features have been designed to minimise required user input in order to aid usability. The smartphone app was designed with a simple, intuitive user interface; navigational complexity was minimised. Functionality has been automated where possible, including tasks such as connecting the smartphone and wearable sensor, recording exercise data, and presenting goal achievement feedback. Further, a custom middleware platform was implemented to manage lower level functions such as authentication, encryption, and connectivity. Appropriate training is also likely to alleviate usability challenges.[137] A face-to-face training module was developed to explain REMOTE-CR platform functionality, and provides opportunities for demonstration and hands on practice. The training module is supported by an illustrated user guide that comprehensively documents platform functionality, and email or telephone support as required (Appendix 1).

4.6.4 Evaluation Of Patient-centred Outcomes

REMOTE-CR has been designed to provide an alternative to traditional centre-based exCR. Prior to recommending mHealth exCR it will be necessary to determine how
the programme compares with existing programmes. As such a non-inferiority randomised controlled trial comparing mHealth and centre-based exCR was planned. This intended evaluation informed aspects of platform and intervention content design, such as exercise prescription, monitoring and coaching, intervention content, and intervention duration. The planned evaluation is currently in progress. In line with the adopted mHealth development framework,[121] the evaluation will assess patient-centred outcomes such as participation, physical activity level, exercise capacity, modifiable cardiovascular risk factors, quality of life, cost, and cardiovascular events. Further details are provided in the trial protocol.[115]

Table 1 REMOTE-CR behaviour change techniques

<table>
<thead>
<tr>
<th>Category</th>
<th>Behaviour Change Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1a,b Goals &amp; planning</td>
<td>Goal setting (behaviour)</td>
</tr>
<tr>
<td>1.2c</td>
<td>Problem solving</td>
</tr>
<tr>
<td>1.3c</td>
<td>Goal setting (outcome)</td>
</tr>
<tr>
<td>1.4a,c</td>
<td>Action planning</td>
</tr>
<tr>
<td>1.5a,b,c</td>
<td>Review behaviour goal(s)</td>
</tr>
<tr>
<td>1.6a,b</td>
<td>Discrepancy between current behaviour &amp; goal</td>
</tr>
<tr>
<td>2.1a,b Feedback &amp; monitoring</td>
<td>Monitoring of behaviour by others without feedback</td>
</tr>
<tr>
<td>2.2a,b</td>
<td>Feedback on behaviour</td>
</tr>
<tr>
<td>2.3a</td>
<td>Self-monitoring of behaviour</td>
</tr>
<tr>
<td>2.4a,c</td>
<td>Self-monitoring of outcome(s) of behaviour.</td>
</tr>
<tr>
<td>2.6a</td>
<td>Biofeedback</td>
</tr>
<tr>
<td>3.1a,b,c Social Support</td>
<td>Social support (unspecified)</td>
</tr>
<tr>
<td>3.3a,b,c</td>
<td>Social support (emotional)</td>
</tr>
<tr>
<td>4.1a,b,c Shaping knowledge</td>
<td>Instruction on how to perform a behaviour</td>
</tr>
<tr>
<td>5.1a,b,c Natural consequences</td>
<td>Information about health consequences</td>
</tr>
<tr>
<td>8.1a</td>
<td>Repetition &amp; substitution</td>
</tr>
<tr>
<td>8.6a</td>
<td>Behavioural practice/rehearsal</td>
</tr>
<tr>
<td>8.7b</td>
<td>Generalisation of a target behaviour</td>
</tr>
<tr>
<td>9.1a,b,c Comparison of outcomes</td>
<td>Credible source</td>
</tr>
<tr>
<td>10.4b</td>
<td>Reward &amp; threat</td>
</tr>
<tr>
<td>10.9c</td>
<td>Social reward</td>
</tr>
<tr>
<td>13.2b</td>
<td>Identity</td>
</tr>
<tr>
<td>15.1b</td>
<td>Self-belief</td>
</tr>
<tr>
<td>15.3c</td>
<td>Verbal persuasion about capability</td>
</tr>
<tr>
<td>a Participant-facing smartphone app</td>
<td>Focus on past success</td>
</tr>
<tr>
<td>b exCR specialist-facing web-based app</td>
<td></td>
</tr>
<tr>
<td>c Behaviour change education content</td>
<td></td>
</tr>
</tbody>
</table>
4.7. PLATFORM DESIGN

Previous mHealth exCR platforms have provided limited exercise monitoring, feedback and coaching capabilities, and this may limit intervention effectiveness in terms of exercise-induced risk factor modification.[103] To address these limitations REMOTE-CR integrates advances in wearable sensor and mobile communications technologies to provide enhanced exercise training and physical activity behaviour change capabilities similar to those provided by traditional centre-based exCR programmes. Components of the REMOTE-CR platform design are described below.

4.7.1 Platform Components

The REMOTE-CR platform comprises a commercially available Android-based smartphone and wearable sensor, custom smartphone and web-based apps, and a custom middleware platform (Figure 8).

Smartphones were considered the optimal communications platform as near ubiquitous mobile broadband availability in many developed countries allows mHealth exCR to be delivered to individuals in almost any location. The Android smartphone operating system (Google Inc., USA) was selected as the basis for the REMOTE-CR smartphone app because it has a majority share of the smartphone operating system market [138] and has the widest range of smartphone handsets, including many low priced models. These attributes ensure REMOTE-CR could be accessible to a broad range of individuals, and will aid translation into practice.

The BioHarness 3 wearable sensor (Zephyr Technology, USA) was selected because its multi-sensor array is well suited for monitoring exercise among people with CHD, inbuilt Bluetooth connectivity enables integration with almost all current smartphones, and commercial availability will assist accessibility and translation into practice. The BioHarness sensor array quantifies electrocardiogram (ECG, including waveform data), heart rate, heart rate variability, respiratory rate, torso posture, and tri-axial acceleration. The capability to monitor heart rhythm in addition to the more ubiquitous heart rate, and respiratory rate were considered advantageous for monitoring cardiovascular workload during exercise among people with CHD. Previous versions of the BioHarness have been validated,[139-144] and a validation of the BioHarness 3 was conducted as part of the REMOTE-CR development process.[114]

The custom software components of the REMOTE-CR platform include a middleware named Odin, a participant-facing Android smartphone app, and a clinical exCR
specialist-facing web-based app. All software components were designed and built by the research team. The Odin middleware sits between smartphone and server-side software to manage communication and logistic functions including data security, network connectivity and device resource usage.[145, 146] By isolating lower level functionalities from the smartphone and web-based apps, Odin enabled development of the participant- and specialist-facing apps to focus on optimising features for mHealth exCR. Further, iterative refinements to the Odin middleware can be rapidly integrated into the REMOTE-CR platform without requiring substantial changes to the smartphone or web-based apps.

The REMOTE-CR smartphone app [147] has been built for Android version 4.0 or higher, which includes most Android smartphones released since 2012. The smartphone app underwent an iterative development process, and was included in a validation of the REMOTE-CR platform in order to determine real-time data transmission reliability.[114] The web-based app is accessible via any internet browser, including desktop and mobile browsers, and does not require installation of specialised software. This enables true mobile capability for both participant- and specialist-facing apps, and allows the REMOTE-CR platform to operate from any location in which the participant and specialist have a mobile or local internet connection. To address the overall design objectives the smartphone and web-based apps were designed to include components that enable real-time remote exercise monitoring and coaching, retrospective exercise performance review, goal setting, behaviour change education, and social support. Specific components of the smartphone and web-based apps are described below, including links to underlying theory- and evidence-based constructs. When possible, related participant- and specialist-facing components have been described together to reinforce the connected, interactive context of the platform.

### 4.7.2 Real-time Remote Exercise Monitoring And Coaching

Exercise monitoring and coaching capabilities have been modelled on centre-based exCR, where exCR specialists provide participants with face-to-face supervision, individualised coaching, behaviour change education and social support. Real-time remote exercise monitoring and coaching is expected to allow more responsive and individualised management of participants’ exercise training in comparison to previous telehealth exCR platforms where specialist interaction with participants has commonly been periodic, and based on asynchronous measurement of physical activity level or exercise adherence. Responsive supervision and coaching will help
to maximise the benefits of exercise with gradual and appropriate progression of exercise prescription parameters, and teach participants how to manage their exercise within suitable ranges of duration and intensity level.\[18\]

A dedicated exercise monitoring component of the participant-facing smartphone app receives wearable sensor data via Bluetooth. Sensor data are displayed continuously alongside geolocation data (provided by the smartphone) and an aggregate measure of training load (i.e. exercise dose).\[148\] The display configuration can be customised to suit participants’ preferences (Appendix 2). Participants initiate real-time data transmission to a remote web server when ready to begin exercise, and all data are synchronised with a secure web server in real-time. Participants are initially greeted with a message from exCR specialists that includes individualised exercise prescription parameters and behaviour change content. Throughout exercise, participants continue to receive individualised messages from exCR specialists via the smartphone app; messages include coaching, feedback about adherence to individualised exercise prescription parameters, encouragement and social support. Real-time interaction allows for responsive modification of exercise behaviour, and provision of individualised competence information that supports exercise-related confidence (i.e. self-efficacy, perceived competence). Immersive real-time social support is expected to enhance perceptions of relatedness. Remotely monitored exCR inherently supports perceived autonomy in a way that face-to-face supervision may not, as participants will develop exercise behaviours in ‘real-world’ environments that remain accessible beyond the duration of the programme. This may streamline the transition to independent exercise, and promote longer term exercise adherence.

During exercise participants can report cardiovascular symptoms including angina, dyspnoea, and light headedness, using an accepted clinical symptom rating scale that has been adapted for use on smartphones.\[149\] ECG waveform data are not transmitted continuously to manage mobile broadband bandwidth requirements but all symptom reports are accompanied by an ECG rhythm strip, and exCR specialists can access on-demand ECG data whenever required via the web-based app.

The exercise monitoring component of the specialist-facing web-based app continuously retrieves participants’ exercise data from a secure web server and visualises them for real-time review. ExCR specialists view participant data within individual monitoring panes that display instantaneous data for all exercise variables, and a configurable time-series graph to enable trend analysis. Simultaneous monitoring of multiple participants is supported. Exercise intensity level is displayed
as a percentage of heart rate reserve (%HRR, the proportional difference between rest and maximal exercise heart rates), which is a more accurate indicator of metabolic demands than a percentage of maximal heart rate. Further, this method simplifies individualisation as exCR specialists are not required to recall resting and maximal exercise data for each participant. If required parameters that underpin %HRR can be edited in the smartphone app. Separate monitoring panes in the web-based app display participants’ location, notification events, and on-demand ECG data (Appendix 2). Location monitoring enables exCR specialists to consider effects of terrain on exercise responses, integrate local terrain into exercise prescription management, and provide accurate information if an emergency response is required. Notification events include newly initiated exercise training sessions, individualised exercise threshold alerts, and participant-reported cardiovascular symptoms. Exercise alert thresholds can be used to identify participants who are noncompliant with prescribed exercise parameters and improve efficiency during multi-user monitoring by allowing exCR specialists to prioritise attention on participants who need the closest supervision.

The web-based app enables exCR specialists to provide participants with real-time individualised coaching, feedback, social support, and instructions related to cardiovascular symptoms via a text-to-audio messaging system. Written messages are processed by a text-to-audio converter before being presented to participants in real-time, typically via earphones. Audio messages will enhance participants’ perceptions of relatedness as they can closely approximate interaction provided during centre-based exCR. Audio messages help to preserve the real-time context of the message content, and enhance usability by eliminating the need for participants to manually check message content via the smartphone. Participants can manually replay audio messages and review message text during exercise if required.

Real-time exercise monitoring and coaching features integrate behaviour change techniques including behaviour goal setting, feedback on behaviour, biofeedback, social support (unspecified and emotional), instruction on how to perform a behaviour, information about health consequences, behavioural practice/rehearsal, graded tasks, credible source of information, social reward, and verbal persuasion about capability.
4.7.3 Evidence-based Clinical Exercise Prescription

Exercise intervention content is informed by evidence-based guidelines for prescribing exercise to people with CVD.\cite{18, 149} Consistent with American College of Sports Medicine guidelines\cite{149} the REMOTE-CR exercise programme comprises three training sessions per week for twelve weeks, and encouragement to be active on most days of the week (i.e. \( \geq 5 \) days). Exercise prescription parameters are individualised and progressed based on participants’ maximal aerobic exercise capacity (\( \dot{V}O_2\text{max} \)), exercise-induced signs and symptoms, age, sex, and exercise tolerance throughout the programme. Participants with higher baseline \( \dot{V}O_2\text{max} \) and no inducible signs or symptoms begin with a more challenging exercise prescription than those with lower capacity and/or inducible signs or symptoms. Exercise duration ranges from 30 to 60 minutes and includes warm up and cool down phases to allow appropriate cardiovascular and musculoskeletal preparation and recovery. Exercise intensity level ranges from 40\% to 65\% HRR, and is adjusted to optimise physiological adaptations while remaining below a metabolic load that induces abnormal clinical signs or symptoms (if present). REMOTE-CR was designed to focus on aerobic exercise modes such as walking, cycling, and stationary ergometry (e.g. rowing, elliptical training). Underwater activities are not supported as wireless communications (e.g. Bluetooth, mobile broadband) do not function underwater. Strength and neuromuscular training are recommended components of exCR,\cite{149} but existing sensor technologies are not capable of quantifying these modes; this remains an important challenge for mHealth exCR to overcome. The REMOTE-CR platform architecture has been designed to enable rapid integration of additional data sources if and when appropriate sensor technologies become available.

4.7.4 Exercise Performance Review

The participant-facing smartphone app and specialist-facing web-based app both include dedicated components for retrospectively reviewing exercise performance data. Both components synchronise with a secure web server; data presentation varies to suit differing needs of participants and exCR specialists. The participant-facing smartphone app summarises exercise duration, distance, speed, heart rate reserve, training load, received messages, reported symptoms, and location for each training session. Information is also aggregated over calendar months (Appendix 2).

The specialist-facing web app allows exCR specialists to view full resolution data for each training session, including cardiovascular symptoms and ECG, and also
summarises participants’ compliance with individualised exercise prescription parameters (Appendix 2). These data allow exCR specialists to review participants’ adherence to exercise prescription goals, can inform decisions about the individualised progression of exercise prescription parameters, and help to identify participants who may need additional support. Web-based app performance review features also allow exCR specialists to review data recorded outside scheduled real-time monitoring operating hours. This provides additional flexibility for participants that may help to sustain regular exercise, while still enabling exCR specialists to track participants’ performance. Similar to previous telehealth exCR programmes, specialists are able to communicate with participants who predominantly exercise outside real-time monitoring windows via telephone, SMS, or email.

Participant- and specialist-facing exercise performance review features provide information that will inform participants’ perceptions of self-efficacy and competence, and integrate behaviour change techniques [127] including reviewing behaviour goals, monitoring behaviours without feedback, feedback on behaviour, self-monitoring (behaviour, outcomes of behaviour), and biofeedback.

4.7.5 Goal Setting

Goal setting components are included in both the participant-facing smartphone app and the specialist-facing web-based app. Participants are able to set individualised weekly goals relating to exercise parameters such as duration, frequency, distance, level of intensity, and training load (Appendix 2). Goal achievement feedback is automated based on recorded exercise performance data; visualised feedback is updated weekly to reflect current goal achievement. Goal setting is encouraged during the initial training module and throughout the programme via behaviour change education content (described below), but is not compulsory. Participants can create, edit, and remove goals at any time.

ExCR specialists can set goals in conjunction with individualised exercise prescription and/or physical activity recommendations. Visual feedback is presented for short and long term goal achievement in order to facilitate monitoring of participants’ adherence to prescribed exercise volumes and recommended physical activity levels.

Participant- and specialist-facing goal setting features are discrete; that is, specialists do not see participants’ goals and vice versa. This allows participants to take ownership of goal setting, and ensure goals are set at a level that will facilitate motivation. Similarly, exCR specialists can monitor participants’ performance against
evidence-based exercise prescription parameters and physical activity guidelines. This helps exCR specialists to optimise exercise prescription, coaching and behaviour change content for individual participants. Participant and specialist goals can be reset or modified as required to align with progress throughout the programme and maintain an optimal motivational effect.

Goal setting features support participants’ perceptions of self-efficacy and competence, and integrate behaviour change techniques such as goal setting (behaviour, outcomes of behaviours), reviewing behaviour goals, and reviewing discrepancies between current and goal behaviours.

4.7.6 Behaviour Change Messages

A suite of behaviour change messages are delivered to participants as audio messages throughout the exercise programme. Messages are received during exercise, and can also be reviewed at any time as part of the exercise performance review features described above. Message content was adapted from previous mHealth CR interventions designed for delivery via SMS,[153, 154] that have demonstrated positive effects on lifestyle behaviours.[103, 155] Message content was grounded in behaviour changes theories, and integrated feedback from CR participants about message content.[137] The tone of SMS messages was adapted for the real-time conversational context of REMOTE-CR, and also took advantage of the larger character allowance to include more natural language (Appendix 3). Messages aimed to enhance participants’ perceptions of exercise self-efficacy, competence, and relatedness, and integrated behaviour change techniques [127] including problem solving, outcome goal setting, action planning, reviewing behaviour goals, self-monitoring (behaviour, outcomes of behaviour), social support (unspecified and emotional), instruction on how to perform a behaviour, information about health consequences, generalisation of a target behaviour, information from a credible source, self-reward, framing/reframing, verbal persuasion about capability, and focus on past success.

4.7.7 Social Support

In the current REMOTE-CR implementation social support is provided via real-time exercise coaching and behaviour change messages, as described above. A dedicated social support component was also designed, but has not yet been implemented. Social support, from other participants in particular, is a highly valued aspect of CR [137] and social support features were designed to enable participants
to interact with each other, both via the REMOTE-CR platform and face-to-face. Prototype social support features include a secure, closed social network, and location aware filtering of exercise route mapping (Appendix 2). Social network functionality was designed to allow both individual and group communication in order to share experiences, provide encouragement, discuss queries or problems, offer advice, and organise face-to-face meetings if desired. Location aware filtering of exercise route maps was designed to help identify participants who exercise in close proximity to each other, which could provide opportunities to exercise together and/or organise face-to-face meetings.

Social support features were designed to support participants’ perceptions of self-efficacy and relatedness, and integrate behaviour change techniques [127] including social support (unspecified, emotional).

4.7.8 Security

To ensure privacy the REMOTE-CR platform requires user accounts to be registered into a database on a secure web server; access to the database is limited to the study team. The participant-facing smartphone app is publicly available via the Google Play Store.[147] Smartphone and web-based app functionalities are contingent on authentication with the secure web server to prevent unauthorised use of the REMOTE-CR platform, and all data transmission is encrypted. Planned improvements to platform security include integration of the secure hypertext transfer protocol for communication between the smartphone app and web server, and the OAuth protocol for communication between the web-based app and web server.
Figure 8 REMOTE-CR platform schematic
4.8. DISCUSSION

This paper outlined the development of an evidence- and theory-based mHealth exCR platform that provides real-time remote exercise monitoring and coaching, social support and behaviour change education. Rather than re-designing the fundamental exCR process, REMOTE-CR aimed to close the current gap between centre- and home-based exCR programmes by mobilising the expertise of exCR specialists. By combining advanced wearable sensor and smartphone technologies the platform can overcome common accessibility barriers that limit participation in centre-based exCR while preserving clinical oversight that is commonly recommended in exCR guidelines.[15, 16, 18] In doing so REMOTE-CR provides an alternative delivery model that may help to broaden the reach of exCR by meeting the needs of participants who are unable or unwilling to attend traditional centre-based exCR programmes. It is important to note REMOTE-CR was not designed to replace existing exCR programmes; rather, it was designed to complement centre-based programmes, and may augment home-based programmes that do not currently provide clinical exercise supervision.

4.8.1 Principle Findings

REMOTE-CR builds on previous telehealth exCR platforms that have commonly relied on periodic telephone, email or SMS interaction between participants and exCR specialists and/or clinicians.[95, 98-107] By enabling more responsive (i.e. real-time) and individualised management of participants’ exercise programming and more immersive social support during exercise, the REMOTE-CR platform may provide a more engaging environment that promotes positive motivational, behavioural and physiological outcomes.

While real-time exercise monitoring and coaching was a primary design focus, the REMOTE-CR platform also includes a strong theoretical foundation. Many elements of the platform design and intervention content are grounded in behaviour change theories that aim to enhance participants’ self-efficacy, competence, autonomy, and relatedness. This empowering approach is expected to build confidence and resilience [18] which may favour sustained positive exercise behaviours throughout and beyond the duration of the exCR programme. Further, adoption of evidence-based clinical exercise prescription and monitoring guidelines [149] will help to ensure participants accrue a sufficient exercise dose to stimulate positive physiological
adaptation, and provide attainable exercise targets that will support perceived self-efficacy and competence via performance accomplishments.[137]

The REMOTE-CR platform was designed to enable rapid and cost-effective scalability. Rural and remote populations typically have reduced access to specialist services,[112] and use of internet-based services allows clinical expertise to be distributed from centralised (often metropolitan) centres across geographically diverse populations. Centralised management of geographically diverse platform deployments may be a more cost-effective way to increase the reach of exCR than establishing additional centre-based programmes. In addition to staff time, hardware (i.e. smartphone and wearable sensor) and mobile broadband subscriptions are the main operating costs. Increasingly ubiquitous smartphone ownership and mobile broadband access, [88-90] and declining mobile broadband costs [156] may reduce operating costs in future; the REMOTE-CR smartphone app[147] can be installed on participants’ personal smartphones (which may promote usability), and bandwidth requirements are low (approximately 2-4 MB per hour). Use of a commercially available wearable sensor also enhances scalability.

4.8.2 Limitations

While the theory- and evidence-based REMOTE-CR platform provides exciting opportunities to improve the provision and uptake of exCR services it is not free from limitations. The REMOTE-CR platform achieved the primary objective to provide comprehensive exercise training and behaviour change features, but does not currently include all core CR components recommended by international guidelines.[15, 16] The platform architecture has been designed to enable modular integration of additional CR components in future, and may be expanded to create a more comprehensive CR programme. At present participants may still access additional CR components via traditional channels such as outpatient clinics and group seminars. Learning to use the smartphone and wearable sensor components of the platform represent potential barriers for people with CHD who are typically older aged. The smartphone app user interface was designed to simplify navigation, and a dedicated training module was developed to familiarise participants with the technologies; however, it is possible some may not be able to overcome the technological barriers. Increasing smartphone use among older age groups [88] suggests this may be a relatively short term barrier, but reinforces a need to retain existing exCR services to provide options for all participants. It is difficult to keep pace with rapidly advancing smartphone and wearable sensor technologies. The
REMOTE-CR smartphone app was initially designed for Android 4.0, but remains compatible with all subsequent updates (v4.0 to 5.1). Moreover, the flexible platform architecture enables rapid integration of new smartphone and wearable sensor capabilities as they become available.

The development framework adopted for this work recommends mHealth platforms should be rigorously evaluated in studies that use randomised controlled trial design, and include patient-centred outcomes to evaluate physical, mental and social health outcomes. The REMOTE-CR platform is currently being evaluated in a non-inferiority randomised controlled trial comparing mHealth and centre-based exCR programmes. The study will assess the effectiveness and acceptability of the REMOTE-CR platform among a CHD population; study outcomes include VO$_2$max, modifiable cardiovascular risk factors (blood pressure, blood lipid and glucose concentrations, body composition, physical activity energy expenditure), exercise-related motivational factors, HRQoL, and satisfaction with the REMOTE-CR platform.

The results of this study will help to determine whether real-time remotely monitored exCR can provide similar benefits compared with centre-based programmes and, therefore, whether it represents a suitable alternative for people whose needs are not being met by existing services. If proven effective, remotely monitored exCR may offer a more cost-effective model for expanding the reach of exCR than establishing additional centre-based programmes. Mobile technologies provide an ideal platform for the provision of real time exercise-based CR and could easily be applied to other chronic disease prevention and management.
4.9. AUTHOR’S CONTRIBUTIONS

JR was primarily responsible for designing the mHealth platform. AM was primarily responsible for technical development. RM, IW, and NG assisted with design and technical development. All authors contributed to the preparation and final approval of the manuscript. We (authors) accept accountability for all aspects of the work.

4.10. CONFLICTS OF INTEREST

None declared.
CHAPTER 5. TELEHEALTH PLATFORM FEASIBILITY AND VALIDITY

5.1. INTRODUCTION TO PUBLICATION

This chapter includes content from a manuscript entitled “Measurement and data transmission validity of a multi-biosensor system for real-time remote exercise monitoring among cardiac patients”, which was published in the Journal of Medical Internet Research: Rehabilitation and Assistive Technologies, 2(1):e2.

Real-time remote exercise monitoring has potential to substantially advance home- and community-based delivery of exCR. However, opportunities are contingent on acceptable sensor measurement validity and real-time remote data transmission integrity; without accurate and reliable source sensor data, and timely and reliable data transmission, remote exercise monitoring will not realise its potential.

This chapter describes the methods and findings of a laboratory-based study that was designed to assess the validity and feasibility of the custom mobile health platform described in Chapter 4. There were two main objectives: 1) evaluate the measurement accuracy and reliability of a commercially available wearable sensor, and 2) evaluate the reliability of multi-stage real-time data transmission.

This piece of research was undertaken to address Objective 3, which was to assess the validity and feasibility of an alternative exCR delivery model.

5.2. AUTHOR CONTRIBUTION

Jonathan Rawstorn was responsible for the study design, ethical approval, data collection, analysis, and interpretation, and wrote the manuscript. Co-authors contributed to interpretation of the results and provided editorial support for the manuscript.
Measurement and data transmission validity of a multi-biosensor system for real-time remote exercise monitoring among cardiac patients.

1,2Rawstorn JC, 2Gant N, 3Warren I, 1,4Doughty R, 4Lever N, 4Poppe K, 1Maddison R

1National Institute for Health Innovation, 2Department of Exercise Sciences, 3Department of Computer Science, 4Department of Medicine, The University of Auckland, Auckland, New Zealand.

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Email addresses: j.rawstorn@auckland.ac.nz, n.gant@auckland.ac.nz, i.warren@auckland.ac.nz, r.doughty@auckland.ac.nz, nlever@adhb.govt.nz, k.poppe@auckland.ac.nz, r.maddison@auckland.ac.nz
5.3. ABSTRACT

Background
Remote telemonitoring holds great potential to augment management of patients with coronary heart disease (CHD) and atrial fibrillation (AF) by enabling regular physiological monitoring during physical activity. Remote physiological monitoring may improve home and community exercise-based cardiac rehabilitation (exCR) programmes, and could improve assessment of the impact and management of pharmacological interventions for heart rate control in individuals with AF.

Objective
To evaluate the measurement validity and data transmission reliability of a remote telemonitoring system comprising a wireless multi-parameter physiological sensor, custom smartphone application (app) and middleware platform, among individuals in sinus rhythm and AF.

Methods
Participants in sinus rhythm and with AF undertook simulated daily activities, low, moderate and/or high intensity exercise. Remote monitoring system heart rate and respiratory rate were compared to reference measures (12-lead ECG and indirect calorimeter). Wireless data transmission loss was calculated between the sensor, smartphone app and remote internet server.

Results
Median heart rate (-0.30 to 1.10 b·min\(^{-1}\)) and respiratory rate (-1.25 to 0.39 br·min\(^{-1}\)) measurement biases were small, yet statistically significant (all P ≤ .003) due to the large number of observations. Measurement reliability was generally excellent (\(\rho = 0.87\) to 0.97, all P < .001; ICC = 0.94 to 0.98, all P < .001; CV = 2.24 to 7.94%), although respiratory rate measurement reliability was poor among AF participants (\(\rho = 0.43,\) P < .001; ICC = 0.55, P < 0.001; CV = 16.61%). Data loss was minimal (<5%) when all system components were active; however, instability of the network hosting the remote data capture server resulted in data loss at the remote internet server during some trials.

Conclusion
System validity was sufficient for remote monitoring of heart and respiratory rates across a range of exercise intensities. Remote exercise monitoring has potential to augment current exCR and heart rate control management approaches by enabling the provision of individually tailored care to individuals outside traditional clinical environments.
5.4. INTRODUCTION

Cardiovascular diseases (CVD) remain the leading cause of morbidity and mortality worldwide, accounting for around one third (~17 million) of deaths globally, with the greatest proportion of deaths attributed to coronary heart disease (CHD).[3] Cardiac rehabilitation (CR) is an essential component of CHD management [157, 158] and international guidelines consistently identify exercise training as a central element of CR.[15, 29, 30] The beneficial effects of exercise-based CR (exCR) on all-cause and cardiac mortality are comparable with comprehensive CR,[31-34] and exercise training can concurrently improve an array of modifiable cardiac risk factors including hypertension, dyslipidaemia, insulin resistance, overweight and obesity, and exercise capacity.[14, 34, 38, 47, 48, 159] Despite these benefits many eligible patients are not referred for CR [58] and uptake is low among those who are referred. [60, 61] Common participation barriers include transport limitations, work commitments and inconvenient programme scheduling.[64] Among those who do undertake CR, adherence to prescribed exercise is poor with up to 50% of participants dropping out of regular exercise within six months of programme completion.[69-71] It is clear traditional CR delivery models do not meet the needs of many eligible patients and innovation is required to enhance participation and adherence.

Home-based exCR has been introduced to broaden access and participation, and confers similar improvements in mortality, cardiac events and cardiac risk factors compared to centre-based CR.[76] Home-based programmes overcome several traditional participation barriers, but many do not include physiological monitoring that is typical during centre-based exCR. In addition to concerns about patient safety, a lack of physiological monitoring also restricts the potential to individualise and optimally manage exercise prescription. As the beneficial effects of exCR are dose-dependent [35, 38, 79] remote physiological monitoring may help home-based exCR participants to achieve recommended exercise training loads, and improve programme outcomes.

Physiological monitoring has recently been identified as a particularly important direction for the future development of home-based exCR [85] but to date most telehealth CR interventions have utilised fixed-line communication tools (e.g. telephone, internet, videoconferencing, transtelephonic ECG) that constrain participants within the home environment. Recent advances in mobile sensor technologies and rapidly growing access to mobile broadband [160] enable real-time
remote physiological monitoring outside fixed-line communication networks, and these technologies should be integrated into telehealth CR.[91]

A survey of wearable physiological monitoring devices identified several key requirements including measurement validity, data transmission integrity, real-time data processing, ease of use and scalability.[87] While few existing monitoring systems addressed all requirements the commercially available BioHarness (Zephyr Technology, USA) scored highly.[87] This multi-parameter wireless biosensor quantifies heart rate, single lead ECG, respiratory rate, tri-axial body acceleration and torso posture via sensors embedded in a textile chest strap or compression-fit vest. On-board memory and Bluetooth connectivity enable data to be stored locally or transmitted wirelessly to compatible devices such as smartphones, tablets and computers. The low-profile design, ease of use and advanced array of sensors make this device well suited for remote exercise monitoring. Early model BioHarness devices have been validated;[139-144] however, the current model has yet to be evaluated in either clinical or non-clinical populations.

Most wearable physiological sensors do not support long-range data transmission to remotely located monitoring stations. Therefore, remote monitoring requires physiological sensors to be combined with devices capable of collating and transmitting sensor data to remote monitoring stations for review and action by health care professionals. Smartphones are a preferable intermediary as, in combination with appropriate mobile or web applications (apps), they provide a ready-to-use mobile platform capable of logging and transmitting data via ubiquitous wireless data networks (e.g. Bluetooth, Wi-Fi, 3G and 4G). Portability, compatibility with several data networks, substantial computational capability and routine integration of motion and location sensors further enhance the potential utility of smartphones for remote exercise monitoring. Moreover, continued rapid global smartphone market penetration growth[88] will likely reduce the necessity for healthcare providers to supply smartphones to would-be remote monitoring system end users. To date there is a paucity of published research combining physiological sensors with mobile data transmission technologies. A system comprising ECG and global positioning system (GPS) sensors, and a smartphone has been evaluated for remotely monitoring cardiac patients during exercise.[67] Remote data transmission was interrupted during 8.6% of completed exercise sessions; however, the amount of data lost and the subsequent impact on real-time remote monitoring were not described.
We have developed a custom mobile app and middleware platform to provide real-time transmission of physiological and clinical data, via smartphones, to remotely located monitoring centres.[161] Bi-directional communication capability enables health care professionals to provide users with instantaneous feedback that could prompt rapid changes in exercise behaviour, enhance exercise self-efficacy, and deliver educational information and provide support. Frequent access to remotely recorded heart rate data during rest, activities of daily living and exercise could enable physicians to assess the impact of pharmacological intervention on heart rate control. In combination with the communication capability this could assist physicians to titrate atrial fibrillation (AF) patients’ medications in order to achieve optimal heart rate control. The platform has shown promise in preliminary proof of concept research; however, a robust assessment of wireless data transmission reliability is required.

This study aimed to evaluate the sensor measurement validity and wireless data transmission reliability of a remote physiological monitoring system comprising the BioHarness, custom app and middleware platform. Validity was assessed among individuals in sinus rhythm and with AF in order to determine whether measurement validity was robust to both normal and abnormal heart rhythms. AF was chosen as it is the most common sustained cardiac arrhythmia, and is a common comorbidity in CHD.[162]

5.5. METHODS

A dual-phase cross sectional study was conducted to assess system validity among convenience samples of healthy recreationally active individuals in sinus rhythm (i.e. systole initiated at the sinoatrial node and proliferated via normal cardiac conduction pathways; Phase One), and individuals with AF (Phase Two). Phase One participants were recruited via contacts and local sport clubs. Phase Two participants were recruited via outpatient cardiology clinics. This dual-phase approach enabled safe assessment of sensor measurement validity across a broad range of exercise intensities. Phase One participants completed constant, intermittent, and incremental intensity exercise at moderate to maximal levels of intensity. Phase Two participants completed constant intensity exercise and simulated daily activities at low to moderate levels of intensity. Phase One was approved by the University of Auckland Human Participants Ethics Committee (2011/7674). Phase Two was approved by the New Zealand Health and Disability Ethics Committee (CEN/11/11058), respectively. All volunteers provided written informed consent. Procedures common to Phases One and Two are outlined below, followed by phase-specific exercise procedures.
5.5.1 Common Procedures

The remote physiological monitoring system comprised the BioHarness (version 3 with chest strap, Zephyr Technology, USA; Figure 9), a smartphone (Xperia Arc S, Sony Ericsson Mobile Communications AB, Sweden) utilising the Android operating system (v2.3.4, Google Inc., USA), a custom mobile app with integrated middleware platform (Figure 10), and a remote monitoring internet server (Odin).[161] Physiological data, transmitted to the smartphone via Bluetooth (1 Hz measurement frequency), were displayed throughout exercise, stored locally, and transmitted to the remote internet server in near real-time (30 s data packet transmission interval).

Upon arrival at the laboratory participants underwent baseline measurement of stature and body mass, and familiarisation with exercise ergometers. Participants were instrumented with a 12-lead electrocardiogram (ECG; AT-110, Schiller AG, Baar, Switzerland), BioHarness and indirect calorimeter (Metalyzer, Cortex Biophysik GmbH, Leipzig, Germany). Adhesive electrodes were applied at standard ECG sites following recommended skin preparation procedures,[163] and electrical cables were secured to minimise signal artefact. Calorimeter gas sensors were calibrated via a two-point procedure using gases of known composition, the volume transducer was calibrated using a 3000 ml calibration syringe (Hans Rudolph, Kansas, USA) and the internal barometer was calibrated against a mercury barometer (SK1256, Sato Keiryoki Manufacturing, Tokyo, Japan).

Activation of ECG, BioHarness and calorimeter data logging followed a standardised procedure to ensure accurate data synchronisation. Data were recorded during 180 s of seated rest prior to, and throughout exercise. A 60 s transition period was included prior to locomotive exercise to enable treadmill initiation.

5.5.2 Phase One Exercise Procedures

During Phase One participants completed three discrete bouts of treadmill running during two laboratory-based trials. During Trial One participants ran on a motorised treadmill (EX200, Powersport, Bridgend, Wales) at 0% incline to determine the velocity eliciting 50% heart rate reserve (V50%HRR). Following instrumentation participants completed an incremental protocol to assess peak oxygen uptake (V̇O₂peak), operationally defined as the highest measured V̇O₂. Treadmill velocity (V50%HRR) remained constant and the incline was increased by 1% every 60 s until volitional exhaustion. Mean V̇O₂ during the final 30 s of each workload was plotted as a function of treadmill incline, and inclines eliciting 50%, 66%, 70% and 90%
$\dot{V}O_2$peak were derived via linear interpolation. After 30 min rest participants completed a 30 min constant intensity treadmill running protocol (C30) at an incline eliciting 66% $\dot{V}O_2$peak. During Trial Two participants completed a 30 min intermittent intensity treadmill protocol (I30) comprising three repetitions of a 10 min exercise block. Each exercise block included five sequential 2 min stages at inclines eliciting 50%, 70%, 90%, 70% and 50% $\dot{V}O_2$peak, respectively. Mean levels of exercise intensity were equivalent in the C30 and I30 protocols.

5.5.3 Phase Two Exercise Procedures

During Phase Two participants completed three bouts of exercise during a single laboratory-based trial. Participants self-selected light-to-moderate levels of exercise intensity during treadmill and cycle ergometer (Velotron, RacerMate Inc., Washington, USA) familiarisation. Following instrumentation participants undertook 10 min of treadmill walking, 10 min of cycling, and sequential 3 min bouts of simulated daily activities (sweeping and vacuuming). Walk, cycle and daily activity bouts were separated by 5 min of seated rest.

5.5.4 Data Analysis

Reference heart rate measures were manually calculated from synchronised ECG waveforms as the average rate during the final 10 seconds of each minute. Reference respiratory rate was captured by the calorimeter at 0.10 Hz. BioHarness and calorimeter data were downloaded using the manufacturers’ software (BioHarness Log Downloader v1.0.24 and MetaSoft v3.9.3, respectively) and exported for manual analysis. BioHarness data were down-sampled to match reference measures. Data outside the manufacturers specified measurement ranges were excluded prior to analysis.

Phase One and Two data were analysed separately following identical procedures using SPSS (v20.0.0, IBM, New York, USA). Consistent with guidelines for assessing measurement validity in this field [164] a multi-faceted approach was undertaken to evaluate BioHarness heart rate and respiratory rate measurement accuracy and reliability. Heart rate and respiratory rate data were non-normally distributed and a nonparametric analytical approach was implemented where necessary. Wilcoxon signed-rank tests for matched pairs were conducted to assess systematic biases between sensor and reference measures. Kruskal-Wallis analyses of variance were performed to assess the effect of ACTIVITY (Phase One; rest, transition, run. Phase Two; rest, transition, walk, cycle, sweep, vacuum) on measurement biases.
Statistically significant main effects were explored using Dunn-Bonferroni corrected paired comparisons.

Spearman’s rank-order correlation coefficients (ρ) and two-way random effects intraclass correlation coefficients for absolute agreement (ICC) were calculated to describe relative measurement reliability. [164] Absolute measurement reliability was assessed by calculating the standard error of measurement (SEM) and coefficient of variation (CV)[164] and a non-parametric approach to the 95% limits of agreement (LoA) similar to that described by Bland & Altman,[165] in which the LoA were calculated as the 2.5th and 97.5th percentile ranked biases. The threshold for statistical significance was set at $\alpha < .05$.

Wireless data transmission reliability was evaluated by determining data loss between the BioHarness, App and remote monitoring server (Odin). Reference sample sizes were calculated as the product of exercise duration and sensor sampling frequency. These analyses utilised data logged at the BioHarness’ native summary frequency (1 Hz) as the aforementioned down-sampling procedures had potential to conceal intermittent data loss.
Figure 9 Zephyr BioHarness
Figure 10 Mobile app screenshot
5.6. RESULTS

Participant characteristics are summarised in Table 2. Ten and eight participants completed all Phase One and Two activity bouts, respectively. Unidentified trial-wide technical errors affected heart rate and respiratory rate measurements during two separate Phase Two trials. The outlying nature of these two data sets was confirmed by two independent investigators and they were excluded from analyses.

5.6.1 Measurement Accuracy

The BioHarness systematically underestimated heart rate ($z = -3.01, P = .003$) and respiratory rate ($z = -21.57, P < .001$) during Phase One, although the median biases were small (Table 3 and Table 4). A statistically significant effect of ACTIVITY on measurement bias was detected for respiratory rate ($H_2 = 40.96, P < .001$), but not heart rate ($H_2 = 0.83, P = .66$). Dunn-Bonferroni corrected paired comparisons revealed systematic differences in respiratory rate measurement biases between all three levels of ACTIVITY (all $P < .001$ to $P = 0.04$; Table 4).

The BioHarness systematically overestimated heart rate ($z = -3.28, P = .001$) and respiratory rate ($z = -4.47, P < .001$) during Phase Two, although negative biases were observed during some activities (Table 3 and Table 4). A statistically significant effect of ACTIVITY was detected on respiratory rate ($H_5 = 203.07, P < .001$; Table 4), but not heart rate ($H_5 = 4.41, P = .49$; Table 3). Dunn-Bonferroni-corrected paired comparisons revealed systematic differences in respiratory rate measurement biases between all levels of ACTIVITY ($P < .001$ to $P = .02$; Table 4) with the exception of walk and cycle ($P = .12$; Table 4).

BioHarness measurement error was relatively consistent across the measurement ranges, although a degree of heteroscedasticity was apparent among Phase Two respiratory rate measures (Figure 11).

5.6.2 Measurement Reliability

BioHarness and reference heart rate measures were strongly correlated during both phases (Table 5), indicating excellent relative measurement reliability. The SEM, CV and LoA for heart rate were similar during both Phases (Table 5). Small SEM and CV indicate acceptable absolute heart rate measurement reliability during both phases; however, the non-parametrically derived LoA were relatively wide (Figure 11). Asymmetric LoA reflect the aforementioned non-normal measurement error...
distributions. BioHarness and reference respiratory rate measures were strongly correlated during Phase One, but not Phase Two (Table 5). Phase One respiratory rate SEM and CV were small, but the LoA were relatively wide (Figure 11). The respiratory rate SEM, CV and LoA were substantially larger during Phase Two (Table 5) and reflect poor absolute measurement reliability. While the magnitude of the Phase Two respiratory rate SEM was comparable to the heart rate SEM during both phases it represents a larger proportion of the total measurement range and; therefore, markedly lower absolute measurement reliability.

5.6.3 Wireless Data Transmission Reliability

Zero biases were observed between BioHarness, App and Odin measurements, indicating sensor measurement validity was unaffected by wireless data transmission. Phase One BioHarness, App and Odin data loss were 4.1%, 0.2% and 21.3%, respectively. Failure to record data throughout two VO2peak bouts accounted for all BioHarness data loss. However, these errors did not compromise BioHarness-to-App data transmission. A terminal App crash during one exercise bout accounted for all Phase One App data loss. Outages of the data network hosting the Odin server precluded App-to-Odin data transmission throughout five exercise bouts, and this instability accounted for 15.5% Odin data loss. Unidentified intermittent data capture errors accounted for the remaining Odin data loss (5.9%).

Phase Two BioHarness, App and Odin data loss were 0.0%, 0.6% and 1.1%, respectively. Phase Two was unaffected by Odin network stability and data loss occurred as a result of intermittent errors similar to those observed during Phase One.
### Table 2 Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>Phase One</th>
<th>Phase Two</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/male</td>
<td>10/6</td>
<td>8/5</td>
</tr>
<tr>
<td>Age (y)</td>
<td>26.68 (3.26)</td>
<td>69.68 (9.53)</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>71.10 (11.53)</td>
<td>77.46 (18.81)</td>
</tr>
<tr>
<td>Stature (m)</td>
<td>1.73 (0.06)</td>
<td>1.69 (0.12)</td>
</tr>
<tr>
<td>VO₂peak (ml·kg⁻¹·min⁻¹)</td>
<td>50.82 (4.51)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Data reported as mean (SD). Phase One = healthy participants; Phase Two = participants with atrial fibrillation. VO₂peak = peak oxygen consumption. N/A = not assessed during Phase Two.

### Table 3 Biases between BioHarness and reference heart rate

<table>
<thead>
<tr>
<th></th>
<th>Heart Rate</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median b·min⁻¹</td>
<td>Bias b·min⁻¹</td>
<td>Bias %</td>
</tr>
<tr>
<td><strong>Phase One</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>REF</td>
<td>72.00 (18.00)</td>
<td>0.00 (4.45)</td>
</tr>
<tr>
<td></td>
<td>BH</td>
<td>70.75 (23.38)</td>
<td></td>
</tr>
<tr>
<td>Transition</td>
<td>REF</td>
<td>108.00 (30.00)</td>
<td>-0.80 (7.20)</td>
</tr>
<tr>
<td></td>
<td>BH</td>
<td>97.00 (31.18)</td>
<td></td>
</tr>
<tr>
<td>Run</td>
<td>REF</td>
<td>162.00 (18.00)</td>
<td>-0.30 (4.60)</td>
</tr>
<tr>
<td></td>
<td>BH</td>
<td>163.50 (16.40)</td>
<td></td>
</tr>
</tbody>
</table>
| Total            | REF        | 162.00 (24.00)    | -0.30 (4.53)
|                  | BH         | 160.70 (13.40)    | -0.20 (2.96) |
| **Phase Two**    |             |                   |    |
| Rest             | REF        | 84.00 (24.00)     | 2.10 (4.55) | 2.06 (5.77) |
|                  | BH         | 89.10 (29.45)     |               |
| Transition       | REF        | 108.00 (6.00)     | 1.10 (9.30)  | 1.67 (8.78) |
|                  | BH         | 91.70 (21.30)     |               |
| Walk             | REF        | 126.00 (40.50)    | 0.65 (9.25)  | 0.49 (7.82) |
|                  | BH         | 130.20 (46.58)    |               |
| Cycle            | REF        | 120.00 (60.00)    | 1.90 (11.50) | 1.79 (9.66) |
|                  | BH         | 121.80 (72.50)    |               |
| Sweep            | REF        | 108.00 (27.00)    | -3.60 (12.00)| -3.75 (9.70) |
|                  | BH         | 103.10 (20.05)    |               |
| Vacuum           | REF        | 108.00 (30.00)    | 3.20 (13.76) | 3.47 (13.46) |
|                  | BH         | 101.30 (33.34)    |               |
| Total            | REF        | 108.00 (48.00)    | 1.10 (9.75)
|                  | BH         | 106.55 (51.68)    | 1.23 (8.61) |

Table reports median (IQR) reference (REF) and BioHarness (BH) heart rates, absolute (b·min⁻¹) and relative (%) biases. Phase One = healthy participants in sinus rhythm; Phase Two = participants with atrial fibrillation. 

A, B Statistically significantly different compared to reference measures (A P = .003, B P = .001).
Table 4 Biases between BioHarness and reference respiratory rate

<table>
<thead>
<tr>
<th>Phase</th>
<th>Median br∙min⁻¹</th>
<th>Bias br∙min⁻¹</th>
<th>Bias %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>REF 17.00 (6.75)</td>
<td>-0.28 (4.00)R</td>
<td>-1.56 (23.42)</td>
</tr>
<tr>
<td></td>
<td>BH 16.15 (5.44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transition</td>
<td>REF 19.30 (7.33)</td>
<td>-2.20 (5.72)R</td>
<td>-12.17 (29.52)</td>
</tr>
<tr>
<td></td>
<td>BH 17.65 (6.32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Run</td>
<td>REF 41.70 (12.00)</td>
<td>-1.36 (4.58)R</td>
<td>-3.30 (10.65)</td>
</tr>
<tr>
<td></td>
<td>BH 40.80 (10.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>REF 39.90 (15.30)</td>
<td>-1.25 (4.65)B</td>
<td>-3.33 (12.01)</td>
</tr>
<tr>
<td></td>
<td>BH 39.02 (13.40)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table reports median (IQR) reference (REF) and BioHarness (BH) respiratory rates, absolute (br∙min⁻¹) and relative (%) biases.

Phase One = healthy participants in sinus rhythm; Phase Two = participants with atrial fibrillation.

A Statistically significantly different compared to reference measures (P < .001).

R Statistically significantly different compared to Phase One rest, transition, run (P < .001 to P = 0.04)

WCV Statistically significantly different compared to Phase Two rest, transition, walk, cycle, sweep and vacuum (P < .001 to P = .02)

Table 5 Relative and absolute reliability of BioHarness heart rate and respiratory rate

<table>
<thead>
<tr>
<th>Relative</th>
<th>ρ</th>
<th>ICC</th>
<th>SEM (br∙min⁻¹)</th>
<th>LoA (br∙min⁻¹)</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase One</td>
<td>HR</td>
<td>0.92</td>
<td>0.98^</td>
<td>5.20 (-21.87, 9.26)</td>
<td>2.24</td>
</tr>
<tr>
<td></td>
<td>RR</td>
<td>0.87</td>
<td>0.94^</td>
<td>2.78 (-13.73, 9.41)</td>
<td>7.94</td>
</tr>
<tr>
<td>Phase Two</td>
<td>HR</td>
<td>0.97</td>
<td>0.98^</td>
<td>4.77 (-13.39, 23.79)</td>
<td>4.05</td>
</tr>
<tr>
<td></td>
<td>RR</td>
<td>0.43</td>
<td>0.55^</td>
<td>4.60 (-11.58, 18.91)</td>
<td>16.61</td>
</tr>
</tbody>
</table>

Table reports Spearman’s rank-order correlation coefficient (ρ), two-way random effects intraclass correlation coefficient (ICC), standard error of measurement (SEM), non-parametric 95% limits of agreement (LoA), and coefficient of variation (CV) for heart rate (HR) and respiratory rate (RR).

A Statistically significant (P < .001)
Figure 11 Sensor measurement error as a function of mean measurement magnitude

Solid reference lines = mean biases, dashed reference lines = 95% limits of agreement.
5.7. DISCUSSION

This study evaluated the sensor measurement and wireless data transmission validity of a remote physiological monitoring system among participants in sinus rhythm and AF. Heart and respiratory rates differed systematically from reference measures across a range of exercise intensities and activities, but the magnitudes of these biases were small. Measurement reliability was generally acceptable, and wireless data capture was excellent when all components of the monitoring system were operational. However, instability of the data network hosting the Odin remote monitoring server resulted in substantial data loss during some exercise bouts.

The small magnitude of heart rate and respiratory rate measurement biases are unlikely to impair interpretation of physiological stress or workload during remote monitoring. As a caveat, larger biases during simulated sweeping and vacuuming may indicate reduced sensor stability and increased movement artefact during activities requiring substantial upper limb movement. Recent evidence suggests conductive fabric sensors embedded in a textile vest are subject to less movement artefact than traditional adhesive ECG electrodes.[166] Thus the BioHarness compression-fit vest may improve sensor measurement validity; however, it was not publicly available during this experiment and could not be assessed.

Heart rate and respiratory rate measurement biases are comparable to some, but not all previous evaluations of similar sensors’ measurement validity. Biases were smaller than those reported for a previous model BioHarness during laboratory- and field-based locomotion,[140, 141, 143] but comparable to those reported during incremental and constant intensity treadmill running.[144] As it is not possible to determine the extent to which iterative hardware and software development contributes to measurement accuracy, caution should be taken when generalising the present results to earlier model devices.

Relative heart rate measurement reliability was excellent across a range of activities and workloads; correlation coefficients compare favourably with evaluations of previous model BioHarness devices [141, 144] and other wearable physiological sensing devices.[167-170] Small SEM, and CV substantially smaller than a previously established criterion for acceptability,[169] indicate good absolute heart rate measurement reliability during both phases. Relatively wide LoA are consistent with previous BioHarness evaluations [143, 144] and reflect infrequent large measurement errors. While high frequency data are attractive for real-time remote
exercise monitoring, the effect of infrequent outlying measurement errors may unnecessarily confound real-time data interpretation. Many wearable physiological sensors support much higher frequency monitoring than is typically provided during centre-based supervised exercise. Thus it may be acceptable to sacrifice some temporal resolution in order to increase measurement reliability. Post-processed down-sampling is recommended to account for the temporal instability of respiratory gas exchange data during exercise,[171, 172] and a similar approach warrants consideration for real-time monitoring of high frequency physiological data. Aggregating individual data packets, which were transmitted every 30 seconds during this experiment, may overcome the effects of infrequent outlying measurement errors. However, further investigation is required to determine the optimal balance between temporal resolution and measurement reliability.

Respiratory rate measurement reliability was comparable with evaluations of previous BioHarness models [140, 144] and other wearable physiological monitors featuring inductive plethysmographs during Phase One,[169, 170, 173] but was notably reduced during Phase Two. This was unexpected, but not without precedent.[142, 143] The major methodological discrepancies between phases were the inclusion of upper body activities (simulated sweeping and vacuuming), lower levels of activity intensity, and older aged participants of lower exercise training status during Phase Two. Activities requiring substantial upper limb movement could impair the BioHarness respiratory rate sensor; however, a post-hoc sensitivity analyses (not presented) did not support this effect. As low intensity activities are associated with small tidal volumes and thoracic wall displacements [174] it is possible the BioHarness respiratory rate sensor may be confounded during low levels of exercise intensity. Again; however, post-hoc sensitivity analyses did not support this effect. Pulmonary mechanics are impaired among older aged individuals (independent of pathophysiological conditions) and those with respiratory muscle weakness.[175, 176] However data describing pulmonary mechanics were not collected during this study and the mechanism(s) underlying poor Phase Two respiratory rate measurement reliability remain unknown.

Remote physiological monitoring is contingent upon reliable data transmission to a remotely located monitoring station. Data capture was generally excellent throughout this experiment; however, several errors were identified. Unresolved data logging errors precluded data storage on the local BioHarness memory during two exercise bouts; however, remote data transmission was unaffected and all data were successfully transmitted to the remote monitoring server during these errors. While
local BioHarness data capture was necessary to assess sensor measurement validity, the middleware platform responds to network instability by temporarily caching all data until a network connection is re-established. Thus local BioHarness data capture would not be required in a production-ready remote monitoring system.

The institutional network that hosted the Odin server throughout this study was subject to inconsistent power supply and undisclosed maintenance events. Resulting Odin server outages affected five exercise bouts during three Phase One trials. Relocating Odin to a robust host network will resolve this issue, and is an immediate priority for future iterations of the monitoring system. After accounting for host network instability Odin captured 94.7% and 98.9% of data during Phases One and Two, respectively. Iterative development is required to resolve the remaining App and Odin data capture errors; however, data capture reliability was sufficient for real-time remote monitoring given that a stable App-to- Odin connection was confirmed before beginning exercise.

### 5.7.1 Limitations

A potential limitation of this study was the small sample size. However, as the unit of analysis was the number of sensor observations, rather than the number of participants, the design had sufficient statistical power to detect clinically significant biases between BioHarness and reference measures of heart rate and respiratory rate.

As with all studies evaluating physiological sensor validity, these results may be confounded by factors influencing the quality of data from the BioHarness and reference sensors. Positional overlap between ECG (V1-V6) and BioHarness electrodes may have impaired BioHarness electrode skin contact, particularly among participants with small chest circumferences requiring ECG electrodes to be closely grouped. Interrupted skin contact could explain the occasional presence of large measurement errors apparent in the relatively wide heart rate LoA.

Similarly, the design of the BioHarness respiratory rate sensor dictated that it was typically located above ECG electrodes V5 and V6. Compression of the respiratory rate sensor against underlying ECG electrodes could impair measurement validity; however, this would be expected to affect both phases and is unlikely to explain the reduced measurement reliability observed during Phase Two.
5.7.2 Implications

Remote physiological monitoring has numerous potential applications in both clinical and non-clinical settings. Remote monitoring has been identified as an important future development in home-based exCR,[85] and may help to bridge the gap between centre- and home-based programmes for individuals who are unable to attend traditional exCR. Real-time remote physiological monitoring could help home-based exCR participants’ to achieve and adhere to recommended exercise training loads, and this may optimise beneficial exercise-induced physiological adaptations. Moreover, bi-directional communication capability will enable exercise physiologists to provide instantaneous individualised feedback, educational information and support based on real-time physiological responses. While remote exCR should not replace centre-based programmes, it may provide a viable alternative for those who are unable or unwilling to attend supervised exCR. Robust trials are now required to determine the efficacy and safety of remotely monitored exCR. Given that centre-based exCR is the gold standard treatment in many countries it seems prudent to compare remotely monitored exCR with centre-based programmes.

Remote physiological monitoring also has potential applications outside of exCR, and could be used to monitor heart rate control in people with AF. Management of patients with AF involves consideration of either a rhythm control approach (attempt to maintain sinus rhythm) or one of rate control, which is often the preferred approach. Reduction of the rapid heart rate in AF increases the diastolic filling periods and left ventricular stroke volume.[162] Current guidelines recommend an individualised approach to AF rate control, using a combination of pharmacological agents such as beta-blockers, calcium channel blockers and digoxin.[162] However, heart rate control during exercise remains problematic for many patients with AF, even when receiving medications. Guidelines recommend that patients who experience symptoms associated with AF during exercise should be assessed during exercise and have their pharmacological treatment titrated to achieve a physiological chronotropic response and avoid bradycardia.[162] The most common approach for monitoring arrhythmias during everyday life is Holter monitoring (24 hours to 7 days).[162] This approach is highly regarded and valuable for clinical decision making; however it is time and resource intensive to monitor data, and can be intrusive for patients. Remote monitoring systems such as the one described herein have several advantages over traditional Holter monitoring. The conductive textile electrodes embedded into wearable physiological sensors overcome the discomfort associated with adhesive electrodes. Moreover, data from integrated motion sensors
could be used to delineate periods of rest and physical activity, and these contextual data may augment interpretation of heart rate control among patients with AF. Finally, embedding automated data collation and processing within remote monitoring servers can eliminate manual data handling and improve the efficiency of data processing and reporting. Collectively these characteristics could assist physicians to assess the effects of pharmacological intervention and titrate AF patients’ medications in order to optimise heart rate control at rest and during exercise. Future research is needed to determine the utility of such remote monitoring in this and other translational contexts.

5.7.3 Conclusion

The remote monitoring system evaluated in this experiment has sufficient measurement accuracy for quantifying heart rate and respiratory rate among individuals in sinus rhythm and with AF when gold standard clinical sensors are unavailable. Wireless data transmission reliability was generally excellent. Remote physiological monitoring has potential application as an alternate method for delivering exercise-based cardiac rehabilitation, and enhancing the management of heart rate control for individuals with atrial fibrillation.
5.8. ACKNOWLEDGEMENTS

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5.9. CONFLICT OF INTEREST

None declared.

5.10. CONTRIBUTORSHIP

All authors contributed to the design, data collection, analysis and interpretation, drafting of the article, and final article approval.
CHAPTER 6. EVALUATING TELEHEALTH CARDIAC REHABILITATION EFFECTIVENESS: STUDY PROTOCOL

6.1. INTRODUCTION TO PUBLICATION

This chapter includes content from a manuscript entitled “The remote exercise monitoring trial for exercise-based cardiac rehabilitation (REMOTE-CR): a randomised controlled trial protocol”, which was published in BMC Public Health, 14:1236.

The custom mobile health platform (Chapter 4) demonstrated acceptable validity for real-time exercise monitoring (Chapter 5), but there is a paucity of evidence evaluating this type of novel intervention. Rigorous evaluation is required to inform implementation decisions, and randomised controlled trials that assess patient-centred outcomes and usability are recommended.

This chapter presents the protocol for an RCT that was designed to evaluate the effectiveness of remotely monitored exercise-based cardiac rehabilitation. As a complementary alternative to existing services, a non-inferiority design was chosen to determine if effects are comparable to existing centre-based programmes. There were three main objectives: 1) compare the effects of remote and centre-based programmes, 2) evaluate within-group effectiveness, and 3) assess usability and acceptability. For this thesis, a pilot trial was planned to be nested within the main RCT. The pilot trial assessed the primary outcome and selected secondary outcomes at the 12 week follow-up time point.

This piece of research was undertaken to address Objective 4, which was to rigorously evaluate the effectiveness and acceptability of an alternative exercise-based rehabilitation delivery model.

6.2. AUTHOR CONTRIBUTION

Jonathan Rawstorn wrote the full study protocol. Co-authors provided editorial support, and the primary publication author reformatted (i.e., abbreviated) the full study protocol for publication.
The Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation: A randomised controlled trial protocol.

1Maddison R, 1,2Rawstorn JC, 3Rolleston A, 1Whittaker R, 4Stewart R, 4Benatar J, 5Warren I, 1Jiang Y, 2Gant N

1National Institute for Health Innovation, 2Department of Exercise Sciences, 5Department of Computer Science, University of Auckland, Auckland, New Zealand
3The Cardiac Clinic, Tauranga, New Zealand
4Department of Cardiology, Auckland City Hospital, Auckland, New Zealand

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Email addresses: r.maddison@auckland.ac.nz, j.rawstorn@auckland.ac.nz, anna@thecardiacclinic.co.nz, r.whittaker@auckland.ac.nz, ralph.stewart@auckland.ac.nz, jbenatar@adhb.govt.nz, i.warren@auckland.ac.nz, y.jiang@auckland.ac.nz, n.gant@auckland.ac.nz
6.3. ABSTRACT

Background
Exercise is an essential component of contemporary cardiac rehabilitation programs for the secondary prevention of coronary heart disease. Despite the benefits associated with regular exercise, adherence with supervised exercise-based cardiac rehabilitation remains low. Increasingly powerful mobile technologies, such as smartphones and wireless physiological sensors, may extend the capability of exercise-based cardiac rehabilitation by enabling real-time exercise monitoring for those with coronary heart disease. This study compares the effectiveness of technology-assisted, home-based, remote monitored exercise-based cardiac rehabilitation (REMOTE-CR) to standard supervised exercise-based cardiac rehabilitation in New Zealand adults with a diagnosis of coronary heart disease.

Methods
A two-arm, parallel, non-inferiority, randomised controlled trial will be conducted at two sites in New Zealand. One hundred and sixty two participants will be randomised at a 1:1 ratio to receive a 12-week program of technology-assisted, home-based, remote monitored exercise-based cardiac rehabilitation (intervention), or a 12-week program of standard supervised exercise-based cardiac rehabilitation (control).

The primary outcome is maximal oxygen uptake ($\dot{V}O_2$ max) at 13 weeks. Secondary outcomes include cardiovascular risk factors (blood lipid and glucose concentrations, blood pressure, and anthropometry), self-efficacy, intentions and motivation to be active, objectively measured physical activity, self-reported leisure time exercise and health-related quality of life. Cost information will also be collected to compare the two modes of delivery. All outcomes are assessed at baseline, 13 and 25 weeks, except for $\dot{V}O_2$ max, blood lipid and glucose concentrations, which are assessed at baseline and 13 weeks only.

Discussion
This novel study will compare the effectiveness of technology-supported exercise-based cardiac rehabilitation to a traditional supervised approach. If the REMOTE program proves to be as effective as traditional cardiac rehabilitation, it has potential to augment current practice by increasing access for those who cannot utilise existing services.
6.4. INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death worldwide - 30% (16.7 million) of total deaths globally.\[2\] The largest proportion of CVD mortality is attributed to coronary heart disease (CHD),\[3, 6\] the prevalence of which is projected to increase 16.6% by 2030.\[177\] Thus there is an increasing need for secondary prevention strategies to reduce the impact of CHD. Cardiac rehabilitation (CR) is a complex secondary prevention intervention that aims to optimise cardiovascular disease risk reduction, promote the adoption and adherence of healthy behaviours and reduce disability among those with established CHD.\[15\] Secondary prevention guidelines recommend a multifaceted CHD risk management approach;\[30, 178, 179\] however exercise is consistently identified as an integral component of CR,\[15, 29, 36, 180\] and its potential as a risk modification strategy extends beyond the effects of physical inactivity alone.

Numerous beneficial cardiovascular and metabolic adaptations enable exercise to concurrently target several established CHD risk factors including blood pressure, blood lipid profile, glucose metabolism, weight status and body composition.\[181\] Moreover, a Cochrane review \[32\] reported 13% (risk ratio [RR]=0.87, 95%CI 0.75, 0.99) and 26% (RR=0.74, 95%CI 0.63, 0.87) reductions in all-cause and cardiovascular mortality, respectively, following exercise-only CR and comprehensive CR incorporating an exercise component. These findings are supported by several other meta-analyses.\[31, 33, 34\]

Despite its documented benefits CR adoption is low in many countries,\[36, 60, 61\] including New Zealand.\[72, 74\] Exercise adherence is also poor, with up to 36% attrition from supervised programs.\[28, 70, 71, 92\] Factors commonly associated with sub-optimal participation include ill health, domestic responsibilities, and difficulty accessing supervised programmes.\[65, 66\] Low accessibility is of particular concern as it is associated with higher levels of cardiac morbidity and mortality.\[182\] A recent HEART journal editorial \[183\] concluded that CR should not only focus on CHD risk factor modification and medication adherence but should also offer a range of different delivery options for people according to their preferences and needs to address the low levels of participation. One such approach that has been investigated for risk factor modification has been the use of telehealth, which involves telephone, internet, and videoconference communication between patient and health-care provider.
A systematic review of 11 telehealth trials (n = 3145) showed significant improvements on CHD risk factors including exercise adherence and volume, total cholesterol, high density lipoprotein cholesterol and systolic blood pressure.[82] While these findings support telehealth, research has been limited to land-based telephone, internet and videoconferencing technologies that confine participants to fixed locations. As such there is a need to explore technologies that support increased programme flexibility. Mobile technologies, including the internet are therefore gaining increased research attention as an alternative approach to support behaviour change, clinical improvement, and improved social functioning.[184]

Emerging evidence to date for mobile interventions for delivering healthcare and improving disease self-management (mHealth) is promising.[184] A number of systematic reviews support the delivery of mobile phone text messaging interventions [135, 185, 186] for achieving behaviour change across a range of behaviours and chronic conditions such as diabetes and asthma.

In terms of CHD, the recently completed HEART randomised controlled trial (n = 171) demonstrated a mobile phone text messaging and internet intervention was effective and cost-effective for increasing leisure time physical activity and walking, but was not effective for increasing maximal oxygen uptake over and above usual care in people with CVD at 6 months.[103] Compared to the usual care control group, the HEART intervention also significantly increased participants’ health-related quality of life (physical health domain), self-efficacy and motivation to be physically active. Structured exit interviews conducted with those who were randomised to the intervention showed the HEART intervention was well received, had positive effects on participant’s physical activity levels, and was not considered burdensome. Most (93%) participants read all or most of their text messages.[187] Whilst this trial demonstrated the feasibility and effectiveness of a text messaging intervention to increase physical activity levels, improvement is needed to ensure interventions achieve positive impacts on exercise capacity and other CVD risk factors. Such improvements include closer exercise monitoring to ensure participants meet the required frequency, intensity and duration to realise beneficial physiological adaptations.

Increasingly powerful mobile technologies, such as smartphones and wireless physiological sensors, may extend the capability of mHealth exercise-based CR (exCR) by enabling real-time remote exercise monitoring for those with CVD. The feasibility of remotely monitored exCR was recently demonstrated using a
smartphone, ECG sensor and GPS receiver.[67] A six-week remote exCR programme improved walking performance (comparable to traditional exCR), cardiac depression and physical health-related quality of life. Furthermore, system usability and reliability were rated highly by participants. These encouraging results demonstrate the feasibility of remote exCR; however, a randomised controlled trial is required to determine the benefits and harms associated with this approach.

6.4.1 Aim

To compare the effectiveness of technology-assisted, home-based, remotely monitored exCR (REMOTE) to standard supervised exCR in New Zealand adults with a diagnosis of CHD.

6.4.2 Hypotheses

The primary hypothesis is that the REMOTE program will be as effective at increasing exercise capacity at 12 weeks compared to standard exCR. Secondary hypotheses are; the REMOTE program will result in similar improvements in other cardiovascular risk factors (blood lipid and glucose concentration, blood pressure, anthropometry) compared to standard exCR. The REMOTE program will result in greater exercise adherence compared to standard exCR.

6.5. METHODS

The study design is a single-blinded, two-arm, parallel, randomized controlled non-inferiority trial. Given the established effectiveness of supervised exCR [181] the REMOTE program is unlikely to result in a substantially greater improvement in exercise capacity; however, it’s advantages in terms of greater reach and participant adherence highlight the appropriateness of a non-inferiority trial design. The protocol is in accord with the SPIRIT 2013 statement,[188, 189] and the intervention is described according to the CONSORT-EHEALTH checklist.[190]

6.5.1 Eligibility And Recruitment

Eligible participants are adults aged 18 years or more, with a diagnosis of CHD (angina, myocardial infarction, percutaneous coronary intervention or coronary revascularisation) within the previous six months. Participants are current outpatients who have been clinically stable for at least six weeks, are able to perform exercise, and can understand and write English. A Motorola (Moto G) smart phone is available
on loan to participants in the REMOTE group. Participants who have been admitted to hospital with heart disease within the previous six weeks, have terminal cancer, are contraindicated for maximal exercise testing, have significant exercise limitations other than CHD, currently meet the recommendations for regular physical activity (150 min/week moderate to vigorous),[191] are currently participating in a supervised exercise programme (including exCR), have a pacemaker or implantable cardioverter-defibrillator, or have contraindications for maximal exercise testing are excluded.

Eligible participants are identified by research nurses or research assistants from a large metropolitan hospital in Auckland, New Zealand (population 1.6 million) prior to discharge, through outpatient clinics and existing databases, as well as existing community CR education sessions. Those agreeing to participate are screened for eligibility and provided a study pack, which includes a participant information sheet and consent form. Contact details of interested participants are sent to the research team. Participants identified in hospital and through outpatient clinics are telephoned approximately one month after discharge or one week after initial contact, respectively, to confirm their interest in the study and schedule a baseline assessment. Eligible participants are also recruited by a research staff at an existing CR clinic in the Bay of Plenty, New Zealand. These participants have been discharged from hospital, are eligible to participate in CR but have not yet enrolled in a program. Interested participants are given a study pack and a baseline assessment is scheduled.

6.5.2 Sample Size Calculation

The target sample size of 162 participants (81 per group) will provide 80% power at 2.5% level of significance (one-sided) to show that the REMOTE and standard exCR programmes do not differ by more than 1.25 ml·kg⁻¹·min⁻¹ on peak oxygen uptake (VO₂max). This sample size is based on the assumption the standard exCR programme will result in an increase of 2.4 ± 2.7 ml·kg⁻¹·min⁻¹ in VO₂max at 12 weeks,[192] and has been inflated to allow for 10% loss to follow up. The non-inferiority margin was chosen because it is clinically significant and is associated with lower CV-mortality.[44, 45]
6.5.3 Ethics Approval

Ethical approval for the trial was received from the University of Auckland Human Participants Ethics Committee (011021). Approval was also obtained from the Metropolitan Hospital’s Research Review Board.

6.5.4 Randomization And Blinding

After written consent is obtained, baseline assessment is completed and then participants are randomized using sealed sequential, opaque envelopes. Participants are randomly allocated to either the control (traditional exCR) or intervention (REMOTE) arms at a 1:1 ratio, stratified by study site and sex. The allocation sequence is overseen by the project statistician (YJ). Assessors of the primary outcomes are blind to treatment allocation; however participants are not blind.

6.5.5 Intervention

The REMOTE intervention is delivered over 12 weeks and comprises a personalised exercise prescription, real-time remote exercise monitoring, and behavioural support to increase exercise adherence (goal setting, exercise scheduling, overcoming barriers), delivered via smartphone. The intervention aims to have individuals participate in moderate to vigorous aerobic-based exercise for at least 30 minutes (preferably more), most days (≥5) of the week, in line with current recommendations [193] and American College of Sports Medicine (ACSM) guidelines.[195]

Specific details are provided below.

6.5.5.1. Exercise Prescription

An individualized exercise prescription, based on personal preferences and current exercise capacity, is a core component of the intervention. Following ACSM guidelines for exercise in cardiac patients,[195] participants are provided with a weekly prescription detailing exercise duration, frequency and intensity, via a smartphone application (app) designed for this study. The prescribed exercise intensity is sufficient to induce a “training effect”, yet below a metabolic load that evokes abnormal clinical signs or symptoms. Exercise duration is increased according to symptoms and clinical status. Exercise intensity is increased gradually as tolerated.[195] Progression of exercise prescription components occurs in the following order: duration, frequency, then intensity.[195] Participants are taught and encouraged to use ratings of perceived exertion (RPE) and the heart rate reserve method (HRR) to achieve the desired intensity. During early stages the level of
intensity targets an RPE of 11 to 13 ("fairly light" and "somewhat hard"; 6-20 scale) \[196\] and/or 40% to 50% HRR. During the latter stages the level of intensity targets an RPE of 13 to 15 ("somewhat hard" to "hard") and/or 55% to 65% HRR. The preferred mode of exercise is walking, although participants are able to choose other modes (e.g. cycling, rowing) if preferred.

6.5.5.2. Remote Monitoring

During pre-defined time windows (e.g. 06:00-11:00) participants connect to the remote exercise monitoring system, which permits a remotely-located exercise physiologist to monitor their location, distance, speed, heart rate, respiratory rate, training load and single-lead ECG in real-time; provide real-time feedback and support via participants’ smartphone (including alerts, messages or telephone calls); respond to adverse events if necessary; provide post-exercise feedback; and modify participants’ exercise prescription as required. Participants can be monitored in any environment with an active broadband connection (mobile, Wi-Fi, Bluetooth).

The REMOTE system, comprising a physiological sensing device, smartphone and web apps, and a middleware platform, supports simultaneous monitoring of multiple participants. Participants are loaned a BioHarness 3 (Zephyr Technologies, USA) physiological sensing device to wear during exercise. The BioHarness enables measurement of a comprehensive range of physiological parameters required for monitoring exercise performance. Bluetooth connectivity permits transmission of data to smartphones. The system including the Zephyr device, smartphone (Android) app, and the Odin middleware platform has been tested for reliability and validity.\[114\] The Odin middleware platform, is an off-the-shelf solution that provides reliable communication, minimises data usage cost and maximises device battery life.\[161\] The smartphone app collects and transmits physiological data to a remotely located web server in real-time. The web app displays these data in remote locations, and enables real-time provision of feedback to moderate participants’ exercise behaviour.

6.5.5.3. Support And Strategies To Facilitate Exercise Adherence

Messages outlining key behaviour change strategies are sent to participants via the smartphone by the exercise physiologist. Three messages per week are sent for the 12 week intervention period. The program is grounded in self-efficacy theory,\[197, 198\] which is the most examined psychological variable within the cardiac setting. Behaviour change strategies focus on increasing confidence and motivation to exercise, overcoming barriers to being physically active, scheduling exercise into daily life, goal setting, and enhancing social support and networks to be active. In
addition, features on the smartphone app allow participants to review their exercise performance and assess progress toward personalised goals.

6.5.6 Control

The active control group receive a 12 week program of supervised exercise, delivered at the University of Auckland or Tauranga CR clinics. Supervised exercise sessions are offered three times per week by trained exercise scientists/nurses. Participants typically complete a 15-minute warm up, 30-45 minutes of moderate-vigorous intensity aerobic exercise on various exercise modalities (e.g., treadmill, cycle ergometer, rowing machine), and a 5 min cool down. Heart rate, blood pressure, and rating of perceived exertion (RPE) are monitored on a regular basis. Exercise prescription for the control group also adheres to ACSM guidelines for exercise in cardiac patients.[195]

6.5.7 Outcome Assessments

All assessments are conducted at the University of Auckland and Tauranga cardiac clinics. Prior to the baseline assessment participants are sent an accelerometer to wear for seven consecutive days. Baseline assessments involve an explanation of study procedures, signed consent and collection of participant-reported secondary outcomes, followed by physical measurements (stature, body mass, body mass index, waist and hip circumference), blood lipid and glucose measurements, and a test of maximal exercise capacity. The baseline assessment concludes with randomization and assignment of participants to the respective study groups.

6.5.7.1. Primary Outcome

The primary outcome is maximal oxygen uptake ($\text{VO}_2\text{max}$) assessed at baseline and 13 weeks. An individualised exercise testing protocol is used to assess $\text{VO}_2\text{max}$ via respiratory gas analysis. A graded protocol is initiated at a comfortable walking speed and 0% gradient. The gradient then increases by 1% every 60 seconds until volitional exhaustion, or the presence of indications for test termination.[195] The target exercise time is 8 to 12 minutes. Individualised walking speeds are replicated at the 13 week follow-up assessment. Participants are encouraged to continue the test until the respiratory exchange ratio exceeds 1.10, indicative of a maximal aerobic performance. The ACSM guidelines for exercise testing cardiac patients are adhered to.[195] Exercise testing is conducted at the University of Auckland Clinics, Tamaki
Campus, and the Tauranga cardiac clinic by trained physiologists. A medical physician is available to deal with any emergencies that may arise.

6.5.7.2. Secondary Outcomes

All secondary outcomes are assessed at baseline, 13 and 25 weeks, except for blood lipid and glucose concentrations, which are assessed at baseline and 13 weeks only. Stature, body mass, waist and hip circumference, and blood pressure are measured using standardized procedures. An electronic sphygmomanometer will be used to assess systolic and diastolic pressure after at least 5 minutes of seated rest. Participants’ height will be measured to the nearest 0.1 cm using a stadiometer, and body mass to the nearest 0.1 kilograms using electronic scales. Body mass index is derived from the weight (kg) divided by height (m) squared. Waist circumference is measured using an anthropometric tape measure placed around the participant’s waist at the level of the umbilicus. Hip circumference is measured around the furthest protrusion of the buttocks as seen from a lateral perspective. Waist-hip ratio calculated according to ISAK protocols.[199]

A fingertip blood sample is obtained from participants for analysis of blood lipid and glucose concentration using automated point of care analysers (Cholestech LDX at the Auckland site, CardioChek at the Tauranga site).

Psychological variables including self-efficacy (situational self-confidence), intentions, and motivation to exercise are assessed to determine their potential mediating effect. Task self-efficacy is assessed using a scale adapted from the Self-Efficacy Scale.[200] Participants rate their confidence to perform physical activities for increasing periods of time (i.e., 10, 30, and 60 min) at three intensities (i.e., light, moderate, and vigorous). A key is provided to define these levels of intensity. Mean scores are calculated with higher values indicating greater efficacy to perform physical activity for longer duration and greater intensity.

Participants’ confidence to exercise in the face of obstacles (barrier efficacy) is assessed using the Barriers Efficacy Scale.[200] Participants rate their confidence to overcome eight common reasons preventing people from participating in exercise sessions (e.g., pain, bad weather) on a scale ranging from 0% (no confidence at all) to 100% (completely confident). Mean scores are calculated with higher values indicating greater efficacy to overcome barriers to exercise.

Self-efficacy to follow their exercise prescription is assessed using 9 items. Participants rate their confidence in their ability to follow the prescribed exercise
regimen on a scale ranging from 0% (no confidence at all) to 100% (completely confident). Mean scores are calculated with higher values indicating greater efficacy to adhere to prescribed exercise.

Intentions to perform physical activity are assessed using two items,[201] which ask participants to rate their level of intention to follow their exercise prescription during the next 3 months (e.g. "I definitely intend to follow my exercise prescription"). The items are scored using a seven point Likert scale ranging from 0 (completely disagree) to 7 (completely agree). A mean score from the two items is used to give an overall measure of intention with higher values indicating greater intention to perform physical activity.

Self-determination to exercise is operationalized using the Locus of Causality for Exercise Scale; a reliable and valid three-item self-report measure of the extent to which participants feel they choose to exercise with no sense of coercion.[202] Participants rate how much they agree or disagree with each statement on a seven-item Likert scale from 1 (Strongly disagree) to 7 (Strongly agree) indicating their motivation to perform exercise. Mean scores are calculated with higher values indicating greater self-determination or a more internal perceived locus of causality.

Leisure time exercise is assessed using the Godin Leisure Time Physical Activity Questionnaire.[203] This simple three-item questionnaire has well-established reliability and validity and has been used in patients undergoing CR (n = 826).[203]

Objective physical activity is assessed using the Actigraph accelerometer ([www.theActigraph.com](http://www.theActigraph.com)), which is sent to participants to wear for 7 consecutive days. The Actigraph is a small, piezoelectric accelerometer and has been validated in healthy and cardiac patients.[204, 205] Raw data are processed according to accepted procedures.[206]

Adherence to the prescribed regimens is assessed by determining the number of sessions attended compared to the number of sessions prescribed. Participants in both programs are encouraged to participate in supervised exercise three times per week. Attendance data are collected weekly and summed to determine total attendance (the numerator) compared to total number of sessions prescribed (denominator).

Cost information is collected and includes the cost of each programme and direct medical costs (including cost of treatment, primary care, secondary care and over-
the-counter medications). The EuroQol five dimension questionnaire [207] is used to obtain a single preference index for calculation of Quality Adjusted Life Years to assess per-unit cost for comparison with other CR programmes. Healthcare utilisation is recorded for adverse events including cardiac events, and other events participants deem likely to be related to their participation in the study (including, but not limited to, musculoskeletal injury).

6.5.8 Statistical analysis

Statistical analyses will be performed using SAS version 9.2 (SAS Institute Inc. Cary NC) and R version 2.11 (R Foundations for Statistical Computing). Baseline characteristics will be summarised using descriptive statistics. Continuous variables will be described as numbers of observed and missing values, mean, standard deviation, median, minimum and maximum. Categorical variables will be described as frequencies and percentages. Treatment evaluation will be performed on the principle of intention to treat, using data collected from all randomised participants. Analysis of covariance (ANCOVA) regression model will be used to evaluate the main treatment effect on the primary outcome between the two treatment groups, adjusting for its baseline measure, age, ethnicity and other potential confounding factors (if they are statistically significant at 5% level). A similar approach will be used for other continuous secondary outcome measures. Logistic regression model will be considered for the analysis of a binary outcome (e.g. meeting physical activity recommendations).

6.6. CONCLUSION

This novel study evaluates a supervised exercise program delivered via a mobile phone and sensor system compared to a traditional model of supervised exCR. REMOTE monitoring may offer the same benefits of a supervised gym-based program, but is potentially more accessible to a broader range of patients and is cost-effective.

The protocol, in accordance with the SPIRIT statement, incorporates findings from recent mobile and telehealth systematic reviews, with the aim of building on this empirical evidence. The REMOTE trial includes an objective assessment of maximal cardiorespiratory fitness, which is the gold standard measurement following exCR. It also includes objective assessment of physical activity, which was lacking in previous research.[103]
The non-inferiority trial design is most suitable because it is unlikely the REMOTE intervention will result in substantially greater improvement in exercise capacity compared to traditional supervised exercise.[208] The non-inferiority margin (\(\dot{\text{V}}\text{O}_2 \text{ 1.25 ml·kg}^{-1} \text{·min}^{-1}\)) is clinically significant and is associated with lower cardiovascular mortality.[14]
6.7. COMPETING INTERESTS

The authors declare that they have no financial or non-financial competing interests.

6.8. AUTHOR CONTRIBUTIONS

RM and JR conceived the study, participated in its design and coordination, and helped draft the manuscript. AR, NG, RW and YJ participated in the design of the study. RS and JB provide clinical oversight for the study. IW participated in the design of the study and created the REMOTE software. All authors read and approved the final manuscript.

6.9. TRIAL REGISTRATION

Australian New Zealand Clinical Trials Registry (ACTRN12614000843651, 07/08/2014)

6.10. SOURCES OF SUPPORT

This is an investigator-initiated study funded by a grant from the Auckland Medical Research Foundation, 1113020. Dr Maddison is supported by a Health Research Council, Sir Charles Hercus Research Fellowship.
CHAPTER 7. EVALUATING TELEHEALTH CARDIAC REHABILITATION EFFECTIVENESS: PILOT TRIAL RESULTS

7.1. INTRODUCTION TO CHAPTER

This chapter presents the findings from a pilot non-inferiority RCT which was nested within the larger trial described in Chapter 6. The pilot trial was planned to include 76 participants, and evaluate the primary and selected secondary outcomes at the 12 week follow-up time point. Differences between the main trial protocol (Chapter 6) and the pilot trial reported in this chapter are specified and rationalise in the methods section, below. There were three main objectives: 1) compare the effects of remote and centre-based programmes, 2) evaluate within-group effectiveness, and 3) assess usability and acceptability.

This piece of research was undertaken to address Objective 4, which was to rigorously evaluate the effectiveness and acceptability of an alternative exercise-based rehabilitation delivery model.

7.2. AUTHOR CONTRIBUTION

Jonathan Rawstorn was responsible for ethical approval, study management, delivery of the mobile health intervention, baseline assessment of the primary outcome, analysis and interpretation of the results, and wrote this chapter. The chapter is written in accordance with guidelines for reporting randomised, non-inferiority and equivalence, and eHealth trials.[190, 209, 210]
7.3. ABSTRACT

Introduction
Mobile health (mHealth) technologies can remotely connect clinical exercise specialists with exercise-based cardiac rehabilitation (exCR) participants to provide real-time supervision and coaching in any location. We compared the effectiveness of remotely delivered exCR with traditional clinical programmes; we hypothesised remote exCR \( \dot{V}O_2 \text{max} \) would be no more than 1.75 ml·kg\(^{-1} \cdot \text{min}^{-1} \) lower than control.

Methods
A non-inferiority, two-arm, parallel pilot RCT compared 12 weeks of remotely monitored exCR (intervention; INT) with centre-based exCR (control; CON) among people with coronary heart disease (CHD). The intervention included real-time remote exercise monitoring, evidence-based coaching from exCR specialists, theory-based behaviour change, and social support. The control treatment included traditional supervised exCR. Maximal aerobic exercise capacity (\( \dot{V}O_2 \text{max} \), primary), cardiovascular risk factors, exercise adherence and self-efficacy changes from baseline were assessed at baseline and three month follow-up.

Results
76 participants (male n=68/86%; New Zealand European n=58/76%; 61.0 ± 13.5 y) were randomised to INT (n=37) or CON (n=39). \( \dot{V}O_2 \text{max} \) was comparable but non-inferiority was inconclusive (adjusted difference=0.16 ml·kg\(^{-1} \cdot \text{min}^{-1} \), [95% CI -1.79 to 2.12], \( P=.87 \)). Both groups improved \( \dot{V}O_2 \text{max} \) (INT\( \Delta \)=2.92 ml·kg\(^{-1} \cdot \text{min}^{-1} \) [1.52 to 4.32]; CON\( \Delta \)=2.76 ml·kg\(^{-1} \cdot \text{min}^{-1} \) [1.39 to 4.12], both \( P<0.001 \)), physical activity energy expenditure (INT\( \Delta \)=2786 METmin·week\(^{-1} \) [1264 to 4308] \( P=.001 \); CON\( \Delta \)=3149 METmin·week\(^{-1} \) [1666 to 4631] \( P<.001 \)), and task self-efficacy (INT\( \Delta \)=12.87% [8.54 to 17.19]; CON\( \Delta \)=12.86% [8.66 to 17.08], both \( P<.001 \)). Exercise adherence was comparable (INT=69.34 ± 5.21%, CON= 57.73 ± 5.35%, \( P=.12 \)). Intervention acceptability and usability were high; 28 (90%) intervention participants would choose remotely monitored exCR if available via usual care.

Conclusions
Real-time remotely monitored exCR was comparable to centre-based exCR; the main RCT will help clarify the non-inferiority hypothesis in a larger sample. Remotely monitored exCR can complement existing exCR services, and may increase utilisation by providing an additional option for people who are unwilling or unable to attend centre-based exCR.
7.4. INTRODUCTION

Cardiac rehabilitation (CR) is an essential component of contemporary coronary heart disease (CHD) management that aims to optimise cardiovascular risk reduction, facilitate adoption and adherence to healthy behaviours, reduce disability, and promote an active lifestyle.[15] International guidelines recommend a multidisciplinary approach that includes patient evaluation, medical and lifestyle risk factor management, cardioprotective therapies, psychosocial management, exercise training, and health behaviour change education.[15, 16]

Exercise training is a central element of CR that reduces mortality and rehospitalisation rates,[15, 32, 211] improves modifiable cardiovascular risk factors, health-related quality of life (HRQoL) and psychosocial wellbeing,[14, 34, 47, 48, 77, 211] and may be more cost-effective for reducing premature death than common CHD medications.[36] Exercise-based CR (exCR) has traditionally been delivered in clinical settings such as hospitals and rehabilitation centres, and commonly comprises two to three months of exercise training supervised by exCR specialists or physical therapists.

Despite the documented health benefits, adoption and adherence to exCR are suboptimal,[58, 60] and participation is frequently limited by a system/service, psychological, and access barriers.[64, 67] Compared with centre-based exCR, home-based programmes overcome several access barriers and provide comparable effects on mortality, recurrent cardiac events, exercise capacity, modifiable cardiovascular risk factors, and HRQoL.[64, 77] However, the opportunity cost of enhanced access is a loss of supervision from exCR specialists. This may limit the magnitude of exercise-induced health benefits,[18] and limits opportunities to support positive exercise motivation via interactive coaching, feedback and social support.

Telehealth programmes have used information and communication technologies to provide CR participants with additional support and this approach has demonstrated promising effects on cardiovascular risk factors, HRQoL, and adverse events.[82-84] However, previous telehealth programmes have relied on periodic telephone, email or SMS contact, which has not allowed the responsive, structured exercise monitoring, coaching, feedback, and social support that are provided by face-to-face supervision during centre-based exCR. Some telehealth exCR interventions have used mobile technologies (mHealth exCR) such as wearable sensors and smartphone applications (apps) to monitor exercise adherence and physical activity.
level,[98, 100-102, 106, 107] but asynchronous data processing and specialist review has precluded the responsive monitoring, coaching and support that is characteristic of centre-based exCR. Addressing these limitations remains a major challenge for telehealth/mHealth exCR to overcome.

Real-time remote exercise monitoring and coaching could address this challenge by combining the accessibility of home-based exCR with the responsive, individualised clinical supervision of centre-based programmes. The requisite technological capability has existed for some time and the feasibility of this approach has been demonstrated among people with CHD.[67, 114] However, there remains a lack of evidence for the effectiveness and acceptability of real-time remotely monitored exCR. The capability to connect exCR specialists with participants in real-time, in almost any location, using mHealth technologies could narrow the gap between home- and centre-based exCR, and has potential to improve reach and utilisation. Real-time remotely delivered exCR could complement existing exCR services by providing an alternative delivery model for people who do not have access to centre-based exCR, and people who do have access to centre-based exCR but would benefit from more flexible programme delivery models. To achieve these two objectives remotely delivered exCR should be more effective than usual care alone, and at least as effective as traditional centre-based exCR programmes.

This pilot study aimed to determine whether real-time remotely monitored exCR (REMOTE-CR) was at least as effective as traditional centre-based exCR for improving maximal exercise capacity (VO2max) in adults with CHD. We adopted a non-inferiority experimental design because, in combination with favourable accessibility, non-inferiority of remotely monitored exCR is expected to be sufficient to support implementation as an additional alternative alongside existing exCR services. For the pilot study, the pre-specified non-inferiority margin was -1.75 ml·kg⁻¹·min⁻¹ (main trial margin = -1.25 ml·kg⁻¹·min⁻¹); this represents a clinically important difference that is associated with reduced mortality.[14, 44, 45] Our primary null hypothesis was H₀: The effect of centre-based exCR on VO2max is at least 1.75 ml·kg⁻¹·min⁻¹ higher than remotely monitored exCR. Secondary objectives were to explore the effects of remotely monitored exCR on modifiable cardiovascular risk factors, exercise adherence, and self-efficacy. Non-inferiority margins were not defined for secondary outcomes.
7.5. METHODS

7.5.1 Design

A nested pilot trial was embedded within a larger ongoing parallel, two-arm, non-inferiority RCT being conducted in New Zealand. The REMOTE-CR study (Chapter 6) is comparing the effectiveness of 12 week programmes of centre-based and real-time remotely monitored exCR. The trial protocol was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12614000843651) and published in 2014.[115] No changes have been made to the main trial protocol during the study; however, the pre-planned scope of this pilot trial was limited to immediate post-exercise programme follow-up (12 weeks) and a subset of outcomes specified in the study protocol (see Outcomes, below). The trial received ethical approval from the University of Auckland Human Participants Ethics Committee (011021). Trial development and reporting was informed by the CONSORT statements for randomised, non-inferiority and equivalence, and eHealth trials.[190, 209, 210]

7.5.2 Participants

Trained researchers identified participants via three metropolitan hospitals, outpatient cardiac rehabilitation clinics, and community-based CR group seminars in Auckland and Tauranga (New Zealand). Eligible participants were English-speaking adults (≥ 18 years) with a documented diagnosis of CHD (atherosclerosis, angina pectoris, myocardial infarction or coronary revascularisation) within the previous six months. Participants were outpatients who had been clinically stable for at least six weeks at baseline, and were able to perform exercise. Participants who had been admitted to hospital with heart disease within the previous six weeks, had terminal cancer, were contraindicated for maximal exercise testing and/or had significant non-CHD exercise limitations, met physical activity recommendations (150 minutes moderate to vigorous activity per week), were currently participating in a supervised exercise programme (including centre-based exCR), or had a pacemaker or implantable cardioverter-defibrillator were excluded. The eligible cohort was comparable to previous trials that have established the efficacy of the reference treatment, centre-based exCR. Smartphone ownership and literacy were not required; intervention group participants received loaned smartphones (with active data connections) and completed a bespoke training module, and on-demand technical support was available via telephone, email and/or face-to-face as required.
7.5.3 Procedures

Eligible participants provided informed consent and completed a face-to-face baseline assessment at University or clinical facilities at least 6 weeks after discharge from hospital. All participants had access to usual care which included inpatient rehabilitation, individualised outpatient clinics, and community-based group education seminars that cover topics such as cardiovascular risk factors, medication, nutrition, physical activity/exercise, and psychosocial support. In addition to usual care, participants completed a 12 week programme of centre-based exCR (control group) or remotely-monitored exCR (intervention group). All participants completed a face-to-face follow-up assessment within two weeks of completing their exercise programme.

7.5.4 Intervention

Exercise programmes for both study groups were informed by evidence-based guidelines for prescribing exercise to people with CVD. Programs comprised three exercise training sessions per week for twelve weeks, and encouragement to be active on most days of the week (i.e. ≥ 5 days). Exercise prescription was individualised and progressed based on participants’ VO$_2$max (assessed at baseline), exercise-induced signs and symptoms, age, sex, and exercise tolerance throughout the programme. Training session duration ranged from 30 to 60 minutes, and included warm up and cool down phases to allow appropriate cardiovascular and musculoskeletal preparation and recovery. Exercise intensity level ranged from 40% to 65% HRR (the difference between rest and maximal heart rates), and was adjusted to optimise physiological adaptations while remaining below a metabolic load that induces abnormal clinical signs or symptoms (if present). Remotely monitored exCR (intervention) predominantly focused on aerobic exercise modes as few participants had access to strength training facilities, and remotely quantifying strength training performance remains a technological challenge. However, strength training was not excluded, and was optionally undertaken by some participants. Centre-based exCR (control group) included strength training when appropriate, and was similar to treatments typically included in studies evaluating the effectiveness of centre-based exCR.

Remotely monitored exCR was delivered via an mHealth platform comprising a commercially available Android-based smartphone and wearable sensor, custom smartphone and web-based apps, and custom middleware (Figure 8).
Platform features and intervention content were grounded in behaviour change theory, including Social Cognitive Theory, Self-determination Theory, and a taxonomy of behaviour change techniques (Table 1).[126, 127, 129] Theory-based platform components were designed to enhance self-efficacy, competence, autonomy, and relatedness (Chapter 4), as these constructs influence exercise adoption and adherence, physical activity level, and clinical outcomes.[130, 132-134]

The commercially available wearable sensor (BioHarness 3, Zephyr Technology, USA) features Bluetooth connectivity and a multi-sensor array that is well suited for monitoring exercise among people with CHD (i.e. ECG including waveform data, heart rate, heart rate variability, respiratory rate, torso posture, tri-axial acceleration). Wearable sensor accuracy and reliability were validated in the target population during platform development.[114]

Commercially available smartphones using the Android (Google Inc., USA) mobile operating system were loaned to intervention group participants for the duration of the exercise programme; mobile data plans were provided free of charge and the REMOTE-CR smartphone app was pre-installed. Periodic updates were deployed via the Google Play Store (https://play.google.com) to optimise app performance and stability; updates did not change intervention content or functionality.

The smartphone and web-based apps were designed specifically for remote delivery of exCR by the research team, via an iterative development process that included validation of real-time data transmission reliability.[114] The participant-facing smartphone app [147] is compatible with Android version 4.0 or higher; the exCR specialist-facing web-based app is accessible via any desktop or mobile internet browser. True mobile capability enables participants and exCR specialists to operate from any location with a mobile or local internet connection.

Smartphone and web-based app features enabled real-time remote exercise monitoring and coaching, retrospective exercise performance review, goal setting, behaviour change education, and social support. Operating hours for remotely monitored and centre-based exCR were matched to ensure equal availability between study groups; exCR specialists were available for real-time remote exercise monitoring at any time during operating hours. During exercise, data from the wearable sensor (physiological) and smartphone (geo-positional) were displayed on the smartphone for participant self-monitoring, and streamed to a web server in real-time via mobile broadband. Data were retrieved by the web-based app and visualised for exCR specialist monitoring, also in real-time. Exercise specialists monitored data
during pre-specified live monitoring time windows, and provided real-time individualised coaching, feedback, and social support throughout exercise via a text-to-audio messaging system. Participants received audio messages via earphones to preserve the real-time context of the communication and aid usability, and could be manually replayed and/or read at any time.

The smartphone app enabled participants to retrospectively review summarised exercise performance data and set individualised exercise and physical activity goals. Performance review allowed participants to assess their progress throughout the intervention; goal achievement feedback was automatically visualised, and updated weekly to reflect current achievement status.

Participants received a suite of behaviour change educational messages throughout the intervention. Message content was adapted from theory-based short message service (SMS) exCR interventions that have demonstrated positive effects on lifestyle behaviours.[103, 155] SMS messages were adapted for the real-time context of REMOTE-CR, and took advantage of a larger character allowance to include more natural language (Appendix 2).

The custom middleware sat between the smartphone app and web server to manage communication and logistic functions including data security, network connectivity and device resource usage.[145, 146] To ensure security and privacy the REMOTE-CR platform included user authentication protocols in both apps, the web server was secure, and all data transmission was encrypted.

7.5.5 Outcomes

All outcomes were pre-specified in the study protocol and remained unaltered during the study; however, the scope of this pilot trial was limited to the primary and selected secondary outcomes, and did not include the specified six month longer term follow-up. Outcomes were assessed at baseline and at the completion of the 12 week exercise programmes. The primary outcome was a non-inferiority outcome; non-inferiority margins were not specified for secondary outcomes as the study could only be powered for the primary non-inferiority margin.

7.5.5.1. Primary Outcome

The primary outcome was \( \dot{V}O_{2\text{max}} \), assessed during an individualised maximal graded treadmill exercise test. The \( \dot{V}O_{2\text{max}} \) protocol was initiated at a brisk (individualised) velocity, and gradient was increased by 1% every 60 seconds until
volitional fatigue or clinical indications for test termination. The baseline protocol was replicated at follow-up until the baseline termination time; modifications (e.g. increased velocity) were permitted after the baseline test duration was exceeded, if required. Respiratory gas exchange was measured throughout using a metabolic cart (Moxus, AEI Technologies, USA); VO$_2$max was defined as the average VO$_2$ during the final 30 seconds prior to fatigue or symptom limited test termination. Exercise testing was completed by blinded, trained exercise physiologists, in accordance with clinical guidelines for maximal exercise testing among people with CVD.[149]

7.5.5.2. Secondary Outcome

Secondary outcomes included blood lipid (total, high-density lipoprotein [HDL-C] and low density lipoprotein cholesterol [LDL-C], triglycerides) and glucose concentrations, body composition (stature, body mass, body mass index, waist and hip circumferences), blood pressure (systolic and diastolic), physical activity energy expenditure, exercise-related task and barrier self-efficacy, and exercise adherence. Measurement of modifiable cardiovascular risk factors followed standardised procedures. Capillary blood lipid and glucose concentrations were measured using Cholestech LDX (Auckland study site) or CardioChek (Tauranga study site) analysers. Blood pressure was measured with a calibrated, automated sphygmomanometer (T9P, Omron Healthcare, Netherlands) after at least 5 minutes of seated rest. Physical activity level was assessed with the Godin Leisure Time Physical Activity Questionnaire.[203] Exercise-related task and barrier self-efficacy were assessed with adapted versions of the Self-Efficacy Scale and Barriers Efficacy Scale.[200] Exercise adherence was assessed as the number of exercise training sessions completed (numerator) compared to those scheduled (denominator). Adverse event data were collected at follow-up. Primary and secondary outcomes are similar to those reported in studies that have established the effectiveness of the reference treatment, centre-based exCR.

7.5.6 Sample Size

For the main RCT we estimated a sample size of 162 (81 per group) would provide at least 80% statistical power at the 2.5% level of significance (1 sided) to detect a difference in VO$_2$max of 1.25 ml·kg$^{-1}$·min$^{-1}$ between the two groups at follow-up, including inflation to allow 10% loss-to-follow-up; that is, a non-inferiority margin of -1.25 ml·kg$^{-1}$·min$^{-1}$. This sample size was based on the assumption the standard exCR programme will result in an increase of 2.4 ± 2.7 ml·kg$^{-1}$·min$^{-1}$ in VO$_2$max at 12 weeks,[192] and was inflated to allow for 10% loss to follow up. For this pilot trial,
using the same data we estimated a sample size of 76 (38 per group) would provide at least 80% statistical power at the 2.5% level of significance (1 sided) to detect a difference in $\dot{V}O_2$ max of 1.75 ml·kg$^{-1}$·min$^{-1}$ between the two groups at follow-up; that is, a non-inferiority margin of $-1.75$ ml·kg$^{-1}$·min$^{-1}$. This margin is clinically significant, and is associated with lower cardiovascular mortality.\cite{14, 44, 45}

### 7.5.7 Randomisation and Blinding

Upon completion of the baseline assessment trained researchers randomised participants to the intervention or control group at a one-to-one ratio, stratified by study site and sex. The randomisation sequence was computer generated by a statistician who was not involved in study procedures, and used a blocked approach (variable block size, 2 or 4). Treatment allocation was concealed in sequentially numbered, sealed, opaque envelopes until completion of the baseline assessment, preserving participant and assessor blinding. Due to the nature of the treatments it was not possible to blind participants to their treatment allocation. Primary outcome assessment was blinded at follow-up.

### 7.5.8 Statistical Methods

Treatment effects were evaluated using analysis of covariance on the change from baseline, adjusted for the baseline outcome value, to enable assessment of within- and between-group effects in the same model. All analyses were conducted according to the principles of intention to treat. The primary hypothesis was assessed using the non-inferiority confidence interval method,\cite{210} whereby non-inferiority required the 95% CI lower bound to be above the $-1.75$ ml·kg$^{-1}$·min$^{-1}$ inferiority margin. Missing data were imputed using the group mean outcome value. This was preferred to carrying the baseline outcome value forward, as assuming no change could bias analyses toward no difference and, therefore, non-inferiority.\cite{208}

In line with recommendations for reporting non-inferiority and equivalence trials,\cite{210} a per protocol analysis of the primary outcome was also conducted to estimate sensitivity of the treatment effect to attrition.

Exploratory analyses of secondary outcomes were not subjected to non-inferiority methods, and were tests of superiority. Statistical analyses were conducted using SPSS (version 22, IBM Corp., USA); all tests were 2-sided with a 5% level of statistical significance. Descriptive statistics were calculated for intervention feedback questionnaire responses.
Additional sensitivity and sub-group analyses were considered inappropriate in this pilot trial as they were likely to be underpowered. Descriptive statistics are reported as mean ± standard deviation (SD) or n / %. Mean treatment effects are reported with 95% CI or SD, as specified. Unadjusted descriptive statistics are also presented for baseline and follow-up time points alongside change from baseline data.

7.6. RESULTS

A total of 334 potential participants were screened for eligibility between May 2014 and May 2015 (Figure 12); 105 were ineligible and 143 declined participation. Of those who declined 49 (34%) expressed treatment group preferences (intervention n = 40; control n = 9) and declined participation to avoid the possibility of randomisation to the non-preferred treatment. Ten participants did not attend the baseline assessment and were unable to be successfully rescheduled. In total, 37 and 39 participants were randomised to the intervention and control groups, respectively. Three participants withdrew after randomisation but prior to being enrolled in a study treatment, 9 were lost to follow-up (withdrawn n = 5, unable to attend follow-up n = 4). At follow-up, 2 participants were unable to complete assessment of the primary outcome but did complete assessment of secondary outcomes (Figure 12).

Participants were predominantly male (n = 68, 89.2%), New Zealand European (n = 58, 76.3%), with a mean age of 61.0 ± 13.5 years (Table 6). Twenty eight (36.8%) participants’ were below the median New Zealand household income (= NZD 70 000 per year). Most participants had been diagnosed with a myocardial infarction (n = 53, 69.7%); 45 (59.2%) had undergone angioplasty, and 21 (27.6%) had undergone CABG surgery. Approximately half the participants were prescribed a beta blocker (n = 42, 55.3%) and angiotensin converting enzyme inhibitor (n = 37, 48.7%). Most participants were prescribed aspirin (n = 70, 92.1%) and a statin (n = 69, 90.8%).

7.6.1 Primary Outcome

After 12 weeks of eXCR there was no statistically significant difference in VO₂max between the intervention or control group (F₁, 73 = 0.03, P = .87, Table 7). The lower bound of the 95% CI extended marginally beyond the a priori non-inferiority margin (Figure 13). Within-group improvements in VO₂max were statistically significant for both the intervention and control groups (both P < 0.001, Table 7).

A per protocol sensitivity analysis of complete cases was consistent with the primary analysis; VO₂max did not differ between groups (adjusted change from baseline = -
0.25 ml·kg⁻¹·min⁻¹, 95% CI -2.25 to 1.75 ml·kg⁻¹·min⁻¹, F₁,₆₂ = 0.06, P = .80), the lower bound of the 95% CI extended beyond the non-inferiority margin, and within-group improvements remained statistically significant for both the intervention (adjusted change from baseline = 2.72 ml·kg⁻¹·min⁻¹, 95% CI 1.25 to 4.19 ml·kg⁻¹·min⁻¹, P = .001) and control groups (2.97 ml·kg⁻¹·min⁻¹, 95% CI 1.61 to 4.33 ml·kg⁻¹·min⁻¹, P < 0.001).

7.6.2 Secondary Outcomes

There were no between-group differences in any secondary outcomes (F₁,₇₃ = 0.00 to 3.43, P = .07 to .99) except for a small difference in waist-to-hip ratio that favoured the control group (F₁,₇₃ = 4.99, P = .03, Table 7).

Self-reported physical activity energy expenditure increased in both the intervention (P = .001) and control groups (P < .001, Table 7). Remotely monitored exCR reduced diastolic blood pressure (P = .02), increased HDL-C (P = .047), and increased exercise-related task self-efficacy (P < .001, Table 7). There was a small but statistically significant increase in waist-to-hip ratio in the intervention group (P = .03, Table 7).

Centre-based exCR reduced systolic blood pressure (P = .04), reduced waist (P = .02) and hip circumferences (P = .01), and increased exercise-related task self-efficacy (P < .001, Table 7). There were no other statistically significant within-group changes in secondary outcomes.

7.6.3 Intervention Fidelity and Acceptability

Three participants (intervention = 2, control = 1) withdrew from the study after randomisation but prior to beginning their study treatment; reasons included changes in personal circumstances, and health concerns after a positive exercise stress test. All other participants were enrolled in the respective exercise programmes. Adherence to scheduled exercise training sessions varied widely in the intervention (range 0 to 100%) and control groups (range 0 to 97%). Mean exercise adherence was higher in the control group but the difference was not statistically significant (69.34 ± 5.21% vs 57.73 ± 5.35%, F₁,₇₄ = 2.42, P = 0.12). Among participants who began exercise programmes, five (3 intervention, two control) completed zero training sessions; reasons included work or family commitments, transport difficulties, and lack of motivation.
Intervention group participants reported the wearable sensor was easy to use and comfortable to wear, and most would have been prepared to use the sensor on an on-going basis if remotely monitored exCR was continued (Table 8). The majority of participants found the REMOTE-CR smartphone app easy to use although some experienced reliability issues; predominantly sub-optimal mobile broadband coverage and temporary server outages for scheduled maintenance outside real-time exercise monitoring operating hours. One third of intervention group participants would have preferred to use their own Android smartphone, rather than the loaned study phones, to simplify device charging, and prevent carrying two phones during exercise. Intervention group participants felt supported (31, 100%) and almost all thought REMOTE-CR was a good alternative exCR delivery model (30, 97%); the majority would choose remotely monitored exCR if it was offered as an alternative to existing centre-based programmes (28, 90%). Some participants indicated they would have benefited from features that facilitated social interaction with other intervention group participants (9, 29%). Features enabling between-participant contact to provide social support, share vicarious experience, organise face-to-face meetings, and plan shared exercise training were included in the original platform design specification, but were unable to be implemented for the trial.

A large majority of participants liked receiving an individualised exercise prescription (28, 90%), real-time exercise monitoring (30, 97%), and feedback messages (26, 84%) from clinical exercise physiologists (Table 8). Similarly, most participants valued self-monitoring and goal setting features. All participants liked the convenience of being able to use the REMOTE-CR platform in any location, and several participants were able to receive real-time exercise monitoring during domestic and international travel.

7.6.4 Adverse events

Eight participants reported 12 adverse events including high blood pressure (n = 2), chest pain (n = 1), musculoskeletal injury (n = 3), depression (n = 1), and other illness (n = 5). Only one adverse event was related to the study treatment; one intervention group participant tripped on uneven ground during exercise and sustained an ankle injury.
Assessed for eligibility: 334

Excluded: 258
  Declined participation: 143
  Not interested: 94
  Intervention preference: 40
  Control preference: 9
  Ineligible: 105
  Did not attend baseline: 10

Randomised: 76

Allocated to intervention: 37
  Received treatment: 35
  Withdrew prior to treatment: 2

Allocated to intervention: 39
  Received treatment: 38
  Withdrew prior to treatment: 1

Lost to follow-up: 6 (7*)
  Withdrew - personal reasons: 3
  Did not attend follow-up: 3
  *Did not complete VO₂ max: 1

Lost to follow-up: 3 (4*)
  Withdrew - personal reasons: 2
  Could not attend follow-up: 1
  *Did not complete VO₂ max: 1

Analysed: 37
  Completed follow-up: 31
  Imputed data: 6 (7*)

Analysed: 39
  Completed follow-up: 36
  Imputed data: 3 (4*)

*Follow-up VO₂ max imputed, remaining follow-up completed.

Figure 12 Trial flowchart
Figure 13 Between-group difference in $\text{VO}_2\text{max}$

Change from baseline, adjusted for the baseline outcome (intervention – control). Error bars indicate 2-sided 95% CI, non-inferiority margin = -1.75 ml·kg⁻¹·min⁻¹.
Table 6 Baseline demographic and clinical characteristics.

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<td>5 / 12.8</td>
<td>11 / 14.5</td>
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<td>21 / 53.9</td>
<td>42 / 55.3</td>
</tr>
<tr>
<td>Don’t know/refuse to answer</td>
<td>4 / 10.8</td>
<td>2 / 5.1</td>
<td>6 / 7.9</td>
</tr>
<tr>
<td>Medical History (n / %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>23 / 62.2</td>
<td>22 / 56.4</td>
<td>45 / 59.2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>13 / 35.1</td>
<td>6 / 15.4</td>
<td>19 / 25.0</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>30 / 81.1</td>
<td>35 / 89.7</td>
<td>65 / 85.5</td>
</tr>
<tr>
<td>Angina</td>
<td>16 / 43.2</td>
<td>17 / 43.6</td>
<td>33 / 43.4</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>28 / 75.7</td>
<td>25 / 64.1</td>
<td>53 / 69.7</td>
</tr>
<tr>
<td>Angioplasty</td>
<td>22 / 59.5</td>
<td>23 / 59.0</td>
<td>45 / 59.2</td>
</tr>
<tr>
<td>CABG</td>
<td>6 / 16.2</td>
<td>15 / 38.5</td>
<td>21 / 27.6</td>
</tr>
<tr>
<td>Never smoked</td>
<td>22 / 59.5</td>
<td>18 / 46.2</td>
<td>40 / 52.6</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>15 / 40.5</td>
<td>21 / 53.8</td>
<td>36 / 47.4</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0 / 0.0</td>
<td>0 / 0.0</td>
<td>0 / 0.0</td>
</tr>
<tr>
<td>Medications (n / %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta blocker</td>
<td>20 / 54.1</td>
<td>22 / 56.4</td>
<td>42 / 55.3</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>4 / 10.8</td>
<td>8 / 20.5</td>
<td>12 / 15.8</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>21 / 56.8</td>
<td>16 / 41.0</td>
<td>37 / 48.7</td>
</tr>
<tr>
<td>Aspirin</td>
<td>32 / 86.5</td>
<td>38 / 97.4</td>
<td>70 / 92.1</td>
</tr>
<tr>
<td>Antiocoagulant</td>
<td>23 / 62.2</td>
<td>25 / 64.1</td>
<td>48 / 63.2</td>
</tr>
<tr>
<td>Statin</td>
<td>33 / 89.2</td>
<td>36 / 92.3</td>
<td>69 / 90.8</td>
</tr>
</tbody>
</table>

\(^a\) Participants could identify with multiple ethnicities.
\(^b\) Categorised above/below the median household income in NZ (≈NZD 70 000).\(^{[212]}\)
NZ = New Zealand; CABG = coronary artery bypass graft; ACE = angiotensin converting enzyme.
### Table 7 Baseline and follow-up outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean ± SD</th>
<th>Intervention Mean ± SD</th>
<th>Change Mean (95% CI)</th>
<th>Control Mean ± SD</th>
<th>Change Mean (95% CI)</th>
<th>INT – CON (n=37) Mean (95% CI)</th>
<th>Change Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂ max (ml·kg⁻¹·min⁻¹)</td>
<td>26.52 ± 7.55</td>
<td>29.56 ± 7.48</td>
<td><strong>2.92 (1.52 to 4.32)</strong>†</td>
<td>27.59 ± 6.94</td>
<td><strong>3.76 (1.39 to 4.12)</strong>†</td>
<td>0.16 (-1.79 to 2.12)</td>
<td><strong>-3.63 (-2.491 to 17.55)</strong>†</td>
</tr>
<tr>
<td>Activity (MET·min·week⁻¹)</td>
<td>2419 ± 3211</td>
<td>5265 ± 3545</td>
<td><strong>2866 (1264 to 4308)</strong>†</td>
<td>2935 ± 3498</td>
<td><strong>6007 ± 6335</strong></td>
<td><strong>3149 (1666 to 4831)</strong>†</td>
<td><strong>-363 (-2491 to 1765)</strong>†</td>
</tr>
<tr>
<td><strong>Body mass composition</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Body mass (kg)</td>
<td>86.15 ± 18.25</td>
<td>85.24 ± 15.21</td>
<td>-0.95 (-2.86 to 1.70)</td>
<td>83.29 ± 15.92</td>
<td>81.69 ± 14.63</td>
<td>-1.92 (-4.14 to 0.30)</td>
<td>1.34 (-1.9 to 4.53)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.90 ± 5.22</td>
<td>28.56 ± 3.99</td>
<td>-0.16 (-0.84 to 0.52)</td>
<td>27.81 ± 3.56</td>
<td>27.41 ± 3.27</td>
<td>-0.57 (-1.24 to 0.09)</td>
<td>0.41 (-0.54 to 1.37)</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>103.11 ± 11.66</td>
<td>102.96 ± 10.42</td>
<td>-0.90 (-1.69 to 1.88)</td>
<td>100.83 ± 10.26</td>
<td>98.84 ± 9.96</td>
<td>-2.23 (-3.97 to -0.50)†</td>
<td>2.32 (-0.18 to 4.82)</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>105.84 ± 9.50</td>
<td>104.50 ± 7.55</td>
<td>-0.76 (-2.38 to 0.44)</td>
<td>103.82 ± 6.47</td>
<td>102.27 ± 5.87</td>
<td>-1.91 (-3.28 to -0.53)†</td>
<td>0.94 (-1.05 to 2.92)</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.97 ± 0.06</td>
<td>0.98 ± 0.05</td>
<td><strong>0.01 (0.01 to 0.02)</strong>†</td>
<td>0.97 ± 0.06</td>
<td>0.96 ± 0.06</td>
<td>-0.01 (-0.02 to 0.01)</td>
<td><strong>0.02 (0.01 to 0.03)</strong>†</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic (mm Hg)</td>
<td>139.14 ± 15.54</td>
<td>135.35 ± 15.72</td>
<td>-2.45 (-6.66 to 1.76)</td>
<td>134.18 ± 17.43</td>
<td>131.17 ± 14.16</td>
<td><strong>-4.28 (-8.37 to -0.18)</strong>†</td>
<td>1.83 (-4.08 to 7.74)</td>
</tr>
<tr>
<td>Diastolic (mm Hg)</td>
<td>81.78 ± 10.23</td>
<td>77.52 ± 8.83</td>
<td><strong>-3.30 (-5.90 to -0.69)</strong>†</td>
<td>77.95 ± 10.40</td>
<td>77.58 ± 9.94</td>
<td><strong>-1.29 (-3.82 to 1.25)</strong>†</td>
<td><strong>-2.01 (-5.68 to 1.66)</strong></td>
</tr>
<tr>
<td><strong>Blood lipids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total-C (mmol·L⁻¹)</td>
<td>3.58 ± 0.78</td>
<td>3.63 ± 0.83</td>
<td>0.06 (-0.13 to 0.25)</td>
<td>3.53 ± 0.66</td>
<td>3.62 ± 0.75</td>
<td>0.08 (-0.10 to 0.27)</td>
<td>-0.02 (-0.29 to 0.24)</td>
</tr>
<tr>
<td>LDL-C (mmol·L⁻¹)</td>
<td>1.87 ± 0.61</td>
<td>1.93 ± 0.62</td>
<td>0.06 (-0.08 to 0.24)</td>
<td>1.69 ± 0.47</td>
<td>1.72 ± 0.41</td>
<td>0.02 (-0.14 to 0.17)</td>
<td>0.06 (-0.16 to 0.29)</td>
</tr>
<tr>
<td>HDL-C (mmol·L⁻¹)</td>
<td>1.02 ± 0.31</td>
<td>1.11 ± 0.34</td>
<td><strong>0.08 (0.01 to 0.15)</strong>†</td>
<td>1.10 ± 0.41</td>
<td>1.13 ± 0.40</td>
<td>0.04 (-0.04 to 0.11)</td>
<td>0.04 (-0.06 to 0.15)</td>
</tr>
<tr>
<td>Triglyceride (mmol·L⁻¹)</td>
<td>1.55 ± 0.85</td>
<td>1.48 ± 0.51</td>
<td>-0.08 (-0.30 to 0.10)</td>
<td>1.65 ± 0.92</td>
<td>1.72 ± 0.93</td>
<td>0.09 (-0.10 to 0.29)</td>
<td>0.18 (-0.47 to 0.09)</td>
</tr>
<tr>
<td>Blood glucose (mmol·L⁻¹)</td>
<td>5.50 ± 1.73</td>
<td>5.98 ± 1.51</td>
<td>0.48 (-0.11 to 1.07)</td>
<td>5.49 ± 1.71</td>
<td>5.85 ± 2.06</td>
<td>0.36 (-0.22 to 0.93)</td>
<td>0.13 (-0.70 to 0.95)</td>
</tr>
<tr>
<td><strong>Self-efficacy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Task (%)</td>
<td>63.39 ± 23.18</td>
<td>79.07 ± 13.57</td>
<td><strong>12.87 (8.54 to 17.19)</strong>†</td>
<td>70.60 ± 14.03</td>
<td>80.77 ± 13.93</td>
<td><strong>12.86 (6.66 to 17.08)</strong>†</td>
<td>0.00 (-6.09 to 6.09)</td>
</tr>
<tr>
<td>Barrier (%)</td>
<td>78.82 ± 18.86</td>
<td>76.21 ± 15.92</td>
<td>-4.26 (-8.54 to 0.01)</td>
<td>83.14 ± 16.64</td>
<td>82.81 ± 11.13</td>
<td>1.24 (-2.92 to 5.40)</td>
<td>-5.50 (-11.49 to 0.48)</td>
</tr>
<tr>
<td>Exercise adherence (%)</td>
<td>57.73 ± 5.35</td>
<td>69.34 ± 5.21</td>
<td>-11.61 (-26.48 to 3.27)</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Baseline and follow-up descriptive data are unadjusted. Within-group changes from baseline are adjusted for the baseline outcome. Between-group differences compare changes from baseline, adjusted for the baseline outcome.

† Statistically significant difference (P < .05).

‡ Godin Leisure Time Physical Activity Questionnaire [203] Light + moderate + vigorous.

§ Self-Efficacy Scale and Barriers Efficacy Scale [200].

VO₂ max = maximal aerobic exercise capacity; Total-C, LDL-C & HDL-C = total, low density lipoprotein, & high density lipoprotein cholesterol.
<table>
<thead>
<tr>
<th>Table 8 REMOTE-CR platform acceptability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wearable sensor</strong></td>
</tr>
<tr>
<td>Easy to use</td>
</tr>
<tr>
<td>Comfortable to wear</td>
</tr>
<tr>
<td>Would use on an ongoing basis</td>
</tr>
<tr>
<td><strong>Smartphone app</strong></td>
</tr>
<tr>
<td>Easy to use</td>
</tr>
<tr>
<td>Easy to understand</td>
</tr>
<tr>
<td>Reliable</td>
</tr>
<tr>
<td>Would have preferred to use on own smartphone</td>
</tr>
<tr>
<td><strong>Remotely delivered exCR</strong></td>
</tr>
<tr>
<td>Felt supported during the programme</td>
</tr>
<tr>
<td>Good exCR delivery model</td>
</tr>
<tr>
<td>Would choose instead of centre-based exCR</td>
</tr>
<tr>
<td><strong>Wanted social features</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Clinical exercise specialist consultation</strong></td>
</tr>
<tr>
<td>Individualised exercise prescription</td>
</tr>
<tr>
<td>Real-time exercise performance monitoring</td>
</tr>
<tr>
<td>Encouragement and social support</td>
</tr>
<tr>
<td>Behaviour change messages</td>
</tr>
<tr>
<td>Report cardiovascular symptoms</td>
</tr>
<tr>
<td><strong>Self-monitoring (via smartphone app)</strong></td>
</tr>
<tr>
<td>Real-time self-monitoring during exercise</td>
</tr>
<tr>
<td>Retrospective performance review after exercise</td>
</tr>
<tr>
<td>Encouragement and social support</td>
</tr>
<tr>
<td>Behaviour change messages</td>
</tr>
<tr>
<td>Report cardiovascular symptoms</td>
</tr>
<tr>
<td><strong>Goal setting</strong></td>
</tr>
<tr>
<td>Set individualised goals</td>
</tr>
<tr>
<td>Receive automated goal achievement feedback</td>
</tr>
<tr>
<td><strong>General</strong></td>
</tr>
<tr>
<td>Mobility, could use anywhere</td>
</tr>
<tr>
<td>Record/review exercise route maps</td>
</tr>
<tr>
<td>View/use route maps recorded by other participants</td>
</tr>
</tbody>
</table>

Responses from 31 intervention group participants who completed follow-up.

* Social features were included in the original REMOTE-CR platform design specification, but were unable to be implemented for the trial. Features were designed to enable participants to contact each other to provide social support, share vicarious experience, organise face-to-face meetings, and plan shared exercise training.
7.7. DISCUSSION

Our nested pilot trial evaluated the effects of real-time remotely monitored exCR on \( \dot{V}O_2 \text{max} \), modifiable cardiovascular risk factors, self-efficacy and exercise adherence in comparison to traditionally supervised centre-based exCR. After 12 weeks of exCR \( \dot{V}O_2 \text{max} \), the primary outcome, did not differ between groups. The lower bound of the 95% CI (-1.79 ml·kg\(^{-1}\)·min\(^{-1}\)) extended slightly below the pre-specified non-inferiority margin (-1.75 ml·kg\(^{-1}\)·min\(^{-1}\)); consistent with non-inferiority trial reporting guidelines [210] this result is inconclusive and it is not possible to either accept or reject the null hypothesis that centre-based exCR would be superior to remotely monitored exCR. Findings from the main trial [115] will provide definitive evidence of whether remotely monitored exCR is at least as effective as centre-based programmes for improving \( \dot{V}O_2 \text{max} \).

Both remotely monitored and centre-based exCR groups demonstrated statistically significant within-group improvements in \( \dot{V}O_2 \text{max} \), and the effect sizes (=10%) were comparable to those commonly reported for centre-based exCR.[14, 109, 192] While the within-group effects of centre-based exCR on exercise capacity are well documented, this is the first trial to evaluate the effectiveness of real-time remotely monitored exercise among people with CHD and provides encouraging evidence for the potential to augment existing exCR services. The REMOTE-CR platform was designed to build on previous telehealth CR research from our own group, and others. Our group has previously demonstrated an SMS-based intervention can improve leisure-time physical activity energy expenditure, but intervention intensity was insufficient to improve \( \dot{V}O_2 \text{max} \).[103] Other groups have demonstrated promising effects of telephone, email, and web-based exCR interventions on a range of outcomes including \( \dot{V}O_2 \text{max} \), blood pressure, cholesterol fractions, glycated haemoglobin, body composition, physical activity level, and HRQoL:[95-107] a recent meta-analysis suggests these treatment effects are at least comparable to centre-based exCR, and in some cases may be superior (Chapter 3).

While some of these interventions used movement and/or physiological sensors to provide high level asynchronous monitoring of physical activity level and exercise adherence,[98, 100-102, 106, 107] telehealth exCR has thus far been unable to provide the responsive, individualised exercise monitoring, coaching and feedback that is commonly provided in centre-based programmes. The REMOTE-CR platform was developed to address this gap in the literature, and aimed to combine the near universal accessibility of home-based exCR with the clinical oversight and interaction
of centre-based programmes. As well as real-time exercise monitoring, the REMOTE-CR platform enabled more frequent interaction between participants and exCR specialists than has previously been possible. This interaction and support from clinical specialists may have beneficial effects that extend beyond exercise-induced adaptations as it provides opportunities to establish interpersonal relationships that may be more comparable to face-to-face supervision than telephone, email, or web-based interaction. Our trial was not designed to compare social dynamics between remotely monitored and centre-based exCR, but qualitative feedback indicates most intervention group participants felt supported and valued real-time interaction with exCR specialists.

Both remotely monitored and centre-based exCR improved self-reported physical activity energy expenditure and task-specific self-efficacy, and these effects did not differ between groups. While exercise adherence was not always optimal, improvements in physical activity across both 12 week exercise programmes are positive. Further, enhanced confidence to exercise may increase the likelihood that exercise and physical activity behaviours will be maintained beyond the 12 week intervention period. The full scale trial will include follow-up treatment effects 12 weeks after the conclusion of the exCR programmes, and will help to clarify whether post-exCR self-efficacy does facilitate longer term exercise adherence.

With the exception of waist-to-hip ratio all secondary outcome treatment effects were comparable between remotely monitored and centre-based exCR. Further, we observed some within-group improvements in physiological cardiovascular risk factors after remotely monitored (blood pressure, cholesterol) and centre-based exCR (body composition, blood pressure). These results are consistent with effects reported for telehealth[98, 99, 105-107] and centre-based exCR.[31] While risk factor modification was modest it is important to note many participants were prescribed medications to regulate blood pressure, and almost all were prescribed medications to manage cholesterol; the intensity of the exCR interventions may have been insufficient to augment standard pharmacological risk factor management. Further, while all participants had access to dietary education (CR group seminars) and consultation (outpatient clinics) as part of usual care neither exCR programme included specific dietary components. Dietary components may have facilitated more positive changes in body composition, and the REMOTE-CR platform architecture has been designed to enable modular integration of additional core CR components in future. Nonetheless as VO$_2$max and physical activity level are established predictors of cardiovascular risk, [13, 14, 43] modest improvements in other
cardiovascular risk factors should not detract from the important role of exCR in CHD secondary prevention.

While remotely monitored exCR improved participants’ exercise-specific task self-efficacy it did not improve their confidence to overcome exercise barriers. This was unexpected as the REMOTE-CR platform was designed to overcome accessibility barriers that commonly limit centre-based exCR participation, and may be a function of the instrument we used to assess barrier efficacy. The Barriers Efficacy Scale [200] does not directly query commonly reported accessibility barriers such as transport restrictions and programme availability.[64, 67] The instrument does include questions about exercise scheduling; however, real-time exercise monitoring and centre-based operating hours were matched in our trial to control for confounding effects of differential availability of monitored/supervised exercise. All intervention group participants valued the convenience and flexibility of the REMOTE-CR platform, and most indicated they would likely choose remotely monitored exCR if it was offered as an alternative option alongside centre-based exCR. Further, a substantial number of individuals who declined participation in the trial would have participated if they had been able to choose the intervention group rather than undergo randomisation. These preferences do not provide direct evidence that remote programme delivery can overcome traditional exCR participation barriers and, therefore, potentially enhance exercise-related barrier self-efficacy. However, they do indicate an appreciable demand for programmes that offer more flexibility than traditional centre-based exCR. Moreover, this demand was demonstrated among a predominantly metropolitan cohort where centre-based exCR can be accessed as part of usual care. Very few participants lived in rural or remote areas which typically have limited access to specialist services,[112] and remotely monitored exCR may have even greater potential to enhance exCR utilisation in those areas. It is also important to note a small number of potential participants who were unwilling to be randomised had expressed a preference for centre-based exCR, and a small number of intervention group participants indicated they would also value centre-based exCR. This demonstrates a demand for both exCR delivery models and, intuitively, a range of options is likely to meet the needs of more people.

Varied programme preferences suggest remotely monitored and centre-based exCR may be suited to slightly different subsets of people with CHD, and reinforces the notion that remotely monitored exCR should not be viewed as a replacement for centre-based exCR. On the contrary, although the REMOTE-CR platform was designed to integrate evidence-based attributes of centre-based exCR its objective
was to provide an additional option for people whose needs are not met by existing services. Centre-based exCR remains well suited to those who value face-to-face support and interaction (and can access those programmes); remotely monitored exCR may be well suited to those who prefer a greater degree of independence and flexibility, and/or could not otherwise access exCR. Given that remotely monitored exCR can provide real-time physiological monitoring, including ECG it remains unclear whether it is any less appropriate for people in higher CHD risk strata, particularly as not all centre-based programmes offer telemetric ECG monitoring. By providing an additional option that complements centre-based exCR, remotely monitored programmes could help to increase overall exCR utilisation rather than redistribute those who currently participate. While beyond the scope of this trial, remotely monitored exCR may also have potential to assist participants’ transition from centre-based exCR into sustainable, independent exercise. Intervention content may require adaptation to reflect the transitional focus, but the current REMOTE-CR platform could support a transitional use case without modification.

Social interaction features were initially included in the design specification for the REMOTE-CR smartphone app, but were unable to be implemented for this trial. The social component would have enabled participants to provide interactive social support, share vicarious experiences, organise face-to-face meetings, and plan shared exercise training. While web-based social interaction components of mHealth CR interventions have not always been well used, participant feedback suggests embedding features in a phone may improve usability.[213] Almost one third of remotely monitored exCR participants indicated they would have liked smartphone app features that allowed them to interact with other participants. Integrating social interaction components into future iterations of the REMOTE-CR platform could enhance the remotely delivered exCR experience for some participants, although opt-out functionality would be necessary to preserve the capability to participate individually. Additional technical training may be required to reduce technical barriers and enhance usability of social components.[213]

7.7.1 Strengths And Limitations

This is the first trial to assess the effectiveness of real-time remotely monitored exCR, and capitalised on recent advances in wearable sensor and smartphone technologies which have not previously been implemented within exCR, and positive findings demonstrate the potential of this approach for augmenting existing services. The trial used a rigorous randomised controlled design to minimise confounding bias. Use of
a non-inferiority experimental design provides valuable information about how remotely monitored exCR compared with gold standard centre-based programmes. In conjunction with future research this could inform clinical practice, including decisions about whether to implement remotely monitored exCR alongside existing services. In line with recommendations both patient-centred and usability outcomes were evaluated [121] and the findings demonstrate positive patient-centred and clinical outcomes.

Many potential participants had strong preferences for the intervention (n = 40) or control groups (n = 9) and were unwilling to be randomised (Figure 8). Our sample was demographically comparable to previous exCR cohorts, but this may limit the generalisability of our findings. Preference arms were nested within an RCT that compared home and centre-based CR.[75] Many participants expressed a preference (n = 126 vs 104 randomised), predominantly for home-based CR (n = 72 vs 54), and preferences did not alter treatment effects. When interventions target different needs, selection biases from non-randomised designs may reflect true, consistent, and important differences that need to be accounted for; this may enhance external validity for real-world implementation contexts that allow people to self-select the exCR programme that best suits their needs. Future research should consider alternative experimental designs to assess effects of individual preferences.

Secondary outcome assessment was not blinded although many were objectively measured. Self-reported physical activity and self-efficacy were subject to recall and social desirability biases; physical activity is being assessed objectively (accelerometry) in the main trial.[115] While powered for the pilot non-inferiority margin this trial included a small sample; the larger main trial (n = 162) will clarify promising pilot results. Participants could not to be blinded to treatment allocation, and the number of secondary outcome analyses increases the risk of type one error. However, assessment of multiple cardiovascular risk factors aligns with the multi-factorial objectives of CR. Finally, a large number of eligible individuals declined participation in the trial, suggesting that while remotely monitored exCR addressed common exCR participation barriers it is not a panacea. Additional approaches will be required to meet the needs of all people who would benefit from exCR.
7.7.2 Conclusions

Real-time remotely monitored exCR can close the gap between home- and centre-based exCR by making responsive, individualised exercise monitoring and coaching, behaviour change education, and social support available to people in almost any location. Treatment effects were comparable with centre-based exCR, and results from the main trial [115] will help to clarify the non-inferiority hypothesis. Remotely monitored exCR can complement existing exCR services, and may increase exCR utilisation by providing an additional option for people who are unwilling or unable to attend centre-based exCR.
7.8. ACKNOWLEDGEMENTS

We wish to acknowledge the contributions of cardiac rehabilitation nurses and research assistants, in particular Melissa Rawstorn and Hannah Lowe. We are grateful to the centre-based exCR programmes that provided the control group treatment, University of Auckland and Counties Manukau cardiac rehabilitation clinics (Auckland site), and Cardiac Clinic (Tauranga site). This investigator-initiated study was funded by the Auckland Medical Research Foundation (AMRF, 1113020); AMRF had no input in the study design and conduct, or the analysis and interpretation of results. Dr Maddison was supported by a Health Research Council Sir Charles Hercus Fellowship.

7.9. CONFLICT OF INTEREST

JR/AM/IW/RM contributed to the design and development of the REMOTE-CR platform.
CHAPTER 8. GENERAL DISCUSSION

Exercise training is a critical component of secondary prevention of CHD [15, 211] yet utilisation of traditional supervised exercise-based cardiac rehabilitation (exCR) remains sub-optimal; participation is limited by service, psychological and physical barriers;[64, 83] physical barriers that limit access to exCR are commonly cited reasons for non-attendance. Alternative delivery models, including telehealth exCR, have been proposed in order to overcome access barriers; however a combination of high accessibility and evidence-based clinical exercise supervision remains elusive. Rapid advances in wearable sensor and mobile communication technologies could help to close this gap, but there has been little research in this area. The overall aim of this thesis was, therefore, to explore novel approaches for enhancing exCR accessibility using pervasive sensing and communication technologies.

In order to achieve this aim a comprehensive body of work was undertaken to scope, develop, validate, and evaluate an alternative exCR delivery model. A systematic review and meta-analysis was conducted to evaluate the effectiveness of telehealth exCR, determine characteristics of existing programmes, and identify opportunities for novel interventions. The systematic review informed development of a mobile health (mHealth) technology platform and intervention that were designed to deliver evidence- and theory-based exCR to participants regardless of their physical location (REMOTE-CR). A feasibility and validation study was conducted to determine the accuracy and reliability of the platform for quantifying physiological responses to exercise, and transmitting data to a remotely located web-server to permit real-time monitoring by clinical exercise specialists. Finally, a non-inferiority, randomised controlled pilot trial was designed and conducted to compare the effectiveness of REMOTE-CR with traditionally supervised centre-based programmes, and assess intervention acceptability.

A number of primary findings were derived from this research:

1. Existing telehealth exCR interventions are as good as centre-based programmes for increasing $\dot{V}O_2\text{max}$ and improving modifiable cardiovascular risk factors.
2. A smartphone and web-based software platform is capable of delivering a multifaceted intervention that integrates evidence-based exCR guidelines and theory-based behaviour change components.

3. Wearable sensors and internet-connected smartphones can accurately and reliably quantify physiological responses to exercise, and reliably transmit data to remote locations for real-time monitoring.

4. Real-time remotely monitored exCR increases $\bar{VO}_2\text{max}$, physical activity energy expenditure and self-efficacy, and effect magnitudes are comparable with traditional centre-based exCR.

This general discussion presents a brief summary of the research findings, demonstrates how the research addressed the thesis aims and objectives, and integrates the findings to inform the major implications. Strengths and limitations of the collective body of work will be discussed, before outlining suggestions for future research and practice.

The discussion addresses Objective 5, which was to synthesis findings from the extant literature and the research presented in Chapters 3 to 7 in order to identify implications for clinical practice, opportunities for further development, and new directions for technology-assisted CR research that can help to augment current services and enhance utilisation.
8.1. OVERVIEW OF KEY RESEARCH FINDINGS

The systematic review and meta-analysis (Chapter 3) aimed to synthesise existing evidence for the effectiveness of telehealth exCR, and identify opportunities for future development. Several previous reviews had examined the use of telehealth technologies for delivering one or more components of CR;[82-84, 93, 112, 121] however, none had explicitly investigated the use of telehealth technologies to deliver or monitor structured, individualised, prescriptive exercise training that is comparable to gold standard centre-based exCR. The meta-analysis demonstrated comparable effects of telehealth and centre-based exCR on VO₂max and modifiable cardiovascular risk factors, with some evidence suggesting telehealth exCR may have greater effects on physical activity and exercise adherence. Counterintuitively there were few differences between telehealth exCR and usual care, possibly because telehealth interventions in those studies were of insufficient intensity. The review also identified two important and related gaps in the literature: 1) telehealth exCR has been unable to emulate evidence-based best practices common in centre-based programmes, and there remains a substantial gap between the way exercise training is prescribed, monitored, and managed in telehealth and centre-based interventions; 2) telehealth exCR has not yet capitalised on advancing technological capabilities that can enable more responsive, tailored, and immersive interventions. Telehealth exCR interventions have predominantly comprised fixed-line telephone, SMS or email interaction with exCR specialists, with limited use of asynchronous sensor data for high level physical activity and adherence monitoring.

Chapter 4 integrated findings from the systematic review with evidence-based exCR guidelines and established behaviour change theories to design an mHealth platform and intervention that addressed identified gaps in the literature. Platform features and intervention content were targeted towards exercise training and did not include other core CR components. This was planned to enable robust evaluation of the exercise intervention on cardiovascular risk factors without potentially confounding effects of a more comprehensive CR intervention. The REMOTE-CR platform was designed to allow exCR specialists to monitor participants’ exercise and provide individualised coaching in real-time, from almost any location, and to provide behaviour change education and social support. The platform overcame identified gaps in the literature by integrating recent advances in wearable sensor and mobile communications devices, and narrows the gap between exercise prescription and monitoring practices in telehealth and centre-based exCR.
The feasibility and validation study (Chapter 5) aimed to determine the accuracy and reliability of the REMOTE-CR platform across a range of exercise modes and levels of intensity, among individuals in sinus rhythm and atrial fibrillation. The main findings were that small sensor measurement biases were present but considered clinically insignificant. Sensor measurement reliability was acceptable during most activities, and wireless data transmission integrity was sufficient to support real-time streaming of high resolution sensor data. This study demonstrated the technical capability required to connect participants with remotely located exCR specialists in real-time. The study also identified a need to transfer the REMOTE-CR web server to a more stable hosting platform to avoid unexpected outages; this was implemented prior to the planned evaluation trial.

Chapter 6 presented the protocol for a large non-inferiority RCT that was designed to evaluate the effectiveness of real-time remotely monitored exCR among people with CHD, in comparison to traditionally supervised centre-based programmes. The protocol described a priori methods including participant eligibility, sample size calculation, treatment allocation procedures, characteristics of the remotely monitored and centre-based exCR interventions, assessment of short and longer term outcomes, and planned statistical analyses. The effects of remotely monitored exCR on VO$_2$max, cardiovascular risk factors, self-efficacy, and exercise adherence were hypothesised to be at least as good as centre-based exCR.

Chapter 7 presents the results from a pilot trial embedded within the non-inferiority RCT described in Chapter 6. The pilot trial was limited to a subset of the outcomes specified in the full study protocol, and only considered the immediate post-exCR follow-up time point. The main findings were that both remotely monitored and centre-based exCR improved VO$_2$max, and effects were comparable between groups but non-inferiority analysis was inconclusive. Both interventions also improved physical activity energy expenditure and exercise-specific task self-efficacy, and these effects did not differ between groups. Modest improvements were observed in other modifiable cardiovascular risk factors. Usability and acceptability of the remotely monitored intervention were highly rated, and demonstrated substantial demand for alternative exCR delivery models. This rigorous pilot RCT provides promising evidence that supports implementation of real-time remotely monitored exCR as a complementary alternative alongside existing services.
8.2. IMPLICATIONS

When considering this body of research in the context of the existing exCR landscape it is important to determine whether the findings of this thesis have helped to achieve the overall aims and, if so, how this might affect clinical practice.

This research aimed to address a two part problem affecting exCR clinical practice. The implications for clinical practice will, intuitively, be dependent on whether or not the research has helped to solve this problem. Firstly, while substantial research evidence supports the efficacy of exCR, the first part of the problem was that many people are unable to access exCR programmes in traditional clinical settings. As a result, individuals who may otherwise choose to participate in exCR are unable to do so. Secondly, while home-based programmes have been available in some regions for many years, the second part of the problem was that more accessible delivery models (including recent telehealth interventions) have overcome access-related participation barriers at the opportunity cost of clinical expertise and oversight. While this has not precluded beneficial health outcomes, it suggests more could be done for people who cannot attend centre-based exCR.

In summary then, this thesis aimed to create an exCR delivery model that combined the clinical expertise and oversight of centre-based exCR specialists with the near universal accessibility of home-based programmes. While this is not the first research to address the problem it is among the first attempts to mobilise gold standard exCR practices, rather than add additional interaction to existing home-based programmes. Moreover, it appears to be the first to extend evaluation beyond the feasibility phase. The findings demonstrate remotely monitored exCR confers beneficial health effects, meets the needs of many people with CHD, and would likely increase exCR utilisation if it was available to choose alongside other usual care programmes. These encouraging early findings have yet to be corroborated by additional research, but present a strong case for integrating real-time remotely monitored exCR alongside existing programme options. The main RCT will confirm preliminary effects in a larger sample, and in this fast-moving field it is likely additional research will emerge in the near future.

The small body of current evidence, however, should not necessarily prevent remotely monitored exCR from being implemented alongside existing programmes. On the basis of strong evidence for the efficacy of exCR, and evidence that centre-based delivery models deny these benefits to many people, researchers have
suggested withholding remotely monitored exCR may be unethical.[85] While remotely monitored exCR could increase the reach of exCR questions about whether it should become the new standard [85] are perhaps over eager, as the findings of this thesis also support previous research demonstrating ongoing demand for traditional face-to-face supervised exCR.[75] There is no reason these two delivery models cannot complement each other, and no reason to relegate gold standard centre-based exCR as a secondary option.

If the question is not so much whether remotely monitored exCR should be implemented, it is surely how it should be implemented. The origins of REMOTE-CR lie in centre-based exCR, with the goal simply being to put as many attributes of existing programmes as possible at participants' fingertips. Intuitively then, it may be best to implement remotely monitored exCR via centre-based facilities in order to capitalise on the knowledge and experience of existing clinical exercise specialists. This may also have other benefits such as cost-effectiveness, expansion of programme capacity, and co-development. While implementing remotely monitored exCR within centre-based facilities would likely require an increase in staff costs the incremental cost would surely be smaller than establishing standalone remote monitoring facilities. Further, remotely monitored exCR could be provided to participants in diverse geographic regions, including rural and remote areas, from centralised facilities that are best equipped to handle an increased programme demand. This may bring additional cost benefits via economies of scale, and also enable centre-based facilities to service larger populations than is currently possible. Finally, implementing remotely monitored exCR within centre-based facilities would provide opportunities for co-development. That is, experience and knowledge gained via centre-based and remotely monitored programmes could inform development of each other. This could ensure both delivery models capitalise on emerging evidence-based knowledge, and help to improve the quality of service delivery. No matter how remotely monitored exCR is delivered, it will require integration into existing referral systems so that individuals are offered the choice of REMOTE-CR as routine service delivery.

8.3. THESIS STRENGTHS AND LIMITATIONS

Strengths and limitations of each specific phase of this research have been discussed previously in the respective chapters; however, the collective body of research has its own strengths and weaknesses. Firstly, this is one of the first pieces of research to address a key limitation of telehealth exCR by specifically attempting to transfer
gold standard centre-based exCR practices for exercise prescription, monitoring, coaching and support outside of the traditional clinical environment. Previous research has led to important improvements in the quality of home-based exCR programmes but has been unable to emulate evidence-based clinical exCR practices; this has likely limited the intensity of exercise interventions, and may have impaired exercise-induced cardiovascular risk factor modification. Existing approaches appear to have been modelled on typical home-based exCR programmes, and subsequently aimed to augment interaction between participants and specialists via traditional communication media such as telephones, email, and SMS. Conversely, this research was modelled on centre-based exCR, and subsequently aimed to best-practice methods available to participants irrespective of their physical location, with minimal loss of fidelity. Approaching exCR accessibility from this slightly different perspective has potential to significantly advance the field of telehealth exCR by enabling more responsive, personalised, and immersive interventions.

Secondly, the research drew attention to a growing disparity between current technological capabilities and innovation within telehealth exCR. This highlights an important challenge for telehealth exCR: to move beyond increasingly outdated, rate-limiting technologies and capitalise on the potential of rapidly advancing, increasingly pervasive tools.

Thirdly, this research highlights a hitherto counterintuitive willingness of an older aged CHD population to engage with cutting edge technologies. The innovative nature of the REMOTE-CR platform was anticipated to present barriers for older people, who are likely to have lower technology literacy than younger populations. This research was originally intended to contribute early evidence about the effects of real-time remotely monitored exCR, that may have become increasingly relevant in coming years as technology use and literacy continues to increase among older aged individuals. However, the findings demonstrate that when appropriate initial training is provided, this population are already sufficiently capable and confident to embrace mHealth technologies. In this respect the aforementioned disparity between technological capability and innovation is even more alarming, as it can no longer be justified on the basis that more advanced telehealth platforms are excessively complex for older people with CHD.

Finally, with the exception of randomised treatment allocation, which would not be imposed in real-world implementation contexts, the pragmatic nature of the
REMOTE-CR intervention was likely to accurately reflect the utilisation patterns and treatment effects that would be observed if it was offered alongside existing exCR services via usual care channels.

There are also a number of limitations that require consideration. Firstly, this research focused only on the exercise training component of CR and, as such, did not align with recommendations for comprehensive multidisciplinary interventions.[15, 211] In light of the gaps identified in the telehealth exCR literature, a decision was made to focus on exercise training because 1) it remains a central component of international CR guidelines that can have multifactorial benefits in terms of cardiovascular risk, and 2) it enabled a more intensive design and development process than would have been feasible if the REMOTE-CR platform and intervention had included all core components of CR. The platform architecture was designed to enable modular expansion in future iterations; this was specified with a view to developing a more comprehensive intervention if the exercise-specific component was demonstrated to be effective and acceptable.

Secondly, while the sample included in the RCT was demographically similar to those in previous exCR research, a large number of individuals declined participation due to strong treatment preferences and unwillingness to undergo randomisation. There may be important and potentially confounding differences in unmeasured characteristics between our sample and the typical CHD population. A passively controlled (i.e. usual care) experimental design may have avoided treatment preference-based refusal to be randomised, but would have reduced the value of the findings. This research aimed to determine the effectiveness of a novel exCR delivery model; comparison to usual care (i.e. no exercise intervention) would primarily have demonstrated the effectiveness of exercise itself and, as such, would have done little to advance the field. Moreover, an obvious and perhaps more important question would have remained unanswered - is real-time remotely monitored exCR as good as existing programmes? With the benefit of hindsight a non-inferiority design remains the most valuable approach and was best suited to addressing the aims of this thesis.

Thirdly, metropolitan-based recruitment and assessment strategies meant the RCT included very few participants who lived in rural or remote regions. Remotely monitored exCR has important advantages for people in metropolitan areas, but the potential to enhance exCR utilisation may be even greater in rural and remote regions that are underserved by specialist clinical services.
Fourthly, while statistically powered for the pre-specified non-inferiority margin, interpretation of the nested pilot RCT results is limited by a modest sample size (n = 76). This was partly due to slower-than-anticipated recruitment, itself a result of an unexpectedly high proportion of individuals who had strong treatment group preferences and were unwilling to undergo randomisation. Nonetheless, the ongoing main RCT will include a larger sample (n = 162),[115] and may help to clarify the encouraging preliminary findings presented in this thesis.

Finally, while qualitative feedback from remotely monitored participants demonstrated encouraging demand for more flexible exCR delivery models, a large number of individuals declined participation in the evaluation study for reasons other than unwillingness to undergo randomisation. Sub-optimal conversion suggests, unsurprisingly, that the remotely monitored exCR approach proposed in this thesis will not meet the needs of all people with CHD who currently decline exCR. Additional options are required, although it is beyond the scope of this research to suggest which specific needs remain unaddressed.

8.4. FUTURE DIRECTIONS

In completing this body of research it has been exciting to think about where it may lead in future: how can the intervention be enhanced? What is required to achieve implementation in usual care settings? What questions remain unanswered?

The first point to address originates from an unimplemented component of the initial REMOTE-CR platform design specification: social interaction. A suite of features were designed to enable participants to interact with each other, both virtually and via arranged face-to-face visits and/or shared exercise. These features were intended to facilitate immersive social support, sharing of vicarious experiences, and social persuasion, which facilitate positive behavioural outcomes.[126, 129] However, it was not logistically feasible to implement those features in time for the RCT. Qualitative feedback from the pilot RCT demonstrated demand for social interaction features, and including them in an expanded version of the participant-facing smartphone app will be a high priority in subsequent iterations of the REMOTE-CR platform. Similarly, it will be important to expand the scope of the REMOTE-CR platform to enable delivery of additional core components of CR [15, 211] to create a more comprehensive, multidisciplinary intervention. The flexible platform architecture was always intended to allow such expansion once the effectiveness of the exCR component had been established. A modular approach to multidisciplinary
intervention design may also enable interventions to be rapidly tailored to individuals’ needs and preferences.

Unique challenges arose from the use of a standard RCT experimental design in the evaluation study, and these challenges will likely affect future research; particularly studies that include active intervention comparison groups. In practice telehealth exCR would most likely be offered as an option alongside existing programmes, and people would be able to self-select the exCR programme that best suits their needs. With appropriate consideration for potential biases, experimental designs that integrate preference-based allocation may provide more accurate and externally valid estimates of effectiveness by acknowledging important differences between subgroups of individuals who would choose different types of exCR programme. Further, the standard RCT approach may be too cumbersome to evaluate the independent and incremental effects of increasingly comprehensive, multidisciplinary telehealth CR programmes. A recent review of adaptive trial designs for telehealth research suggests multi-arm multi-stage, and sequential phase II/III designs may help to improve efficiency when evaluating complex telehealth interventions.[214] A multi-arm multi-stage design could enable evaluation of different intervention components or configurations simultaneously, and allow adaptive changes to group allocation based on pre-specified interim analyses. Adding sequential phase II/III designs could allow exploratory aspects of early research to inform which intervention components or configurations are carried forward to confirmatory trials (based on interim analyses). While biases would need to be considered, such designs may be more efficient for assessing intervention usability and compliance, multiple outcomes, and exploring heterogeneity of responses to telehealth interventions.[214] Optimising experimental efficiency may be particularly important to keep pace with rapid progression of technologies, and appetite for telehealth.

While the current REMOTE-CR platform was designed within a CR context many individuals would likely benefit from remotely supervised exercise programmes, and there is potential to adapt the platform for the needs of other clinical (e.g. diabetes, metabolic syndrome), healthy and athletic populations. Intervention content would require adjusting for these contexts, but the fundamental platform capability is already in place and could easily be replicated. Moreover, while this research focused on connecting participants with exCR specialists, some individuals (and other population groups) may benefit from less intensive monitoring. People transitioning out of real-time remotely monitored or centre-based exCR may have developed sufficient skills to manage their exercise with a greater degree of independence, but could still benefit
from ongoing specialist support. The REMOTE-CR platform currently provides retrospective exercise performance review and goal achievement feedback; however, there is potential to expand platform capability beyond supervision from real exCR specialists. The field of machine learning presents exciting opportunities to develop pattern recognition algorithms that could be matched to adaptive, intelligent intervention content that would not require active supervision from real exCR specialists. Such interventions have not yet appeared in the exCR literature, but have been demonstrated for managing stress-induced muscle tension,[215] monitoring individuals with Parkinson’s disease,[216] and predicting acute exacerbation of coronary obstructive pulmonary disorder.[217] In a sense this would represent a form of real-time artificial intelligence, which may be well suited to the needs of people transitioning into sustainable long-term exercise. The safety and acceptability of this approach remain unknown although as long as participants were aware of the artificial intelligence engine, automated individualised feedback and coaching may be preferable to no information at all. As automated platforms would have largely uncapped programme capacity they could provide participants with sustainable ongoing support over the longer term, perhaps even indefinitely.

Wearable sensors and remote data collection provide unique opportunities to measure physiological responses during exercise in environments and contexts that have not previously been possible. High resolution data capture will enable increasingly accurate quantification of acute and cumulative exercise dose in free-living environments. In combination with change from baseline health outcomes these data will allow estimates of dose-response relationships to move beyond assumptions that all participants complete exercise as prescribed. This could provide more sensitive estimates of dose-responsiveness, and advance understanding about optimal exercise prescription strategies.

This research indicates an urgent need to embrace recent technological development, rather than shy away from it. This will remain an important consideration for future research, but may also be a double edged sword. Wearable sensors have become mainstream commodities since this research began and while many current consumer devices are unsuitable for remotely monitored exCR, this rapidly developing field will likely provide opportunities to refine, enhance, and expand remote exercise monitoring platforms. However, rapid development and short product lifecycles suggest constant pursuit of the latest hardware developments may be detrimental to advancing the field. This research capitalised on emerging technologies that had not previously been used in telehealth exCR but a decision was
made early in the design phase to ensure REMOTE-CR was primarily a software platform with integrated wearable sensors, not a hardware platform with complementary software components. This was anticipated to provide some resilience against obsolescence each time new hardware becomes available. We should not lose sight of the fact that remote monitoring platforms are simply an alternative model for delivering responsive, individualised, immersive interventions. This objective should remain at the forefront of telehealth platform design and guide decisions about adoption of emerging technologies.

Nonetheless, validated models for predicting technological progress suggest the cost of wearable sensors and smartphones will likely decrease exponentially over time,[218] and opportunities to reduce hardware costs can only strengthen the business case for real-world implementation. Indeed, the cost of suitably powerful smartphones has fallen substantially throughout this research (≈NZD 400-600, Q1 2013; ≈NZD 100, Q4 2015). Continued growth in smartphone ownership (including older age groups) [88-90] may provide further cost savings, as many individuals may already own compatible smartphones. This would enhance cost-effectiveness; however, the cost of establishing and maintaining a remotely monitored exCR programme remains unknown and this should be a priority for future research. The ongoing main RCT (Chapter 6) will provide cost estimates for the REMOTE-CR programme, but costs will likely vary as a function of telehealth exCR platform characteristics and geographic location. This will limit the validity of extrapolating cost analyses across different programmes, and future research should include cost analyses whenever possible.

It was not feasible to include rural and remote regions in the evaluation of the REMOTE-CR intervention. The potential impact of remotely monitored programmes on exCR utilisation and health outcomes is perhaps greatest in these areas as they are typically underserved by specialist services and traditional exCR access barriers are amplified.[112] Further, non-attendance is associated with lower cardiovascular risk factor knowledge and more adverse risk factor profiles.[68] Remotely monitored exCR is well suited to overcoming access barriers, and programmes in rural/remote areas could even be managed from larger urban or metropolitan centres in order to capitalise on existing exCR specialist expertise. This capability to reach underserved population groups should be prioritised in future research.

Finally, the findings of this research indicate that while remotely delivered programmes would likely increase uptake, they will not single-handedly address sub-
optimal utilisation. Given the large proportion of people with CHD who currently do not participate in exCR it is not surprising that remotely monitored programmes cannot address all unmet needs. Additional options are still required to reach utilisation saturation (i.e. the total number of eligible people with CHD less those who are uninterested in any form of exCR).

8.5. CONCLUSION

A novel mHealth platform that embraces recent advances in wearable sensor and mobile communication technologies can bring near universal accessibility to clinically supervised, evidence- and theory-based exCR. Early evidence suggests real-time remotely monitored exCR compares favourably with gold standard centre-based programmes, and presents a strong case for implementation. Promising health outcomes are likely dependent on specific mHealth platform and intervention content characteristics, and need to be verified by additional research. However, alternative exCR delivery models are urgently needed to meet the needs of those who currently decline exCR, and this promising evidence indicates remotely monitored exCR can help to address this problem. The future appears bright for remotely monitored exCR but challenges remain: understanding how remotely monitored exCR can be implemented alongside existing services, and how to expand the scope of mHealth platforms to include a more comprehensive array of evidence-based CR components. Addressing these challenges will help to realise the potential for remote programme delivery to improve global exCR utilisation.
If you always do what you always did,
You will always get what you always got.

Albert Einstein

Some men look at things the way they are and ask why?
I dream of things that are not and ask why not?

Robert Kennedy
APPENDIX 1: SYSTEMATIC REVIEW & META-ANALYSIS SUPPLEMENTARY MATERIAL

Appendix 1.1 Search Strategies – final search date: 31/05/2015

Appendix 1.2 Characteristics of Included Studies [ordered by study ID]

Appendix 1.3 Characteristics of Excluded Studies [ordered by study ID]

Appendix 1.4 Risk of bias summary: review authors' judgements about each risk of bias item for included studies

Appendix 1.5 Additional Outcome Data
Appendix 1.1 Search Strategies [final search 31/05/2015]

MEDLINE
1. exp telemedicine/ OR exp telemetry/ OR exp telephone/ OR exp wireless technology/ OR exp computers, handheld/ OR exp internet/
2. (telemedicine OR telemetry OR telephone OR wireless technology OR computers, handheld OR internet OR telehealth OR telemonitor* OR telerehab* OR web*).tw.
3. ((tele* OR remote OR mobile) ADJ3 (medicine OR health OR monitor* OR rehab*)).tw.
4. (mhealth OR m-health OR mobile-health).tw.
5. (((mobile OR cell* OR smart) AND phone) OR smartphone).tw.
6. (tablet and (computer or app) or ipad).tw.
7. (mobile AND app*).tw.
8. OR/ 1-7
9. exp myocardial ischemia/
10. (myocardial ADJ3 (isch?em* OR infarct*)).tw.
11. (coronary ADJ3 (disease OR bypass OR syndrome) OR angioplasty OR percutaneous coronary intervention OR angina OR stent).tw.
12. OR/ 9-11
13. exp rehabilitation/ OR exp exercise/ OR exp physical fitness/
14. ((rehabilitation OR exercise OR fitness) AND (therap* OR train* OR program* OR treatment OR interven*)).tw.
15. OR/ 13-14
16. 8 AND 12 AND 15

CINAHL
1. MH telehealth+ OR MH telemetry+ OR MH telephone+ OR MH wireless technology+ OR MH computers, handheld+ OR MH internet+
2. telehealth OR telemetry OR telephone OR wireless technology OR computers, handheld OR internet OR telemedicine OR telemonitor* OR telerehab* OR web*
3. (tele* OR remote OR mobile) N3 (medicine OR health OR monitor* OR rehab*)
4. mhealth OR m-health OR mobile-health
5. ((mobile OR cell* OR smart) AND phone) OR smartphone
6. tablet AND (computer OR app) OR ipad
7. mobile AND app*
8. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7
9. MH myocardial ischemia+
10. myocardial N3 (isch#em* OR infarct*)
11. coronary N3 (disease OR bypass OR syndrome) OR angioplasty OR percutaneous coronary intervention OR angina OR stent
12. S9 OR S10 OR S11
13. MH rehabilitation+ OR MH exercise+ OR MH physical fitness+
14. (rehabilitation OR exercise OR fitness) AND (therap* OR train* OR program* OR treatment OR interven*)
15. S13 OR S14
16. S8 AND S12 AND S15
The Cochrane Library
1. [Telemedicine]
2. [Telemetry]
3. [Telephone]
4. [Wireless Technology]
5. [Computers, Handheld]
6. [internet]
7. telemedicine OR telemetry OR telephone OR wireless technology OR computers, handheld OR internet OR telehealth OR telemonitor* OR telerehab* OR web*
8. (tele* OR remote OR mobile) NEAR/3 (medicine OR health OR monitor* OR rehab*)
9. mhealth OR m-health OR mobile-health
10. ((mobile OR cell* OR smart) AND phone) OR smartphone
11. tablet AND (computer OR app) OR ipad
12. mobile AND app*
13. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
14. [Myocardial Ischemia]
15. myocardial NEAR/3 (isch*m* OR infarct*)
16. coronary NEAR/3 (disease OR bypass OR syndrome) OR angioplasty OR percutaneous coronary intervention OR angina OR stent
17. #14 OR #15 OR #16
18. [Rehabilitation]
19. [Exercise]
20. [Physical Fitness]
21. (rehabilitation OR exercise OR fitness) AND (*therap* OR train OR program* OR treatment OR interven*)
22. #18 OR #19 OR #20 OR #21
23. #13 AND #17 AND #22

Embase
1. exp telemedicine/ OR exp telemetry/ OR exp telephone/ OR wireless communication/ OR microcomputer/ OR exp internet/
2. (telemedicine OR telemetry OR telephone OR wireless communication OR microcomputer OR internet OR telehealth OR telemonitor* OR telerehab* OR web*).tw.
3. ((tele* OR remote OR mobile) ADJ3 (medicine OR health OR monitor* OR rehab*)).tw.
4. (mhealth OR m-health OR mobile-health).tw.
5. ((mobile or cell* or smart) and phone) or smartphone).tw.
6. (tablet AND (computer OR app) OR ipad).tw.
7. (mobile and app*).tw.
8. OR/ 1-7
9. exp ischemic heart disease/ OR exp heart muscle ischemia/ OR exp coronary artery disease
10. (myocardial ADJ3 (isch?em* OR infarct*)).tw.
11. (coronary ADJ3 (disease OR bypass OR syndrome) OR angioplasty OR percutaneous coronary intervention OR angina OR stent).tw.
12. OR/ 9-11
13. exp rehabilitation/ OR exp exercise/ OR exp fitness/
14. ((rehabilitation OR exercise OR fitness) AND (therap* OR train* OR program* OR treatment OR interven*)).tw.
15. OR/ 13-14
PsycINFO
1. exp telemedicine/ OR exp telemetry/ OR exp telephone systems/ OR exp mobile devices/ OR exp computer assisted therapy/ OR exp internet/
2. (telemedicine OR telemetry OR telephone systems OR mobile devices OR computer assisted therapy OR internet OR telehealth OR telemonitor* OR telerehab* OR web*).tw.
3. ((tele* OR remote OR mobile) ADJ3 (medicine OR health OR monitor* OR rehab*)).tw.
4. (mHealth OR m-health OR mobile-health).tw.
5. (((mobile OR cell* OR smart) AND phone) OR smartphone).tw.
6. (tablet AND (computer OR app) OR ipad).tw.
7. (mobile and app*).tw.
8. OR/ 1-7
9. exp myocardial infarctions/ OR exp ischemia/ OR exp angina pectoris/
10. (myocardial ADJ3 (isch?em* OR infarct*)).tw.
11. (coronary ADJ3 (disease OR bypass OR syndrome) OR angioplasty OR percutaneous coronary intervention OR angina OR stent).tw.
12. OR/ 9-11
13. exp rehabilitation/ OR exp exercise/ OR exp physical fitness/ OR exp active living/ OR exp lifestyle changes/
14. ((rehabilitation OR exercise OR fitness) AND (therap* OR train* OR program* OR treatment OR interven*)).tw.
15. Or/ 13-14
16. 8 AND 12 AND 15

PubMed
3. (tele* [tw] OR remote [tw] OR mobile [tw]) AND (medicine [tw] OR health [tw] OR monitor* [tw] OR rehab* [tw])
4. mhealth [tw] OR m-health [tw] OR mobile-health [tw]
5. ((mobile [tw] OR cell* [tw] OR smart [tw]) AND phone [tw]) OR smartphone [tw]
6. tablet [tw] AND (computer [tw] OR app [tw]) OR ipad [tw]
7. mobile [tw] AND app* [tw]
8. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
9. myocardial ischemia [mh]
10. (myocardial [tw] AND (isch* [tw] OR infarct* [tw]))
12. #9 OR #10 OR #11
13. rehabilitation [mh] OR exercise [mh] OR physical fitness [mh]
14. (rehabilitation [tw] OR exercise [tw] OR fitness [tw]) AND (therap* [tw] OR train* [tw] OR program* [tw] OR treatment [tw] OR interven* [tw])
15. #13 OR #14
16. #8 AND #12 AND #15
Appendix 1.2 Characteristics of Included Studies [ordered by study ID]

Arthur 2002

<table>
<thead>
<tr>
<th>Design</th>
<th>RCT – two arm, parallel groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol/trial registration</td>
<td>No / No</td>
</tr>
<tr>
<td>Participants</td>
<td>n = 122 (96 male, 79%) in TexCR, n = 120 (101 male, 83%) in CBexCR. Age = 63 ± 9 y.</td>
</tr>
<tr>
<td>Inclusion: Post-CABG (25-49 d post-procedure); 40-80% age-predicted MET\text{max} during GXT; read/write English</td>
<td></td>
</tr>
<tr>
<td>Exclusion: Recurrent angina; positive GXT; unable to attend 3 exCR sessions per week; physical limitations; previous participation in outpatient CR.</td>
<td></td>
</tr>
<tr>
<td>Treatments</td>
<td>TexCR (intervention)</td>
</tr>
<tr>
<td>ICT</td>
<td>Telephone (exercise prescription, monitoring, behaviour change, social support).</td>
</tr>
<tr>
<td>Exercise</td>
<td>6 months. 5 sessions per week (10-15 min warm-up, 40 min aerobic training, 10-15 min cool-down). 60% VO\text{2}peak (0-3 months), 70% VO\text{2}peak (4-6 months). Bi-weekly telephone calls from exercise specialist to monitor progress/adherence and revise exercise prescription. Exercise log reviewed monthly. Consult with exercise specialist at baseline &amp; 3 months.</td>
</tr>
<tr>
<td>Other</td>
<td>Bi-weekly telephone calls from exercise specialist to provide support and education.</td>
</tr>
<tr>
<td>CBexCR (active control)</td>
<td>Exercise</td>
</tr>
<tr>
<td>Other</td>
<td>No additional programme components reported.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Primary: Exercise capacity (VO\text{2}peak).</td>
</tr>
<tr>
<td>Secondary: Blood pressure, exercise adherence.</td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>Post-treatment (6 months) and long-term follow-up (1.5 and 7.2 years post-randomisation)</td>
</tr>
<tr>
<td>Country</td>
<td>Canada.</td>
</tr>
<tr>
<td>Risk of Bias</td>
<td>Support for judgement</td>
</tr>
<tr>
<td>Sequence generation</td>
<td>Low risk</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Low risk</td>
</tr>
<tr>
<td>Blinding – outcome assessment</td>
<td>Unclear risk</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>Unclear risk</td>
</tr>
<tr>
<td>Intention-to-treat analysis</td>
<td>Low risk</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>Unclear risk</td>
</tr>
</tbody>
</table>

Support for judgement

“The study coordinator randomly assigned patients to study groups using a concealed randomization process. A data analyst, who had no role in this project, prepared the randomization schedule using a blocked format.”

“The resulting group assignments were then sealed in opaque envelopes that were opened in sequence after consent and baseline data were obtained.”

Baseline outcomes assessed prior to treatment allocation. Primary outcome (VO\text{2}peak) assessment at low risk of bias. “The physicians who evaluated the primary outcome variable were blind to patients’ assignment.” Blinding of follow-up outcome assessors not specified.

Results show dropout/loss to follow up (n = 20/242 at 6 months, n = 24/222 at 18 months, n = 52/196 at ~7.2 years, see methods regarding latter 2 time points). No detail provided about treatment of missing data at 6/18 months. Imputation of primary outcome missing data at ~7.2 years.

“Analyses were performed on an intention-to-treat approach.” ITT consistent across all three study reports.

Specified primary and secondary outcomes are reported, not all reported outcomes were specified in methods.
<table>
<thead>
<tr>
<th>Other sources of bias</th>
<th>Unclear risk</th>
<th>Long-term follow-up time points included declining sub-samples of the original randomised sample.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frederix 2013a</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>RCT – two arm, parallel groups</td>
<td></td>
</tr>
<tr>
<td><strong>Protocol/trial registration</strong></td>
<td>No / Yes</td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>n = 40 (32 male, 80%) in TexCR, n = 40 (34 male, 85%) in CBexCR. Age = 61 ± 10 y.</td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion:</strong> PCI or CABG following ACS; computer/internet access.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exclusion:</strong> &gt;80 y; ICD or pacemaker; severe arrhythmia; persistent exertional ischaemia after revascularisation therapy; NYHA class III/IV; neuro-musculoskeletal exercise limitations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>TexCR (intervention)</td>
<td></td>
</tr>
<tr>
<td><strong>ICT:</strong> Accelerometer, website (exercise monitoring); email, SMS (exercise prescription/feedback).</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exercise:</strong> 1.5 months centre-based exCR followed by 3 months home-based TexCR. Accelerometer data uploaded to website. Weekly automated personalised physical activity feedback via email/SMS. Exercise prescription details not reported.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other:</strong> No additional programme components reported.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CBexCR (active control)</strong></td>
<td>Exercise: 4.5 months supervised centre-based exCR. Exercise prescription details not reported.</td>
<td></td>
</tr>
<tr>
<td><strong>Other:</strong> No additional programme components reported.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary:</strong> Exercise capacity ((\dot{V}O_2)peak).</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Secondary:</strong> Blood pressure, blood lipid/glucose concentrations, body composition, physical activity, clinical events.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>Belgium.</td>
<td></td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td>Judgement</td>
<td>Support for judgement</td>
</tr>
<tr>
<td>Sequence generation</td>
<td>Unclear risk</td>
<td>“Randomization was done using blind envelopes.” No further detail about sequence generation methods.</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Unclear risk</td>
<td>“Randomization was done using blind envelopes.” Allocation concealment not explicitly stated by appeared likely to have occurred. No details provided regarding sequential opening.</td>
</tr>
<tr>
<td>Blinding – outcome assessment</td>
<td>Unclear risk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>High risk</td>
<td>“Data from dropout patients were omitted. Missing values for patients not considered to be dropout patients were [imputed].” Dropout reported (intervention n = 8, control n = 6). Numbers/reasons comparable between groups. Unclear how many participants were considered lost to follow-up.</td>
</tr>
<tr>
<td>Intention-to-treat analysis</td>
<td>High risk</td>
<td>Intention-to-treat not explicitly stated. Results appeared to be presented according to original treatment allocation, but dropouts were excluded from analyses.</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>High risk</td>
<td>Not all outcomes specified in methods/trial registration are reported.</td>
</tr>
<tr>
<td>Other sources of bias</td>
<td>Low risk</td>
<td>No other risks identified.</td>
</tr>
<tr>
<td>Gordon 2002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>RCT – three arm, parallel groups. 1 group excluded from review due to unclear telehealth fidelity</td>
<td></td>
</tr>
<tr>
<td><strong>Protocol/trial registration</strong></td>
<td>No / No</td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>n = 52 (38 male, 73%; 54 randomised, 2 not reported) in TexCR, n = 45 (34 male, 76%; 52 randomised, 7 not reported) in CBexCR. Age = 61 ± 10 y.</td>
<td></td>
</tr>
<tr>
<td>Inclusion:</td>
<td>Diagnosed CAD (MI, PCI, CABG, angina); low to mod recurrent event risk; ≥4 weeks post-hospitalisation; clinician approval to participate; 21-75 years; able to complete a maximal treadmill test; absence of non-cardiac life-threatening illness; absence of significant/prohibitive psychological illness; able to attend 3 exCR sessions per week CR; understands English.</td>
<td></td>
</tr>
<tr>
<td>Exclusion:</td>
<td>Exclusion criteria not explicitly documented.</td>
<td></td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>TexCR (intervention)</td>
<td></td>
</tr>
<tr>
<td>ICT:</td>
<td>Telephone (exercise prescription, education).</td>
<td></td>
</tr>
<tr>
<td>Exercise:</td>
<td>3 months. 2 centre-based exCR sessions (week 1/6). ≥3 sessions per week. 30-60 minutes. 60-85% HR$\text{peak}$. Telephone calls (week 2/4/8/10) from nurse case manager to update exercise prescription.</td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td>Telephone calls (week 2/4/8/10) from nurse case manager to provide education and behaviour change counselling.</td>
<td></td>
</tr>
<tr>
<td>CBexCR (control)</td>
<td>Exercise: 3 months. 3 centre-based supervised exCR sessions per week. 30-60 min. 60-85% HR$\text{peak}$.</td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td>Education and behaviour change counselling.</td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Primary: Primary outcome not specified.</td>
<td></td>
</tr>
<tr>
<td>Secondary:</td>
<td>Exercise capacity (VO$_2$peak), blood pressure, blood lipid concentrations, body mass, exercise adherence.</td>
<td></td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Post-treatment (3 months).</td>
<td></td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>USA</td>
<td></td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td>Judgement</td>
<td></td>
</tr>
<tr>
<td><strong>Support for judgement</strong></td>
<td>&quot;…patients were randomized to 1 of the following 3 programs for 12 weeks:&quot; No further detail about sequence generation methods.</td>
<td></td>
</tr>
<tr>
<td><strong>Sequence generation</strong></td>
<td>Unclear risk</td>
<td></td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td>Unclear risk</td>
<td></td>
</tr>
<tr>
<td><strong>Blinding – outcome assessment</strong></td>
<td>Unclear risk</td>
<td></td>
</tr>
<tr>
<td><strong>Incomplete outcome data</strong></td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>&quot;…142 (91.6%) underwent testing at baseline and again after 12 weeks of intervention.&quot; Dropout reported (intervention n = 2, control n = 7). Data presented for complete cases</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intention-to-treat analysis</strong></td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Intention-to-treat not explicitly stated. Results appeared to be presented per-protocol.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Selective reporting</strong></td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>All outcomes specified in methods are reported.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other sources of bias</strong></td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>No other risks identified.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Guiraud 2012**

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>RCT – two arm, parallel groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protocol/trial registration</strong></td>
<td>No / No</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>n = 19 (17 male, 89%) in TexCR, n = 10 (7 male, 70%) in Usual Care. Age = 57 ± 12 y.</td>
</tr>
<tr>
<td><strong>Inclusion:</strong></td>
<td>Acute cardiac event; noncompliance with recommended physical activity; CR participation; computer at home.</td>
</tr>
<tr>
<td><strong>Exclusion:</strong></td>
<td>Unstable angina; uncontrolled hypertension; severe arrhythmia; neuro-orthopaedic disease affecting exercise capacity.</td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>TexCR (intervention)</td>
</tr>
<tr>
<td>ICT:</td>
<td>Telephone (counselling and exercise feedback); accelerometer, web portal (exercise monitoring).</td>
</tr>
<tr>
<td>Exercise:</td>
<td>2 months. Weekly upload of daily accelerometry data to web portal. Data retrospectively reviewed by kinesiologist. Bi-weekly telephone calls from kinesiologist to provide physical activity feedback. Exercise prescription details not reported.</td>
</tr>
<tr>
<td>Other:</td>
<td>Bi-weekly telephone calls from kinesiologist to provide counselling.</td>
</tr>
<tr>
<td><strong>Usual Care (control)</strong></td>
<td>2 months. No detail provided.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Primary: Physical activity duration and estimated energy expenditure.</td>
</tr>
<tr>
<td><strong>Secondary:</strong></td>
<td>No secondary outcomes specified or reported.</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Post-treatment (2 months).</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>France.</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td>Judgement</td>
</tr>
<tr>
<td><strong>Support for judgement</strong></td>
<td>“…patients were randomly assigned to an intervention group (n=19) or a control group (n=10).” No further detail about sequence generation methods.</td>
</tr>
<tr>
<td><strong>Sequence generation</strong></td>
<td>Unclear risk</td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td>Unclear risk</td>
</tr>
<tr>
<td><strong>Blinding – outcome assessment</strong></td>
<td>Unclear risk</td>
</tr>
<tr>
<td><strong>Incomplete outcome data</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td><strong>Intention-to-treat analysis</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td><strong>Selective reporting</strong></td>
<td>High risk</td>
</tr>
<tr>
<td><strong>Other sources of bias</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td><strong>Other sources of bias</strong></td>
<td>No other risks identified.</td>
</tr>
</tbody>
</table>
### Kraal 2014

**Design**  
RCT – two arm, parallel groups.

**Protocol/trial registration**  
Yes / Yes

**Participants**  
$n = 25$ (22 male, 88%; 29 randomised, 4 not reported) in TexCR, $n = 25$ (21 male, 84%; 26 randomised, 1 not reported) in CBexCR.  
Age: $58 \pm 8$ y.  
**Inclusion:** MI, angina or revascularisation; low to moderate recurrent event risk; home internet and PC access  
**Exclusion:** Exclusion criteria not explicitly documented.

**Treatments**  
TexCR (intervention)  
ICT: Telephone (exercise prescription, behaviour change), biosensor, computer, website (exercise monitoring).  
**Exercise:** 3 months. 3 centre-based exCR visits to familiarise with biosensor, data upload, data review. ≥2 sessions per week. 45-60 minutes. 70-85% HRpeak. Weekly telephone calls from physical therapist to provide feedback on exercise frequency, duration and level of intensity.  
**Other:** Weekly telephone calls to provide behaviour change counselling.

CBexCR (control)  
**Exercise:** 3 months. 3 centre-based supervised exCR sessions per week. 45-60 min. 70-85% HRpeak.  
**Other:** Education and behaviour change counselling.

**Outcomes**  
**Primary:** Exercise capacity ($\dot{V}O_2$ peak), physical activity level.  
**Secondary:** Exercise adherence, HRQoL, clinical events.

**Follow-up**  
Post-treatment (3 months).

**Country**  
The Netherlands.

**Risk of Bias**

<table>
<thead>
<tr>
<th>Source of Bias</th>
<th>Judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequence generation</td>
<td>Low risk</td>
<td>“Allocation is based on randomization with variable block size (two or four), performed with dedicated computer software by a researcher (NP) who is not present at the time of allocation.”</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Low risk</td>
<td>“To conceal allocation, numbered and sealed opaque envelopes are opened between the baseline cardiopulmonary exercise test and the start of exercise training”</td>
</tr>
<tr>
<td>Blinding – outcome assessment</td>
<td>Unclear</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>High risk</td>
<td>“One patient in the CT group and one in the HT group were not able to perform an exercise test at 12 week…Three patients in the HT group dropped out…” Data presented for complete cases</td>
</tr>
<tr>
<td>Intention-to-treat analysis</td>
<td>High risk</td>
<td>Intention-to-treat stated in the study protocol, but results appeared to be presented per-protocol.</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>High risk</td>
<td>Not all outcomes specified in methods/study protocol are reported.</td>
</tr>
<tr>
<td>Other sources of bias</td>
<td>High risk</td>
<td>The HRQoL measure specified in the study protocol and this study report differ.</td>
</tr>
</tbody>
</table>
### Lee 2013

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>RCT – two arm, parallel groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protocol/trial registration</strong></td>
<td>No / No</td>
</tr>
</tbody>
</table>
| **Participants** | n = 30 (22 male, 73%) in TexCR, n = 30 (22 male, 73%) in Usual Care. Age = 56 ± 8 y.  
*Inclusion*: PCI following ACS; 18-80 y.  
*Exclusion*: Chronic stable angina pectoris; NYHA class III/IV, LVEF < 30%; chronic renal failure; inability to exercise. |
| **Treatments** | TexCR (intervention)  
*ICT*: Telephone (counselling and exercise prescription), mobile phone, wireless heart rate monitor (exercise monitoring).  
*Exercise*: 3 months. 1-2 centre-based exCR sessions during intervention. 4-5 home-based exCR sessions per week with wireless remote heart rate monitoring (10 min warm-up, 30 min walking, 10 min cool-down). 40% HRR (0.5-1 months), 50% HRR (1-1.5 months), 60% HRR (1.5-2 months), 70% HRR (2-2.5 months), 80% HRR (2.5-3 months). Weekly telephone calls to revise exercise prescription.  
*Other*: Weekly telephone calls to provide counselling. Ordinary medical therapy.  
Usual Care (control)  
3 months. Home-based exercise without participation in CR. Ordinary medical therapy. |
| **Outcomes** | Primary: Exercise capacity (sub-maximal metabolic equivalents).  
Secondary: Exercise duration, sub-maximal rate-pressure product, sub-maximal perceived exertion, blood pressure, quality of life. |
| **Follow-up** | Post-treatment (3 months).  
Country: Korea. |
| **Risk of Bias** |  
| **Sequence generation** | Unclear risk  
*Support for judgement*: “Patients were randomly allocated to either the CR group or the usual care (UC) group.” No further detail about sequence generation methods. |
| **Allocation concealment** | Unclear risk  
| **Blinding – outcome assessment** | Unclear risk  
| **Incomplete outcome data** | High risk  
*Support for judgement*: “Twenty six patients in the CR group and 29 patients in the UC group completed follow-up and were available for endpoint analysis.” |
| **Intention-to-treat analysis** | High risk  
| **Selective reporting** | Low risk  
| **Other sources of bias** | Low risk  
| **Support for judgement**: Intention-to-treat not explicitly stated. Results appeared to be presented per-protocol.  
**Support for judgement**: All outcomes specified in methods are reported.  
**Support for judgement**: No other risks identified. |
### Maddison 2014

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>RCT – two arm, parallel groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protocol/trial registration</strong></td>
<td>Yes / Yes</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>n = 85 (69 male, 81%) in TexCR, n = 86 (70 male, 81%) in Usual Care. Age = $60 \pm 9$ y.</td>
</tr>
<tr>
<td></td>
<td><em>Inclusion:</em> Angina pectoris, MI or revascularisation (PCI, CABG/stent) within 3-24 months; clinically stable outpatients; internet access; able to exercise; read/write English.</td>
</tr>
<tr>
<td></td>
<td><em>Exclusion:</em> heart disease-related hospital admission within 6 weeks; terminal cancer; significant non-coronary exercise limitations.</td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>TexCR (intervention)</td>
</tr>
<tr>
<td></td>
<td><em>ICT:</em> SMS (exercise prescription, behaviour change), website (exercise monitoring, behaviour change, education, social support).</td>
</tr>
<tr>
<td></td>
<td><em>Exercise:</em> 6 months. $\geq 30$ min moderate to vigorous exercise on $\geq 5$ days per week. Regular exercise prescription via SMS.</td>
</tr>
<tr>
<td></td>
<td><em>Other:</em> Behaviour change SMS (motivation, self-efficacy, social support) - 6 per week (1-3 months), 5 per week (3-4.5 months), 4 per week (4.5-6 months). Website featuring self-monitoring tools, video messages, lifestyle and CVD risk education, links to relevant organisations’ websites. Access to usual care CR services (see Usual Care, below).</td>
</tr>
<tr>
<td><strong>Usual Care (control)</strong></td>
<td>6 months. Optional access to usual care CR services including community CR education sessions, encouragement to be physically active and join a cardiac club.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Primary: Exercise capacity ($V\dot{O}_{2}$peak).</td>
</tr>
<tr>
<td></td>
<td>Secondary: Blood pressure, body composition, physical activity, health-related quality of life.</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Post-treatment (6 months).</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>New Zealand.</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td><strong>Support for judgement</strong></td>
</tr>
<tr>
<td><strong>Sequence generation</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>“On completion of the baseline assessment, eligible participants were randomly allocated at a 1:1 ratio to either intervention or control group by means of a central computerised service. Randomization was conducted using the minimization method...”</td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>Central computer service use to ensure “Allocation concealment was maintained up to the point of randomisation.”</td>
</tr>
<tr>
<td><strong>Blinding – outcome assessment</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>“Outcome assessors were blinded to treatment allocation.”</td>
</tr>
<tr>
<td><strong>Incomplete outcome data</strong></td>
<td>Unclear risk</td>
</tr>
<tr>
<td></td>
<td>“Multiple imputations method was applied to the missing data for the primary outcome only.” Missing secondary outcome data appeared likely due to LTFU/dropout reported in CONSORT flow diagram.</td>
</tr>
<tr>
<td><strong>Intention-to-treat analysis</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>“Treatment evaluations were performed on the principle of intention to treat (ITT), using data collected from all randomized participants.”</td>
</tr>
<tr>
<td><strong>Selective reporting</strong></td>
<td>High risk</td>
</tr>
<tr>
<td></td>
<td>One secondary outcome specified in trial registration (6 minute walk test) not reported.</td>
</tr>
<tr>
<td><strong>Other sources of bias</strong></td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>No other risks identified.</td>
</tr>
</tbody>
</table>
## Reid 2012a

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>RCT – two arm, parallel groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protocol/trial registration</strong></td>
<td>No / Yes</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>n = 115 (95 male, 83%) in TexCR, n = 108 (93 male, 86%) in Usual Care. Age = 56 ± 9 y.</td>
</tr>
<tr>
<td>Inclusion:</td>
<td>PCI following ACS; 28-80 y; not planning to enrol in CR; home internet access.</td>
</tr>
<tr>
<td>Exclusion:</td>
<td>CABG; ICD; NYHA class III/IV, no English, unable/unwilling to provide consent.</td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>TexCR (intervention)</td>
</tr>
<tr>
<td>ICT:</td>
<td>Accelerometer, website, email (exercise prescription and monitoring, behaviour change, education).</td>
</tr>
<tr>
<td>Exercise:</td>
<td>12 months. Weeks 1-20 - daily website activity log, revision of exercise prescription after online tutorials (see Other, below). Weeks 21-56 = New exercise prescription every 6 weeks, sustained website access, exercise feedback based on patient data logging. Exercise prescription details not reported.</td>
</tr>
<tr>
<td>Other:</td>
<td>Weeks 1-20 - 5 online education/behaviour change tutorials (weeks 2/4/8/14/20, exercise planning, monitoring, goal setting, overcoming barriers, relapse prevention). Emails from exercise specialist between tutorials with motivational feedback. Automated reminder/engagement emails, email question/answer service.</td>
</tr>
<tr>
<td>Usual Care (control)</td>
<td>12 months. Physical activity guidance and a booklet provided by cardiologist.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Primary: Physical activity.</td>
</tr>
<tr>
<td>Secondary:</td>
<td>Health-related quality of life, clinical events.</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Post-treatment (12 months).</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>Canada.</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td>Judgement</td>
</tr>
<tr>
<td>Sequence generation</td>
<td>Low risk</td>
</tr>
<tr>
<td>“Participants were randomized in a 1:1 ratio to CardioFit or usual care using a random sequence that was computer generated by a statistician in blocks of 4, 8 and 10.”</td>
<td></td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Low risk</td>
</tr>
<tr>
<td>“Sequences were generated for Ottawa and London and placed in sealed, numbered envelopes to ensure that treatment allocation was concealed until after baseline data collection.” Sequential opening not explicitly stated by appeared likely.</td>
<td></td>
</tr>
<tr>
<td>Blinding – outcome assessment</td>
<td>Low risk</td>
</tr>
<tr>
<td>Baseline assessments were completed prior to randomisation. “Research assistants, blinded to the participants’ treatment allocation, conducted follow-up assessments.”</td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>Low risk</td>
</tr>
<tr>
<td>“Missing outcome values were replaced with multiple imputations after confirming that the data were missing at random.”</td>
<td></td>
</tr>
<tr>
<td>Intention-to-treat analysis</td>
<td>Low risk</td>
</tr>
<tr>
<td>Intention-to-treat not explicitly stated. Results appeared to be presented according to original treatment allocation.</td>
<td></td>
</tr>
<tr>
<td>Selective reporting</td>
<td>High risk</td>
</tr>
<tr>
<td>Not all outcomes specified in methods/trial registration are reported. Some outcomes not reported at all specified time points.</td>
<td></td>
</tr>
<tr>
<td>Other sources of bias</td>
<td>Low risk</td>
</tr>
<tr>
<td>No other risks identified.</td>
<td></td>
</tr>
</tbody>
</table>
**Salvetti 2008**

| **Design** | RCT – two arm, parallel groups |
| **Protocol/trial registration** | No / No |
| **Participants** | n = 19 (14 male, 74%) in TexCR, n = 20 (15 male, 75%) in Usual Care. Age = 54 ± 8 y. |
| **Inclusion:** | < 70 y; resident in Sao Paulo; NYHA class I/II; maximal functional capacity > 6 MET; normal response to exercise testing; LVEF > 50%; absence of congestive heart failure, recurrent angina, complex ventricular arrhythmias, advanced CAD, antecedents of cardiac arrest or ≥ 2 MI. |
| **Exclusion:** | PVD; COPD; orthopaedic limitation; stroke; concurrent limiting non-cardiac illness; unable to attend 3 exCR sessions per week. |
| **Treatments** | TexCR (intervention) |
| **ICT:** | Telephone (exercise monitoring and feedback). |
| **Exercise:** | 3 months. 2 initial supervised centre-based exCR sessions (60-80% peak HR). 3 home-based exCR sessions per week, stretching and walking (30 min, 60-80% peak HR). Bi-weekly telephone calls from doctor to monitor adherence and progress. Exercise log completed weekly, reviewed by doctor monthly. |
| **Other:** | Bi-weekly telephone calls from doctor to provide support. |
| **Usual Care (control)** | 3 months. Encouraged to increase physical activity. |
| **Outcomes** | Primary: Exercise capacity (V̇O₂peak). |
| **Secondary:** | Blood pressure, health-related quality of life, clinical events. |
| **Follow-up** | Post-treatment (3 months). |
| **Country** | Brazil. |
| **Risk of Bias** | Judgement |
| **Sequence generation** | Low risk |
| **Allocation concealment** | Low risk |
| **Blinding – outcome assessment** | Unclear risk |
| **Incomplete outcome data** | Low risk |
| **Intention-to-treat analysis** | Unclear risk |
| **Selective reporting** | Low risk |
| **Other sources of bias** | Low risk |

**Support for judgement**

- **Sequence generation**
  - Low risk
  - “A researcher, who did not participate in this study, prepared the randomization schedule using a blocked format.”

- **Allocation concealment**
  - Low risk
  - “The resulting group assignments were then sealed in opaque envelopes that were opened after consent and baseline data were obtained.”

- **Blinding – outcome assessment**
  - Unclear risk
  - Not reported.

- **Incomplete outcome data**
  - Low risk
  - Treatment of missing data not explicitly specified but no reported attrition, and results appeared to include data from all randomised participants.

- **Intention-to-treat analysis**
  - Unclear risk
  - Intention-to-treat not explicitly stated but no attrition reported. Results appeared to be presented according to original treatment allocation.

- **Selective reporting**
  - Low risk
  - All outcomes specified in methods are reported.

- **Other sources of bias**
  - Low risk
  - No other risks identified.
**Varnfield 2014**

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>RCT – two arm, parallel groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protocol/trial registration</strong></td>
<td>No / Yes</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>n = 60 (48 male, 80%) in TexCR, n = 60 (34 male, 57%) in CBexCR. Age = 56 ± 10 y.</td>
</tr>
<tr>
<td></td>
<td><em>Inclusion:</em> MI; referred for CR.</td>
</tr>
<tr>
<td></td>
<td><em>Exclusion:</em> Unable to participate in a self-management programme; no experience with or unable to operate a smartphone; unable to attend centre-based exCR; involved in another trial.</td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td><strong>TexCR (intervention)</strong></td>
</tr>
<tr>
<td></td>
<td><em>ICT:</em> Telephone (exercise and goal feedback), website, smartphone/apps, accelerometer, weigh scale, blood pressure monitor (exercise and health monitoring), SMS and pre-installed media (social support, education).</td>
</tr>
<tr>
<td></td>
<td><em>Exercise:</em> 1.5 months. ≥ 30 min moderate activity (mostly walking) most days per week.</td>
</tr>
<tr>
<td></td>
<td><em>Other:</em> Weekly telephone calls from mentors to provide feedback. Physical activity, blood pressure, body weight monitoring via smartphone apps. SMS and pre-installed media files provided social support and educational materials.</td>
</tr>
<tr>
<td></td>
<td><strong>CBexCR (active control)</strong></td>
</tr>
<tr>
<td></td>
<td><em>Exercise:</em> 1.5 months supervised centre-based exCR 2 centre-based supervised exCR session per week (circuit-based aerobic and resistance exercise). RPE = 6-10 and 11-13.</td>
</tr>
<tr>
<td></td>
<td><em>Other:</em> 6 x weekly 1 hour educational sessions.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td><strong>Primary:</strong> Exercise uptake, adherence and completion.</td>
</tr>
<tr>
<td></td>
<td><strong>Secondary:</strong> Blood pressure, blood lipid/glucose concentrations, body composition, physical activity, clinical events.</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Post-treatment (1.5 months) and long-term follow-up (6 months post-randomisation).</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>Australia.</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td><strong>Judgement</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Sequence generation</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Allocation concealment</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Blinding – outcome assessment</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Incomplete outcome data</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intention-to-treat analysis</strong></td>
<td>Unclear risk</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Selective reporting</strong></td>
<td>High risk</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other sources of bias</strong></td>
<td>High risk</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Zutz 2007

| **Design** | RCT – two arm, parallel groups, + non-randomised historic control arm. |
| **Protocol/trial registration** | No / No |
| **Participants** | n = 8 (7 male, 80%) in TexCR, n = 7 (5 male, 71%) in Usual Care. Age = 59 ± 9 y.  
*Inclusion:* MI/PCI/CABG; referral to centre-based CR; live < 60 km from CR centre; no prior CR; fluent in English.  
*Exclusion:* Depression; smoking; >2 mm ST depression or significant arrhythmia during exercise test; uncontrolled diabetes. |
| **Treatments** | TexCR (intervention)  
ICT: laptop computer, heart rate and blood pressure monitors (exercise monitoring), online chat (exercise prescription and feedback, education), website (task list)  
Exercise: 3 months. Exercise heart rate data uploaded ≥ 2 twice per week. Pre- and post-exercise blood pressure and blood glucose concentration uploaded periodically. Exercise prescription details not reported. Scheduled online chat with exercise specialist (3 x 1 h) to provide exercise prescription and progress feedback.  
Other: Scheduled online chat with dietician and nurse (3 x 1 h sessions each) to provide dietary recommendations and risk factor management. Monthly ask-an-expert group online chat. Website with weekly task list.  
Usual Care (control)  
3 months. No contact between researchers or centre-based exCR and participants. Participants underwent 12 week centre-based exCR after completing the control treatment.  
Matched historic CBexCR (control)  
Hospital-based exCR. Matched to intervention (2:1) based on age, gender, and disease presentation. Ineligible for inclusion in this review due to non-randomised sampling method. |
| **Outcomes** | Primary: Exercise capacity (estimated MET<sub>max</sub>)  
Secondary: Blood pressure, blood lipid concentrations, body composition, physical activity. |
| **Follow-up** | Post-treatment (3 months). |
| **Country** | Canada. |
| **Risk of Bias** |  
**Judgement** | Support for judgement |
| **Sequence generation** | Unclear risk | “…randomized to either the internet-based CRP (vCRP) or to the observational control group” |
| **Allocation concealment** | Unclear risk | Not reported. |
| **Blinding – outcome assessment** | Unclear risk | Not reported. |
| **Incomplete outcome data** | High risk | Drop-outs reported. No method for treating missing data specified. |
| **Intention-to-treat analysis** | High risk | Intention-to-treat not explicitly stated. Results appeared to be presented excluding reported dropouts. |
| **Selective reporting** | Low risk | All outcomes specified in methods are reported. |
| **Other sources of bias** | Low risk | No other risks identified. |

**Abbreviations:**  
ACS = Acute coronary syndrome  
CABG = Coronary artery bypass graft  
CAD = Coronary artery disease  
CBexCR = Centre-based exCR  
COPD = Chronic obstructive pulmonary disease  
CR = Cardiac rehabilitation  
exCR = Exercise-based cardiac rehabilitation  
GXT = Graded exercise test  
HR(peak) = Heart rate (peak)  
HRR = Heart rate reserve (i.e. level of exercise intensity)  
ICD = Implantable cardioverter defibrillator  
ICT = Information and communication technologies  
ITT = Intention-to-treat analysis  
LVEF = Left ventricular ejection fraction  
MET = Metabolic equivalent of task  
MI = Myocardial infarction  
NYHA = New York Heart Association functional classification  
PCI = Percutaneous coronary intervention  
PVD = Peripheral vascular disease  
RCT = Randomised controlled trial  
SMS = Short message service  
TexCR = Telehealth exCR  
VO2peak = Peak oxygen consumption  
V̇O₂peak = Peak oxygen consumption
### Appendix 1.3 Characteristics of Excluded Studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason For Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ades 2000[219]</td>
<td>Non-randomised design</td>
</tr>
<tr>
<td>Barnason 2003[221]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Barnason 2013[222]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Beatty 2013[121]</td>
<td>Systematic review and/or meta-analysis</td>
</tr>
<tr>
<td>Bidargaddi 2008[223]</td>
<td>No outcome data</td>
</tr>
<tr>
<td>Blair 2011[112]</td>
<td>Systematic review and/or meta-analysis</td>
</tr>
<tr>
<td>Bosak 2007[224]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Brennan 2001[225]</td>
<td>No outcome data</td>
</tr>
<tr>
<td>Brough 2014[226]</td>
<td>Non-randomised design</td>
</tr>
<tr>
<td>Brubaker 2000[227]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Carr 2008[228]</td>
<td>Ineligible participant group</td>
</tr>
<tr>
<td>Chow 2012[117]</td>
<td>No outcome data</td>
</tr>
<tr>
<td>Dalal 2007[75]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Dalleck 2011[229]</td>
<td>Non-randomised design</td>
</tr>
<tr>
<td>Dantas 2002[230]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>DeBusk 1994[231]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Dennis 2013[232]</td>
<td>Systematic review and/or meta-analysis</td>
</tr>
<tr>
<td>Devi[233]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Fletcher 1984[234]</td>
<td>Ineligible or absent comparison group</td>
</tr>
<tr>
<td>Frederix 2011[235]</td>
<td>Ineligible or absent comparison group</td>
</tr>
<tr>
<td>Frederix 2012[236]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Frederix 2013b[237]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Frederix 2013c[238]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Frederix 2014[239]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Frederix 2015[116]</td>
<td>No outcome data</td>
</tr>
<tr>
<td>Friedman 1998[240]</td>
<td>Ineligible participant group</td>
</tr>
<tr>
<td>Giallauria 2006[241]</td>
<td>Non-randomised design</td>
</tr>
<tr>
<td>Hanssen 2007a[242]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Hanssen 2007b[243]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Hanssen 2009[244]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Harris 2003[245]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Holmes-Rovner 2008[246]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Honeyman 2014[247]</td>
<td>Systematic review and/or meta-analysis</td>
</tr>
<tr>
<td>Huang 2014[93]</td>
<td>Systematic review and/or meta-analysis</td>
</tr>
<tr>
<td>Hwang 2011[248]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Jiang 2013[249]</td>
<td>Abstract or dissertation</td>
</tr>
<tr>
<td>Jolly 2007[250]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Kortke 2006[251]</td>
<td>Ineligible participant group</td>
</tr>
<tr>
<td>Korzeniowska-Kubacka 2011[252]</td>
<td>Non-randomised design</td>
</tr>
<tr>
<td>Korzeniowska-Kubacka 2014[253]</td>
<td>Non-randomised design</td>
</tr>
<tr>
<td>Kotb 2014[254]</td>
<td>Systematic review and/or meta-analysis</td>
</tr>
<tr>
<td>Kouidi 2006[255]</td>
<td>Ineligible or absent comparison group</td>
</tr>
<tr>
<td>Kraal 2013[256]</td>
<td>No outcome data</td>
</tr>
<tr>
<td>Lear 2001[257]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Lear 2002[258]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Lear 2003[259]</td>
<td>No telehealth exCR</td>
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<tr>
<td>Lear 2006[260]</td>
<td>No telehealth exCR</td>
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<tr>
<td>Lear 2013[261]</td>
<td>Abstract or dissertation</td>
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<tr>
<td>Leemrijse 2012[262]</td>
<td>No telehealth exCR</td>
</tr>
<tr>
<td>Lewes 1967[263]</td>
<td>No telehealth exCR</td>
</tr>
</tbody>
</table>
Lieber 2012[264] Ineligible participant group
Lindsay 2008[265] No telehealth exCR
Lombard 1995[266] Abstract or dissertation
Maddison 2011[153] No outcome data
Mayer-Berger 2014[267] No telehealth exCR
Miller 1984[268] No telehealth exCR
Mittag 2006[269] No telehealth exCR
Moore 2007[270] Non-randomised design
Najafi 2015[271] Non-randomised design
Naser 2008[272] No telehealth exCR
Neubeck 2009[82] Systematic review and/or meta-analysis
Neubeck 2011[273] Abstract or dissertation
Nolan 2011[274] No telehealth exCR
Ozahowski 1986[275] No outcome data
Patja 2012[276] No telehealth exCR
Phillips 2014[277] Systematic review and/or meta-analysis
Pietrzak 2014[278] Systematic review and/or meta-analysis
Pinto 2013[279] No telehealth exCR
Piotrowicz 2011[280] Abstract or dissertation
Redfern 2009[281] No telehealth exCR
Redfern 2010[282] No telehealth exCR
Reid 2012b[283] No telehealth exCR
Richardson 2010[284] Ineligible participant group
Sanderson 1990[285] Abstract or dissertation
Southard 2003[286] No telehealth exCR
Sparks 1998[287] No outcome data
Squires 1991[288] Ineligible or absent comparison group
Tirimacco 2014[289] Abstract or dissertation
Turkstra 2013[290] No telehealth exCR
Ueshima 2002[291] Ineligible or absent comparison group
Vale 2005[292] Systematic review and/or meta-analysis
Varnfield 2011[136] No outcome data
Varnfield 2012[293] Abstract or dissertation
Vernooij 2012[294] Ineligible participant group
Widmer 2014[295] Abstract or dissertation
Wister 2007[296] No telehealth exCR
Worringham 2011[67] Ineligible or absent comparison group
Wu 2006[297] No telehealth exCR

exCR = exercise-based cardiac rehabilitation.
<table>
<thead>
<tr>
<th>Study</th>
<th>Sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding of outcome assessment</th>
<th>Incomplete outcome data</th>
<th>Intention-to-treat analysis</th>
<th>Selective outcome reporting</th>
<th>Other Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthur 2002</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>?</td>
</tr>
<tr>
<td>Frederix 2013a</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Gordon 2002</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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<tr>
<td>Guiraud 2012</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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<td>↑</td>
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<tr>
<td>Kraal 2014</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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</tr>
<tr>
<td>Lee 2013</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Maddison 2014</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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<tr>
<td>Reid 2012a</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Salvetti 2008</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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<tr>
<td>Varnfield 2014</td>
<td>↑</td>
<td>↑</td>
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<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Zutz 2007</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

↓ = low risk of bias; ? = unclear risk of bias; ↑ = high risk of bias
## Appendix 1.5 Additional Outcome Data

### Summary of additional body composition data at post-intervention follow-up

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Group Mean</th>
<th>Difference (95% CI)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maddison 2014</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>84.36 ± 13.65</td>
<td>0.65 (-4.18 to 5.48)</td>
<td>TexCR = UC</td>
</tr>
<tr>
<td>UC</td>
<td>83.71 ± 16.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circ. cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>100.70 ± 10.43</td>
<td>0.49 (-3.32 to 4.30)</td>
<td>TexCR = UC</td>
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<tr>
<td>UC</td>
<td>100.21 ± 13.13</td>
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<td></td>
</tr>
<tr>
<td>Hip circ. cm</td>
<td></td>
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<tr>
<td>TexCR</td>
<td>105.30 ± 9.37</td>
<td>0.55 (-2.38 to 3.48)</td>
<td>TexCR = UC</td>
</tr>
<tr>
<td>UC</td>
<td>104.75 ± 8.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>0.96 ± 0.05</td>
<td>0.01 (-0.01 to 0.03)</td>
<td>TexCR = UC</td>
</tr>
<tr>
<td>UC</td>
<td>0.95 ± 0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Zutz 2007</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circ. cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>84.70 ± 6.40</td>
<td>-4.1 (-13.56 to 5.36)</td>
<td>TexCR = UC</td>
</tr>
<tr>
<td>UC</td>
<td>88.80 ± 9.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Arthur 2002</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Waist:hip ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>0.90 ± 0.06</td>
<td>-0.02 (-0.03 to – 0.01)</td>
<td>TexCR &lt; CBexCR</td>
</tr>
<tr>
<td>CBexCR</td>
<td>0.92 ± 0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gordon 2002</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔBody mass kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>-1.00 ± 2.31</td>
<td>-0.14 (-1.05 to 0.77)</td>
<td>TexCR = CBexCR</td>
</tr>
<tr>
<td>CBexCR</td>
<td>-0.86 ± 2.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Varnfield 2014</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>89.10 ± 21.10</td>
<td>0.70 (-8.42 to 9.82)</td>
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<tr>
<td>CBexCR</td>
<td>88.40 ± 11.30</td>
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<td></td>
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<tr>
<td>Waist circ. cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>101.10 ± 14.40</td>
<td>0.40 (-5.80 to 6.60)</td>
<td>TexCR = CBexCR</td>
</tr>
<tr>
<td>CBexCR</td>
<td>100.70 ± 8.70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TexCR/CBexCR = telehealth/centre-based exercise-based cardiac rehabilitation; UC = Usual care

- Hypothesis manually calculated following accepted methods.[298]
- Gordon 2002 data presented as change from baseline.
### Summary of blood glucose control data at post-intervention follow-up

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Group Mean</th>
<th>Difference (95% CI)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frederix 2013a</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood glucose mmol·L⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>5.78 ± 0.44</td>
<td>-0.11 (-0.43 to 0.20)</td>
<td>TexCR = CBexCR</td>
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<tr>
<td>CBexCR</td>
<td>5.89 ± 0.78</td>
<td>P = .44</td>
<td></td>
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<tr>
<td>HbA1c %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TexCR</td>
<td>0.90 ± 0.06</td>
<td>-0.10 (-0.35 to 0.15)</td>
<td>TexCR = CBexCR</td>
</tr>
<tr>
<td>CBexCR</td>
<td>0.92 ± 0.07</td>
<td>P = .06</td>
<td></td>
</tr>
</tbody>
</table>

TexCR/CBexCR = telehealth/centre-based exercise-based cardiac rehabilitation

### Summary of clinical event counts at post-intervention follow-up

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Event Count (%)</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maddison 2014</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac event</td>
<td>TexCR 4/85 (4.7%)</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>UC 3/86 (3.5%)</td>
<td>1.2</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>TexCR 2/85 (2.4%)</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>UC 0/86 (0.0%)</td>
<td>2.4</td>
</tr>
<tr>
<td>Rehospitalisation</td>
<td>TexCR 11/85 (12.9%)</td>
<td>-5.7</td>
</tr>
<tr>
<td></td>
<td>UC 16/86 (18.6%)</td>
<td>-5.7</td>
</tr>
<tr>
<td><strong>Reid 2012a</strong></td>
<td></td>
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</tr>
<tr>
<td>Mortality</td>
<td>TexCR 0/115 (0.0%)</td>
<td>-1.9</td>
</tr>
<tr>
<td></td>
<td>UC 2/108 (1.9%)</td>
<td>-1.9</td>
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<tr>
<td>Revascularisation</td>
<td>TexCR 0/115 (0.0%)</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>UC 1/108 (0.9%)</td>
<td>-0.9</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>TexCR 4/115 (3.5%)</td>
<td>-2.1</td>
</tr>
<tr>
<td></td>
<td>UC 6/108 (5.6%)</td>
<td>-2.1</td>
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<tr>
<td><strong>Salvetti 2008</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary event</td>
<td>TexCR 0/19 (0.0%)</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>UC 0/20 (0.0%)</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Frederix 2013</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehospitalisation</td>
<td>TexCR 4/32 (12.5%)</td>
<td>-14.0</td>
</tr>
<tr>
<td></td>
<td>CBexCR 9/34 (26.5%)</td>
<td>-14.0</td>
</tr>
<tr>
<td><strong>Kraal 2014</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total adverse events</td>
<td>TexCR 0/25 (0.0%)</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>CBexCR 0/25 (0.0%)</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Varnfield 2014</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revascularisation</td>
<td>TexCR 1/60 (1.7%)</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>CBexCR 1/60 (1.7%)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

TexCR/CBexCR = telehealth/centre-based exercise-based cardiac rehabilitation; UC = Usual care

^Summary conclusions not drawn due to the small numbers of reported events.
APPENDIX 2: REMOTE-CR PLATFORM
SUPPLEMENTARY MATERIAL

Appendix 2.1 REMOTE-CR User Guide

Appendix 2.2 REMOTE-CR Platform Screenshots

Appendix 2.3 Behaviour Change Messages
Appendix 2.1 REMOTE-CR User Guide

IMPORTANT INFORMATION

For Zephyr goldtouch motion, zephyr & remote cr

REMOTE-CR exercise monitoring system

Using the Bioharness

Do not stretch beyond your comfort level.

185
REMOTE-CP APP: GOALS

1. Frequency
2. Volume
3. Duration

Touch here to access the GOAL TYPE selection page.
Touch "START" to begin your training session.
REMOTE-CR APP: WORKOUT

Receive during your training session

Touch NOTIFICATIONS to reply or read messages

Touch GADD to open the workout session menu.

Return to the workout session window. Touch BACK to go back (see above).

Touch here to access the symptoms severity pop-up.

Select the symptom severity from this list.

REMOTE-CR APP: WORKOUT
Appendix 2.2 REMOTE-CR Platform Screenshots
Friday 29th

Duration
01:01:15

Distance
5.88 km

Training Load
136.37

Speed
- Min: 0 km/h
- Avg: 5.77 km/h
- Max: 0 km/h

Heart Rate
- Min: 66 bpm 11.11 %HRR
- Avg: 108 bpm 69.44 %HRR
- Max: 140 bpm 113.89 %HRR
Goals for Monday 24th - Sunday 30th

- **Distance:** 10 kms (0%)
- **Duration:** 180 mins (4%)
- **Frequency:** 5 pw (40%)
- **Intensity:** 60 %HRR (18%)
- **Load:** 20 (8%)
Appendix 2.3 Behaviour Change Messages

1.1 Task Self-efficacy
Hi NAME, welcome to the REMOTE-CR programme! Over the next 12 weeks we'll coach you through your very own exercise programme. Each morning we'll tell you how long, and how hard to exercise. You'll hear a time, in minutes, and an exercise intensity, in percentage of heart rate reserve. The REMOTE-CR app shows percentage of heart rate reserve as %HRR. Take a look at the screen now. Your programme this week is 3 training sessions of X minutes at X to X% HRR. It's important to warm up before exercise to prepare your heart for training, and cool down afterward to ease your heart back our of training mode. Keep your heart rate below 40 %HRR for the first 5 minutes to prepare your heart and muscles for training. Finish each training session with 5 minutes below 40 %HRR, and some stretches, so your body can gradually recover. Let's get started!

1.2 Outcome expectations, Task self-efficacy
Good morning NAME. Today's training targets are X minutes at X to X% HRR. Don't forget to warm up first and cool down after. Starting an exercise programme can be the most difficult part. Take it one step at a time and if you stick at it, you'll quickly notice the benefits. Following the prescribed duration and intensity will help ensure you exercise at a level that is safe for you, and improves your fitness. Use the REMOTE-CR app to monitor your intensity to make sure you to get the most out of your programme.

1.3 Task Self-Efficacy
Welcome back NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up first. During exercise your heart beats faster, you breathe harder, you feel your muscles working, and you may start sweating. These are completely normal and safe responses to exercise. Chest pain, dizziness or excessive shortness of breath can mean you are pushing too hard. Use the SYMPTOMS button to let us know if you experience any of these and will adjust your exercise programme to keep you safe and on track to improving your fitness. If you get chest pain when exercising, STOP and follow your angina action plan. Resting and using your GTN spray should ease the pain. It's safe to keep exercising if the pain eases, but if it continues it's best to call for help.

2.1 Understanding prescription
Good morning NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR. Don't forget to warm up first and cool down after. Your body adapts to the exercise you do quickly so it's important to keep challenging yourself by increasing your level of effort. Each week we'll make your programme a bit tougher to keep challenging your body and your fitness.

2.2 Goal Setting
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up first. Not sure where to start? Setting small goals each week can help motivate you to continue your exercise programme. You can use the REMOTE-CR app to set weekly exercise goals and monitor your progress towards achieving them. To help get you started try setting an exercise frequency goal of 3 sessions per week. Make sure to review your goals regularly, achieving them will help to increase your exercise self-confidence and keep you on track to increase your fitness.
2.3 Self-Monitoring/ Self-Regulation
Great to see you NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up first. The REMOTE-CR app records your exercise. Use the REVIEW menu to track your progress - it inspires you to do just a little bit more each time. You can view DURATION, DISTANCE, TRAINING LOAD, HEART RATE, a map, and any symptoms or messages for each session. You can also see how well you've done so far this month at the top of the screen.

3.1 Social Support
Welcome back NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR. Don't forget to warm up and cool down. Support from your friends and family can be a huge help when you're following an exercise programme. Ask them to help you stay active when you need it.

3.2 Scheduling Efficacy
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up first. Fitting exercise into your life can be challenging, but the results are worth it! Scheduling exercise in the morning is a great way to make sure your programme isn't interrupted if unexpected events come up later in the day.

3.3 Coping Efficacy
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up first. Sometimes life makes it hard to stick to your exercise programme but remember, there's a fitter healthier you waiting beyond every obstacle that stands in your way. Planning ahead is crucial. Having a simple plan to overcome obstacles helps make sure they don't hold you back. Don't let bad weather stop you, plan to wear a jacket or carry an umbrella when it's wet outside.

4.1 Self-Monitoring/ Self-Regulation
Hi NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. It's time to REVIEW your progress in the REMOTE-CR app. Look back at the improvements in DISTANCE, DURATION and TRAINING LOAD. You should be proud of your progress, well done!

4.2 Social Support
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Support from friends and family can really help to keep you focused and motivated. Encourage your friends and family to be active with you and they will urge you on when you need it.

4.3 Goal Setting
Great to see you NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. You're 4 weeks into the programme so it's a great time to check in on your goals. Celebrate the goals you've achieved, well done! Set the bar a little higher next week to really challenge yourself. Setting small goals and revising them each week will help to keep you on track to increase your fitness.

5.1 Task self-efficacy
Good morning NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. Regular exercise helps to reduce blood pressure, improve your heart function and control your weight – remember you're working towards a fitter healthier you. Stick at it and you'll see.

5.2 Coping Efficacy
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. If you're heading away from home for a few days, remember the REMOTE-CR system works anywhere you have an internet connection. Take the system with you and stay on track with your programme.
5.3 Self-Monitoring/ Self-Regulation
Great to see you NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. You've been following the programme for 5 weeks now, do you feel yourself improving? Use the REMOTE-CR app to REVIEW your progress and see just how far you've come in a short time.

6.1 Scheduling Efficacy
Welcome back NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. It can be difficult to schedule exercise into your life if you think of it as an added extra. Try looking at things differently. Making exercise a priority and fitting your life around your training programme helps keep you on track to a fitter and healthier lifestyle.

6.2 Social Support
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Have you shared your goals with friends or family? A support person can help provide the support you need to achieve your goals, and motivate you to stay active when it gets tough.

6.3 Goal setting
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. You're 6 weeks into the programme and it's a good time to take another look at your goals. Reward yourself for the ones you've achieved by doing something you enjoy, you've earned it! Are there any goals you haven't quite achieved? Setting small goals each week can help you work towards bigger goals, you'll be there in no time!

7.1 Coping Efficacy
Welcome back NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. It's important to have a plan for obstacles that can stop you from exercising. Think of any things that might hold you back, such as a lack of time to exercise, and write down strategies to help overcome them. Having a plan makes it much easier to stick to your programme.

7.2 Self-Monitoring/ Self-Regulation
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Have you REVIEWED your exercise this week? Check the DISTANCE, and TRAINING LOAD for this week's training sessions and see if you can beat them next week!

7.3 Self-monitoring/Self-Regulation
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Remember to use the REMOTE-CR app to monitor your exercise intensity. Sticking to your prescribed intensity will help to make sure you are exercising at a level that is safe for you, and improves your fitness.

8.1 Self-Monitoring/Self-Regulation
Great to see you NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. Timing yourself around a favourite exercise route is a great way to see how much fitter you are now than when you started. The REMOTE-CR app can show you how much you have improved.

8.2 Social Support
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. There are 160 other people in this study who have also had a cardiac event and are trying to get active. You are not alone.
8.3 Goal Setting
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. You're now 8 weeks into the REMOTE-CR programme, it's time to check in on your goals to see how much progress you are making. Celebrate your successes and then raise the bar a little higher. Regularly challenging yourself by resetting your goals will help keep you motivated, confident, and on track to increase your fitness.

9.1 Coping efficacy
Welcome back NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. What are the things that tempt you to miss your exercise session? Working out a plan to deal with them is a great way to make sure they don't interrupt your progress. Think of some simple strategies that you can fall back on when obstacles stand in your way.

9.2 Task Self-Efficacy
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Each week you've been getting fitter and healthier, you should be noticing a difference in how you feel. Your exercise programme will really start to challenge you in the next few weeks, but you can do it! Your hard work over the last 9 weeks has built a great foundation, stick with it and you will really start to reap the benefits as the challenge increases.

9.3 Self-Monitoring/Self-Regulation
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. What was your TRAINING LOAD this week? Was it more than last week? Keep aiming higher and higher, your well on your way to a healthy lifestyle!

10.1 Coping Efficacy
Welcome back NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. After a while exercise can become repetitive, but don't let that slow your progress or stop you from achieving your goals. Plan to mix things up by trying out new exercise routes and training with friends or family. Both are great strategies to keep exercise fresh and interesting.

10.2 Social Support
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Have you shared your progress with friends or family? Use the REMOTE-CR app to show them how much progress you're making, their support and encouragement can help motivate you to stick with the programme and achieve your goals when it gets tough.

10.3 Goal Setting
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. You're 10 weeks into the programme. Stay motivated by setting new goals. Is there something you'd like to do but are worried about your fitness? Setting goals will help you work towards it!

11.1 Coping Efficacy
Welcome back NAME. This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. When life gets busy your exercise programme can be one of the first things to suffer. Think back to the strategies you planned in week 3 for overcoming obstacles that stop you from exercising. Has your plan been working? Now is a great time to update your plan to make sure nothing stands in the way of your goals.
11.2 Plan for Relapse
Hi NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. You're into the 11th week of your programme now, well done for sticking with it! Coming to the end of an exercise programme can make it difficult to carry on, but it's very important that you keep it up on your own. Having a plan can help stop you falling off the exercise wagon. Think about the progress you've made in the past 11 weeks and set a goal to carry that momentum on!

11.3 Self-Monitoring/Self-regulation
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Take a moment to REVIEW your progress in the REMOTE-CR app. Were your TRAINING LOAD and %HRR higher than last week? Time yourself around your favourite exercise route again, and see how much you've improved since back in week 8.

12.1 Plan for Relapse
Hi NAME. Welcome to the final week of the programme, well done for sticking with it! This week's programme is 3 training sessions of X minutes at X to X% HRR, don't forget to warm up for a few minutes. You've come such a long way over the past 3 months, but it doesn't stop here. Keep using the strategies you've planned for overcoming exercise obstacles, they'll help to make sure you don't lose all the progress you've worked so hard for.

12.2 Social Support/Plan for Relapse
Good morning NAME. Today's training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. With just two more training sessions to go, now is a great time to encourage your friends and family to be involved in your exercise. If you share your goals and progress with them, they'll give you the support and encouragement you need to keep getting fitter and healthier.

12.3 Self-monitoring and Goal Setting
Congratulations NAME, you've made it to the last training session in your programme. Your last training targets are X minutes at X to X% HRR, don't forget to warm up for a few minutes. Use the REMOTE-CR app to REVIEW your progress over the last 12 weeks. You'll be amazed how far you've come in such a short time! It doesn't end here though, now is the time to use the strategies you have learned throughout this programme to make a plan to keep going on your own. Remember to set goals and review them regularly. If you keep challenging yourself the rewards will keep coming!

Missed Sessions
It's normal to miss some exercise sessions but don't let it derail your progress. Look back at what you've achieved so far and pick up right where you left off.

Missing a training session every now and then is normal, sometimes it's unavoidable. It can be a good time to think about the things that stop you from exercising, revisit your plan to overcome those obstacles, and get right back into your programme.
APPENDIX 3: ETHICAL APPROVAL LETTERS

Appendix 3.1 Ethical Approval: Feasibility & Validation Study

Appendix 3.2 Ethical Approval: Randomised Controlled Trial
Appendix 3.1 Ethical Approval: Feasibility & Validation Study

21 December 2011

Dr Ralph Maddison
Clinical Trials Research Unit
Tamaki Campus,
University of Auckland
Private Bag 92 019 Auckland

Dear Dr Maddison -

Re: Ethics ref: CEN/11/11/055 (please quote in all correspondence)
Study title: Telehealth Application for Controlling Ventricular Rate in People with Atrial Fibrillation
Investigators: Dr Ralph Maddison, Professor Rob Doughty, Dr Ian Warren, Dr Nicholas Gant, Mr Jonathan Rawstron

This study was given ethical approval by the Central Regional Ethics Committee on 21st December 2011. A list of members of the Committee is attached.

Approved Documents

- National Application Form (for the above study) with the requested amendments
- Part 4: declaration signed by Dr Ralph Maddison
- Form A: signed
- Interview guidelines, version 2, dated 17/05/2010
- Participant Information Sheet, Version 2, dated 8 November 2011
- Consent Form, Version 2, dated 8 November 2011
- Signed Locality Assessments for Auckland Hospital
- Signed Locality Assessment for Tamaki Campus, Auckland University
- Evidence of Maori Consultation - Letter signed and dated 24 November 2011 by Dr Anna Rolleston, The Cardiac Clinic, Mt Maunganui

This approval is valid until 21st December 2016, provided that Annual Progress Reports are submitted (see below).

Access to ACC

For the purposes of section 32 of the Accident Compensation Act 2001, the Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out. Participants injured as a result of treatment received in this trial will therefore be eligible to be considered for compensation in respect of those injuries under the ACC scheme.

Amendments and Protocol Deviations

All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:

- the researcher responsible for the conduct of the study at a study site
- the addition of an extra study site
- the design or duration of the study
UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE

19-Dec-2011

MEMORANDUM TO:

Dr Nicholas Gant
Sport & Exercise Science

Re: Application for Ethics Approval (Our Ref. 7674)

The Committee considered your application for ethics approval for your project titled Validation of a wireless physiological sensing device, and software platform for remote physical activity monitoring on 19-Dec-2011.

Ethics approval was given for a period of three years.

The expiry date for this approval is 19-Dec-2014.

If the project changes significantly you are required to resubmit a new application to the Committee for further consideration.

In order that an up-to-date record can be maintained, you are requested to notify the Committee once your project is completed.

The Chair and the members of the Committee would be happy to discuss general matters relating to ethics approvals if you wish to do so. Contact should be made through the UAHPEC secretary at humanethics@auckland.ac.nz in the first instance.

All communication with the UAHPEC regarding this application should include this reference number: 7674.

(This is a computer generated letter. No signature required.)

Secretary
University of Auckland Human Participants Ethics Committee

c.c. Head of Department / School, Sport & Exercise Science
Jonathan Rawston
Associate Professor James Janon
Dr Jane Magnusson

Additional information:
1. Should you need to make any changes to the project, write to the Committee giving full details including revised documentation.
2. Should you require an extension, write to the Committee before the expiry date giving full details along with revised documentation. An extension can be granted for up to three years, after which time you must make a new application.

3. At the end of three years, or if the project is completed before the expiry, you are requested to advise the Committee of its completion.

4. Do not forget to fill in the ‘approval wording’ on the Participant Information Sheets and Consent Forms, giving the dates of approval and the reference number, before you send them out to your participants.

5. Send a copy of this approval letter to the Manager - Funding Processes, Research Office if you have obtained funding other than from UniServices. For UniServices contracts, send a copy of the approval letter to: Contract Manager, UniServices.

6. Please note that the Committee may from time to time conduct audits of approved projects to ensure that the research has been carried out according to the approval that was given.
Appendix 3.2 Ethical Approval: Randomised Controlled Trial

UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE

06-Dec-2013

MEMORANDUM TO:

Assoc Prof Ralph Maddison
SOPH Administration

Re: Application for Ethics Approval (Our Ref. 011021)

The Committee considered your application for ethics approval for your project entitled REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation.

Ethics approval was given for a period of three years.

The expiry date for this approval is 06-Dec-2016.

If the project changes significantly, you are required to submit a new application to UAHPEC for further consideration.

In order that an up-to-date record can be maintained, you are requested to notify UAHPEC once your project is completed.

The Chair and the members of UAHPEC would be happy to discuss general matters relating to ethics approvals if you wish to do so. Contact should be made through the UAHPEC Ethics Administrators at humanethics@auckland.ac.nz in the first instance.

All communication with the UAHPEC regarding this application should include this reference number: 011021.

(This is a computer generated letter. No signature required.)

UAHPEC Administrators
University of Auckland Human Participants Ethics Committee
c.c. Head of Department / School, SOPH Administration
Mr Brendan Roxburgh
Dr Nicholas Gant
Jonathan Ravstorn

Additional information:

1. Do not forget to fill in the 'approval wording' on the Participant Information Sheets and Consent Forms, giving the dates of approval and the reference number, before you send them out to your participants.

2. Should you need to make any changes to the project, write to the UAHPEC Administrators by email (humanethics@auckland.ac.nz) giving full details of the proposed changes including revised documentation.
3. At the end of three years, or if the project is completed before the expiry, please advise UAHPEC of its completion.

4. Should you require an extension, write to UAHPEC by email before the expiry date, giving full details along with revised documentation. An extension can be granted for up to three years, after which a new application must be submitted.

5. If you have obtained funding other than from UniServices, send a copy of this approval letter to the Manager - Funding Processes, UoA Research Office. For UniServices contracts, send a copy of the approval letter to the Contract Manager, UniServices.

6. Please note that UAHPEC may from time to time conduct audits of approved projects to ensure that the research has been carried out according to the approval that was given.
UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

18-Feb-2014

MEMORANDUM TO:

Assoc Prof Ralph Maddison
SOPH Administration

Re: Request for change of Ethics Approval Ethics Approval (Our Ref. 011021): Amendments Approved

The Committee considered your request for change for your project entitled REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation and approval was granted for the following amendments on 18-Feb-2014.

The Committee approved the following amendments:

1) To add new investigators Dr Anna Rolleston, Prof Ralph Stewart, Dr Robyn Whittaker, Dr Iain Warren to the research study.

2) Inclusion of additional study site, The Cardiac Clinic in Tauranga.

3) Inclusion of revised participant recruitment procedures.

4) To include the proposed study site, The Cardiac Clinic, for data storage, security and destruction.

5) To replace Jonathan Rawstorn with Associate Prof Ralph Maddison as the person carrying out research procedures.

The expiry date for this approval is 06-Dec-2016.

If the project changes significantly you are required to resubmit a new application to the Committee for further consideration.

In order that an up-to-date record can be maintained, it would be appreciated if you could notify the Committee once your project is completed.

The Chair and the members of the Committee would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at ro-ethics@auckland.ac.nz in the first instance.

Please quote reference number: 011021 on all communication with the UAHPEC regarding this application.
UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

10-Jun-2014

MEMORANDUM TO:
Assoc Prof Ralph Maddison
SOPH Administration

Re: Request for change of Ethics Approval Ethics Approval (Our Ref. 011021): Amendments Approved

The Committee considered your request for change for your project entitled REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation and approval was granted for the following amendments on 10-Jun-2014.

The Committee approved the following amendments:
1) To correct a typographical error in the study PIS from $20 voucher to $10 voucher.

The expiry date for this approval is 06-Dec-2016.

If the project changes significantly you are required to resubmit a new application to the Committee for further consideration.

In order that an up-to-date record can be maintained, it would be appreciated if you could notify the Committee once your project is completed.

The Chair and the members of the Committee would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at ethics@auckland.ac.nz in the first instance.

Please quote reference number: 011021 on all communication with the UAHPEC regarding this application.

(This is a computer generated letter. No signature required.)

UAHPEC Administrators
University of Auckland Human Participants Ethics Committee

c.c. Head of Department / School, SOPH Administration
Dr Robyn Whittaker
UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

25-Jun-2014

MEMORANDUM TO:

Assoc Prof Ralph Maddison
SPH Administration

Re: Request for change of Ethics Approval Ethics Approval (Our Ref. 011021): Amendments Approved

The Committee considered your request for change for your project entitled REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation and approval was granted for the following amendments on 25-Jun-2014.

The Committee approved the following amendments:

1) To ask participants to attend a third assessment, 12 weeks after completing their study treatment in order to evaluate sustained effects of the intervention and control treatments (both treatments are exercise programmes).

2) To ask participants to wear a movement sensor during waking hours for 7 days prior to each assessment to obtain objective measures of physical activity.

3) To administer health and physical activity questionnaires (appended) during assessments.

The expiry date for this approval is 06-Dec-2016.

If the project changes significantly you are required to resubmit a new application to the Committee for further consideration.

In order that an up-to-date record can be maintained, it would be appreciated if you could notify the Committee once your project is completed.

The Chair and the members of the Committee would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at re-ethics@auckland.ac.nz in the first instance.

Please quote reference number: 011021 on all communication with the UAHPEC regarding this application.
02-Jul-2014

MEMORANDUM TO:

Assoc Prof Ralph Maddison
SOPH Administration

Re: Request for change of Ethics Approval Ethics Approval (Our Ref. 011021): Amendments Approved

The Committee considered your request for change for your project entitled REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation and approval was granted for the following amendments on 02-Jul-2014.

The Committee approved the following amendments:

1) To add a new investigator; Dr Jocelyne Benator, research cardiologist at Cardiovascular Research Unit at Auckland City Hospital.

2) To obtain hospital discharge summaries for consenting potential participants to help confirm their eligibility for the study.

3) To extend the post-cardiac event eligibility period from 3 to 6 months in order to include a larger pool of eligible patients in need of cardiac rehabilitation.

4) To change the wording in PIS to state that the participants will receive a $10 voucher instead of $20 vouchers at each study visit.

The expiry date for this approval is 06-Dec-2016.

If the project changes significantly you are required to resubmit a new application to the Committee for further consideration.

In order that an up-to-date record can be maintained, it would be appreciated if you could notify the Committee once your project is completed.

The Chair and the members of the Committee would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at re-ethics@auckland.ac.nz in the first instance.

Please quote reference number: 011021 on all communication with the UAHPEC regarding this application.
UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

23-Oct-2014

MEMORANDUM TO:

Assoc Prof Ralph Maddison
SOPH Administration

Re: Request for change of Ethics Approval Ethics Approval (Our Ref. 011021): Amendments Approved

The Committee considered your request for change for your project entitled REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation and approval was granted for the following amendments on 23-Oct-2014.

The Committee approved the following amendments:

1) To include additional community-based strategies for identifying potential participants.

The expiry date for this approval is 06-Dec-2016.

If the project changes significantly you are required to resubmit a new application to the Committee for further consideration.

In order that an up-to-date record can be maintained, it would be appreciated if you could notify the Committee once your project is completed.

The Chair and the members of the Committee would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at rq-ethics@auckland.ac.nz in the first instance.

Please quote reference number: 011021 on all communication with the UAHPEC regarding this application.

(This is a computer generated letter. No signature required.)

UAHPEC Administrators
University of Auckland Human Participants Ethics Committee

c.c. Head of Department / School, SOPH Administration
Dr Robyn Whittaker
UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

20-Nov-2014

MEMORANDUM TO:

Assoc Prof Ralph Maddison
SOPH Administration

Re: Request for change of Ethics Approval Ethics Approval (Our Ref. 011021): Amendments Approved

The Committee considered your request for change for your project entitled **REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation** and approval was granted for the following amendments on 20-Nov-2014.

The Committee approved the following amendments:

1) Additional study localities for control group treatment delivery in Auckland.

2) To include an additional supervised exercise programme, delivered at Middlemore hospital by the Counties-Manukau District Health Board (CMDHB) as a treatment option for participants randomised to the control group.

The expiry date for this approval is 06-Dec-2016.

If the project changes significantly you are required to resubmit a new application to the Committee for further consideration.

In order that an up-to-date record can be maintained, it would be appreciated if you could notify the Committee once your project is completed.

The Chair and the members of the Committee would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at ro-ethics@auckland.ac.nz in the first instance.

Please quote reference number: **011021** on all communication with the UAHPEC regarding this application.

(This is a computer generated letter. No signature required.)
APPENDIX 4: PARTICIPANT INFORMATION SHEETS

Appendix 4.1 PIS Feasibility & Validation Study (Chapter 5)

Appendix 4.2 PIS Randomised Controlled Trial (Chapter 6 and 7)
Appendix 4.1 PIS Feasibility & Validation Study

Participant Information Sheet

Validation of a wireless physiological sensing device, and software platform for remote physical activity monitoring

Researchers:
Dr Nicholas Gant - Senior Lecturer Dept. Sport & Exercise Science
Dr Ralph Maddison - Programme Leader, Physical Activity, Clinical Trials Research Unit
Dr Ian Warren - Senior Lecturer, Dept. Computer Science
Mr. Jonathan Rawstorn - BSc (Hons), Doctoral student

You are invited to participate in the above named study. The aim of the study is to examine the validity of the Bioharness (Zephyr Technologies, USA) physiological monitoring device, and Odin middleware platform for remotely quantifying physical activity. Please take your time to think about the information provided below and feel free to discuss it with your whanau, family or significant other support people before deciding whether to take part. Taking part is completely voluntary (your choice).

What is the study about?

Regular physical activity is an important modifiable risk for the prevention of chronic health conditions. Accurate assessment of free-living physical activity is essential for monitoring everyday activity levels, and to determine the effectiveness of interventions aimed at increasing physical activity. We intend to establish the validity of novel physical activity measurement tools by comparing them against equivalent gold-standard measures.

Am I eligible to participate?

You are eligible to participate in this study if you are aged between 18 and 50 years, and have no history of medical illness. You are not eligible to participate if you have: risk factors for physical activity; sustained an injury which impacts your ability to perform walking or running exercise in the previous three months, or a chronic lower limb condition such as tendinitis or arthritis; any other significant limitation which prevents you from completing vigorous exercise. If you volunteer for this study, you will be asked to complete a safety checklist to ensure that you are eligible to participate.

What does the study involve?

This study involves three experimental trials. Two trials will be conducted at the Exercise Metabolism Laboratory at the Tamaki Innovation Campus of The University of Auckland and one trial will be conducted during your normal daily activities. These trials will be scheduled over a period of 4 weeks and involve assessments of physical performance during exercise and daily activities. All assessments are described in detail below.
Physical performance assessments

**Trial 1**

**Maximal graded treadmill running test**

During the first visit to the laboratory you will be asked to complete a graded treadmill running test comprising 1 minute exercise stages at increasing exercise intensities until fatigue. The test will last approximately 8-12 minutes, dependent upon your fitness level. 

**Constant intensity treadmill running test**

After 30 minutes of rest you will be asked to complete a 30 minute treadmill running test at an exercise intensity equivalent to 66% of your maximal capacity, determined during the first test.

**Trial 2**

**Intermediate intensity treadmill running test**

During a second visit to the laboratory you will be asked to complete a 30 minute treadmill running test comprising 2 minute stages at fluctuating exercise intensities equivalent to 50%, 70% and 90% of your maximum capacity. The average intensity of this test will be equivalent to the constant intensity treadmill running test.

**Trial 3**

Following the completion of Trial 2 you will be asked to wear the BioHarness for up to 48 hours during normal daily activities. You will not be required to complete any specific exercise or physical activities during this trial. You will be asked to manually initiate the smartphone and BioHarness devices at the beginning of this trial. Once initiated the devices will detect, record and transmit data without your input, so you will experience minimal disruption to your normal daily activities. Following this monitoring period you will be asked to return the smartphone and BioHarness devices to the Department of Sport & Exercise Science.

You may experience mild discomfort and fatigue during exercise, mild dehydration during and after exercise, and mild soreness for up to 2 days after the exercise tests (Trials 1 & 2). These sensations are similar to those you may have experienced during and after recreational sports or vigorous exercise. To minimise the risk of adverse effects associated with exercise you will complete a safety screening checklist prior to participation.

**Physiological measures**

During experimental trials we will use a number of safe and painless techniques to measure your physiological responses to exercise and daily activities.

During Trials 1 and 2 these measurements will be made using the BioHarness device and equivalent gold-standard reference sensors. The BioHarness is an elasticised strap worn around the chest, against the skin, in a similar manner to a common heart rate monitor. It contains non-invasive sensors to measure the electrical activity of your heart (ECG), breathing rate, skin temperature, body acceleration, and posture. It is worn around the chest, against the skin, You will also be fitted with reference sensors including 12-lead ECG, a respiratory gas analyser, a skin thermistor and an accelerometer.

12-lead ECG is a safe, non-invasive technique which uses small adhesive sensors positioned on the skin over the heart to measure its electrical activity. The skin must first be prepared by shaving any hair and lightly abrading the areas where the sensors will be placed. This may cause mild transient skin irritation which does not require treatment.

In the event that a condition which is assessed to be a clinical abnormality is detected by an ECG, we are obliged to inform you of this and you will be advised to consult your personal practitioner. If you do not wish to be informed of any abnormalities detected, you should not participate in this experiment. Because the ECGs are not routinely reviewed by a cardiologist we are unable to perform diagnostic scans for medical purposes.

Respiratory gas analysis is a safe, non-invasive technique which measures oxygen and carbon dioxide exchange across the lungs. You will be asked to wear a mask over your nose and mouth to collect expired air for analysis. Occasionally people experience mild anxiety when wearing the mask for the first time, however, the mask does not impair your ability to breathe normally and the anxiety usually subsides quickly with familiarisation. If you feel uncomfortable at any time during the experiment, please notify the investigator.
During Trial 3 you will be asked to wear the Bioharness device alone. You are encouraged to remove the device during washing and bathing, and at any other time if it causes embarrassment or physical discomfort. There are no other specific risks associated with the procedures and equipment used in the study.

Accidents and Injury
In the unlikely event of physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act (2002). ACC cover is not automatic and your case will need to be assessed by ACC, according to the provisions of the Injury Prevention Rehabilitation and Compensation Act (2002). If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. For more details, refer http://www.acc.co.nz. If you have any questions about ACC please feel free to ask the researcher for more information before you agree to participate in this study or contact ACC (04) 918 7700.

Participation
Your participation is voluntary and may be withdrawn at any time without reason. At your request we will stop the experiment. You have the right to withdraw your data from the study up to 3 months after completing the trials. If you are a student, any decision to participate, not participate or withdraw from this study will not affect in any way how you will be evaluated in any of your own studies. Trials 1 and 2 will take no longer than 2 hours (~45 minutes of exercise) and 1.5 hours (30 minutes of exercise) of your time, respectively. Trial 3 will last 24-48 hours, and will be completed during your normal daily activities. There will be no form of compensation for your participation in this study. Data obtained from this study will be stored to disk for up to six years, and will be used for publication in scientific journals, presentation at academic conferences and to inform a doctoral thesis. After six years, your data will be deleted from the disk, and your consent form and all related paperwork will be destroyed. No material that could personally identify you will be used in any reports of this study. No audio or video recording will take place during any trials. The information and data collected from you will be stored securely in locked cabinets and on secure computer networks, and only the investigators will have access to this information. Your data will be made anonymous by assigning a unique code to it. You may request a summary of the study results, which we can send you once the project is complete.

Summary of Your Rights
- Your participation is entirely voluntary.
- You may withdraw from the project at any time without providing a reason.
- If you are a student your decision to participate, not participate or withdraw from this study will not affect in any way how you will be evaluated in any of your studies.
- You may have your data withdrawn from the study within three months of your participation.
- You may request results regarding the outcome of the project from the experimenters upon completion of the study.
- Your identity will be kept strictly confidential and no identification of you or your data will be made at any time during data collection or in subsequent publication of the research findings.
- You may experience temporary discomfort during and after each exercise trial. If the procedures cause you concern you may withdraw from the project at any time.
- You are encouraged to consult with your whana/family, hapu or iwi regarding participation in this project.

Who should I contact if I have further questions?
If you have any further questions please contact
Mr Jonathan Rawstorn, phone 373-7599 ext 82241, email jrawstorn@auckland.ac.nz
Dr Nicholas Gant, phone 373-7599 ext 86607, email n.gant@auckland.ac.nz
A Prof. Greg Anson, phone 373-7599 ext 82975, email gason@auckland.ac.nz

For any queries regarding ethical concerns please contact:
The Chair,
University of Auckland Human Participants Ethics Committee
APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE
on 13/12/2011, for a period of 3 years from 13/12/2011 to 19/12/2014. Reference number 2011/7674.
Appendix 4.2 PIS Randomised Controlled Trial

Participant Information Sheet

Title of Project:
REMOTE-CR: Remote Exercise Monitoring Trial for Exercise-based Cardiac Rehabilitation

Researchers:
AFR Ralph Maddison (Principal Investigator) Dr Ian Warren (Co-investigator)
Dr Nicholas Gart (Co-investigator) Dr Joelleyn Benatar (Co-investigator)
HP Ralph Stewart (Co-investigator) Mr Jonathan Rowboth (Doctoral student)
Dr Anna Rolleston (Co-investigator) Mr Brendan Roxburgh (Cardiac rehabilitation
Dr Robyn Whittaker (Co-investigator) exercise practitioner)

You are invited to participate in the above named study. The study aims to compare the effects of a remotely monitored exercise-based cardiac rehabilitation programme on exercise capacity, cardiovascular risk factors and exercise adherence against traditional centre-based programmes. Please take your time to think about the information provided below and feel free to discuss it with your whānau, family or significant other support people before deciding whether to take part. Taking part is completely voluntary (your choice).

What is the study about?
Exercise-based cardiac rehabilitation reduces mortality and improves several cardiovascular risk factors, but uptake and adherence to these programmes are low. Remote exercise monitoring may improve uptake and adherence by overcoming several common participation barriers while still enabling real-time supervision by exercise professionals, similar to that provided in cardiac rehabilitation centres. This approach may enable people who cannot attend traditional cardiac rehabilitation to access the benefits of professionally prescribed and monitored exercise. We intend to compare the effects of remotely delivered exercise-based cardiac rehabilitation with a traditional programme delivered in cardiac rehabilitation centers in Auckland and Tauranga. We aim to show that remotely delivered exercise-based cardiac rehabilitation produces similar benefits compared to the traditional centre-based programme.

Am I eligible to participate?
To be eligible to participate in this study you should be aged over 16 years, have diagnosed coronary heart disease, be eligible for referral to outpatient exercise-based cardiac rehabilitation and be able to safely complete a vigorous fitness test. You are not eligible to participate if you have unstable coronary heart disease, diagnosed heart failure, a surgically implanted pacemaker or automated defibrillator, very high blood pressure, or an injury preventing you from safely exercising. To help confirm your eligibility we will obtain a copy of your most recent hospital discharge summary. We will also ask a cardiologist to review your discharge summary to determine whether it is safe for you to participate in this study.

What does the study involve?
You will be asked to attend 3 assessment sessions and complete a 12 week exercise-based cardiac rehabilitation intervention. Assessments will take place immediately before and after the exercise programme, and 6 months after beginning the exercise programme. Assessments 1 and 2 may last up to 2.5 hours. Assessment 3 may last up to 1.5 hours. Assessments will be held at the Health and Performance Clinics at the Tamaki Campus of The University of Auckland (Auckland participants), and the Cardiac Clinic or Department of Sport and Recreation of the Bay of Plenty Polytechnic (Tauranga participants). You will be asked to wear a non-invasive movement sensor for 7 days prior to each assessment. This will not interrupt your normal activities. Sessions will involve assessment of exercise capacity, cardiovascular risk factors including blood pressure, cholesterol and blood glucose, and questionnaires about your health and physical activity. Assessments are described in further detail below.

Upon completion of the first assessment you will be randomly allocated to one of two groups:
1. Remote: Participants in this group will receive an individualised exercise-based cardiac rehabilitation programme delivered using wireless physiological sensors and smartphones over 12 weeks. The programme consists of individualised exercise prescription, real-time exercise
monitoring, and tools to help you integrate exercise into your lifestyle. Participants can be monitored during exercise in any location with an internet connection (mobile or Wi-Fi).

2. **Centre**: Participants in this group will receive an individualised exercise-based cardiac rehabilitation programme delivered at the University of Auckland Cardiac Rehabilitation Clinic (Tamaki Campus, University of Auckland), Middlemore Hospital or The Cardiac Clinic, Tauranga.

Exercise prescriptions for both groups will follow the same guidelines.

**Assessments**

We will use a number of safe techniques to measure your exercise capacity, cholesterol, blood glucose, blood pressure, body composition and physiological responses to exercise. These measurements are to assess your exercise performance and cardiovascular risk factors, and to ensure your safety during exercise. Measurements will be made using finger prick capillary blood sampling, a blood pressure cuff, an electrocardiogram (ECG), a BioHarness device, and an indirect calorimeter.

You will be asked not to eat or drink anything except water for 12 hours (overnight) before each assessment. This is to make sure your cholesterol and blood glucose can be measured accurately. This may cause you to feel hungry.

**Finger prick capillary blood sampling (assessments 1 and 2)**

Your cholesterol, blood glucose and blood lactate concentration will be measured via finger prick capillary sampling, which involves making a very small puncture in your finger tip and drawing a drop of blood into an analyser. The puncture may cause momentary discomfort, but this will resolve immediately and no treatment is required. As with any needle puncture there is an increased risk of infection. This risk will be minimised by experienced researchers who comply with guidelines for this technique. We will try to use a single puncture to draw all samples; however, it may be necessary to make more than one puncture.

**Blood pressure (assessments 1, 2 and 3)**

Your blood pressure will be measured using a standard inflatable blood pressure cuff, similar to that used by physicians. This technique will be used before, during and after exercise.

**Body composition (assessments 1, 2 and 3)**

You height, weight, waist and hip circumferences will be measured.

**Electrocardiogram (assessments 1 and 2)**

ECG is a safe, non-invasive technique which uses small adhesive sensors positioned on the skin over the heart to measure its electrical activity. Sensor sites must first be prepared by shaving any hair and lightly abrading the skin. This may cause mild transient skin irritation which does not require treatment. This technique will be used before, during and after exercise.

**BioHarness (assessments 1 and 2)**

The BioHarness is a noninvasive device that measures the electrical activity of your heart and your breathing rate. Short range radio (Bluetooth) capability enables these data to be monitored wirelessly during exercise. The BioHarness is an elastomeric strap worn around the chest, against the skin, in a similar manner to a common heart rate monitor. This technique will be used during exercise.

**Indirect calorimetry (assessments 1 and 2)**

Indirect calorimetry is a safe, non-invasive technique that measures oxygen and carbon dioxide exchange across the lungs via a face mask. Occasionally some people experience mild anxiety when wearing the mask for the first time; however, it does not impair your breathing and the anxiety usually subsides quickly with familiarisation. This technique will be used during exercise.

**Exercise capacity tests (assessments 1 and 2)**

You will be asked to complete up to five 3 minute exercise stages separated by 1 minute, in order to measure changes in blood lactate concentration. Stages will range from light to moderate intensity. Blood lactate concentration will be measured between each stage using the technique outlined above. You will also be asked to complete a graded exercise test lasting approximately 10 - 15 minutes, dependent upon your fitness level, in order to determine your exercise capacity. The test will get a little harder each minute until you no longer feel able to continue, although you may stop at any time during exercise if you feel uncomfortable or do not wish to continue for any other reason. Indirect calorimetry will be conducted throughout, and blood lactate concentration will be measured at the end of this test. You may experience temporary discomfort during and after exercise. These sensations are typical of exercise-induced fatigue.
which you may have experienced during and after previous exercise and physical activity. There is an acute
and transient increase in the risk of adverse events during exercise in individuals with diagnosed coronary
heart disease. This risk will be minimised by ensuring you meet strict eligibility criteria prior to undertaking
exercise. We will monitor your physiological responses before, during and after exercise to further lessen the
risk of adverse events. Doctors will be on hand to provide supervision or emergency support if necessary.

In the event an undiagnosed clinical abnormality is detected we will inform you of this, and advise you to
consult your general practitioner. If you do not wish to be informed of any detected abnormalities you should
not participate in this study. Researchers are not trained to clinically interpret abnormalities and will not be
able to perform diagnostic assessments for medical purposes. If you have concerns or questions about your
health please consult your general practitioner.

Questionnaires (assessments 1, 2 and 3)
Questionnaires will ask about your health and physical activity (all assessments). If you are allocated to the
Remote group you will be asked to provide feedback about the programme (assessment 2).

Interventions
Both interventions comprise individualised programmes of exercise based on American College of Sports
Medicine guidelines. There is no financial cost to participate in either intervention.

Remote
The remote intervention comprises real-time exercise monitoring and behavioural support delivered using
wireless physiological sensors, smartphones and the internet. Participants will use an Android smartphone
app to transmit sensor data to a supervising exercise practitioner in real time during exercise. If you are
randomised to this group and do not own an android smartphone you will be loaned one for the duration of
the study. You will also be loaned a BioHarness wireless physiological sensing device, and a mobile
broadband plan will be purchased for you. Real-time exercise monitoring will be provided on Mondays,
Wednesdays and Fridays between 06:00am and 11:00am, in line with the centre-based intervention. During
these times an exercise practitioner will monitor your heart rate, respiratory rate, speed and distance, and
may make recommendations to adjust your exercise behaviour and/or prescription. You may also choose to
exercise or be physically active outside these times, and are encouraged to do so using the smartphone and
BioHarness whenever you exercise. If you choose to exercise outside the prescribed times when real-time
monitoring is available your exercise data will still be logged to your personal profile in the smartphone app,
in order to provide you with individualised feedback about your training. The smartphone app also contains
behavioural support tools to help you to monitor your progress, set goals, and access support.

Centre
The centre-based intervention comprises face-to-face supervised exercise, and will be conducted at the
University of Auckland Cardiac Rehabilitation Clinic (Tamaki Campus, University of Auckland), Middletone
Hospital or The Cardiac Clinic, Tauranga. If you received hospital treatment at Middletone hospital and you
are randomly allocated to the ‘centre’ study group, you may be able to choose whether to complete your
exercise programme at the University of Auckland Cardiac Rehabilitation Clinic or Middletone hospital. You
can choose to attend the clinic at any time during standard operating hours, and can choose how many
times per week you attend the clinic. You may also choose to exercise or be physically active outside of
these times.

Participation
Your participation is voluntary and may be withdrawn at any time during the experiment without reason. You
have the right to withdraw your data up to three months after completing the study. Your decision to
participate, not participate or withdraw your participation will have no effect on the care you receive from your
health care provider(s). You will be given a $10 shopping voucher to reimburse your time for assessments.
Individual information will be kept for six years in a locked cabinet or on a secure computer network at the
University of Auckland, after which time it will be destroyed. The principal investigator (Dr Ralph Maddison)
will control access to this information during the six-year period. If you wish to gain access to your data,
contact the principal investigator and it will be provided to you. Group-level findings from this study may be
presented at scientific conferences, published in peer reviewed scientific journals, and will inform a doctoral
thesis. No material that could personally identify you will be used in any reports or presentations relating to
this study. You can request a summary of the results, which we can send to you once the study is complete.
Compensation
In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Accident Compensation Act 2001. ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the Accident Compensation Act 2001. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors, such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses, and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.

Funding
Funding to support this study has been provided by the Auckland Medical Research Foundation.

Summary of Risks:
Acute and transient increase in the risk of cardiac events during exercise.
Mild momentary discomfort during finger prick blood sampling

Summary of Your Rights
- Your participation is entirely voluntary.
- You may withdraw from the study at any time without providing a reason.
- You may be withdrawn from the study by an investigator at any time for your own safety.
- You may withdraw your data from the study within three months of your participation.
- You may obtain a report about the study outcomes from the researchers following study completion.
- Your identity will be kept strictly confidential and no identification of you or your data will be made at any time during collection of the data or in subsequent publication of the research findings.
- You may experience temporary discomfort during and after exercise. These sensations are typical of exercise-induced fatigue, which you may have experienced during and after previous exercise. If the procedures cause you concern you may withdraw from the study at any time.
- You are encouraged to consult with your whanau/family, hapu or iwi regarding participation in this study.

Who should I contact if I have further questions?
If you have any further questions please contact:

Jonathan Rawston
Department of Sport and Exercise Science, University of Auckland, Tamaki Campus.
Phone: 373 7599 ext 84498
Email: jrawston@auckland.ac.nz

A/Prof Ralph Maddison
National Institute for Health Innovation, University of Auckland, Tamaki Campus.
Phone: 373 7599 ext 54767
Email: r.maddison@nihi.auckland.ac.nz

For any queries regarding ethical concerns please contact:
The Chair, University of Auckland Human Participants Ethics Committee
University of Auckland
Private Bag 92019, Auckland
Tel: 373 7599 ext 87830

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 06/12/2013 for (3) years FROM 06/12/2013 TO 06/12/2016, Reference Number 011021.
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