PROTOCOL VERSION 0.5 DATE: 11.01.13

CONTENTS

1. FULL TITLE OF STUDY

The use of cardiac rehabilitation services to aid the recovery of colorectal cancer patients: A pilot randomised controlled trial (RCT) with embedded feasibility study.

2. SUMMARY OF RESEARCH

Background

Over 2 million people are living with cancer in the UK. This figure is rising by 3% per annum [1] and includes approximately 150,000 people diagnosed with colorectal cancer [2]. Increasing incidence and survival means that there is growing demand for rehabilitation. Around 30% of colorectal cancer patients report on-going physical and psychological impairments [2; 4]. A high proportion are overweight, insufficiently active, and high risk drinkers [5], putting them at risk of poor recovery and risk of recurrence and comorbidities. Yet, the challenge is implementing sustainable and effective rehabilitation as part of routine care.

Aim

The aim of the research is to assess whether using an existing cardiac rehabilitation service an acceptable model of rehabilitation to aid the recovery of cancer patients?

Phase 1: Feasibility study objectives

1. To assess the feasibility of delivering rehabilitation to cancer patients within a cardiac rehabilitation setting.
2. To assess the acceptability of the intervention for patients and clinicians (cancer and cardiac).
3. To assess the acceptability and adequacy of the training and support provided by a cancer-exercise specialist for cardiac physiotherapists running the rehabilitation exercise classes.
4. To assess the feasibility and acceptability of the main trial components (e.g. recruitment procedures, rehabilitation referral procedures and proposed outcomes and process measurement tools) and proposed tools for measuring impacts on outcomes and costs.

Phase 2: Pilot study objectives

5. To determine eligibility, consent, recruitment and retention rates and speed of recruitment.
6. To determine likely contamination across trial arms.
7. To determine completion rates for proposed effect outcomes measurement tools at baseline and follow up.
8. To provide data for sample size calculations for a definitive RCT.
9. To assess intervention fidelity according to study protocol.
10. To assess the extent to which intervention and trial procedures can be integrated into routine clinical practice.
11. To conduct a preliminary economic evaluation of the cancer rehabilitation programme.

Design

This is a two-arm pilot RCT with embedded feasibility study that will be undertaken as a phased programme of work comprising of intervention testing and feasibility work (Phase 1) and a pilot trial with a process evaluation (Phase 2). This design is in line with MRC guidance on the development and evaluation of complex interventions [6] to ensure that both the intervention and trial procedures are optimised and can be incorporated into routine clinical practice [7].

Sample

The sample size in Phase 1 is 12 cancer patients and their nominated family member, 6 cardiac patients and 12 clinicians. In Phase 2 the estimated sample size is 66 colorectal cancer patients.

Research sites

The study will be conducted in three cardiac rehabilitation facilities in NHS Highland, NHS Wales and Forth Valley: i) Highland Heartbeat Centre, Raigmore Hospital, ii) University Hospital of Wales and Maindy Sports Centre, Cardiff, and iii) NHS Hub at the Peak sports and leisure complex, Stirling.

Cancer Patient Eligibility

Adults who have been i) diagnosed with primary colorectal cancer, and ii) are in the recovery period following surgery; and may or may not be receiving adjuvant chemotherapy.

Exclusion criteria

Adults who: i) have advanced disease; or ii) fail clinical/risk assessment for rehabilitation and therefore deemed by clinicians as unsafe to participate in exercise classes; or iii) have a severe cognitive impairment and are therefore unable to give informed consent to participate in the study; or iv) are unable to communicate in English.

Intervention

The intervention is rehabilitation for colorectal cancer patients in a cardiac rehabilitation setting. An 8/12-week (number of weeks depending on site) post-hospital rehabilitation programme will be delivered by a member of the cardiac multi-disciplinary team to a mixed class of cancer/cardiac patients in a cardiac rehabilitation setting with some components specifically tailored for cancer patients and delivered by a cancer nurse. The rehabilitation programme comprises 60/90 minutes of exercise training (aerobic and muscle strengthening) delivered to a mixed class of cancer/cardiac patients by a cardiac physiotherapist who will receive additional training and on-going support from a cancer-exercise specialist. Participants will set individual physical activity goals with advice and support from the physiotherapist. The exercise class will be followed by 30/60 minutes of education (e.g. stress management, diet, drug therapy, smoking cessation, benefits of exercise and relaxation). A member of the cardiac multi-disciplinary team will deliver educational sessions to a mixed class of cancer/cardiac patients (e.g. smoking cessation, relaxation) but with some educational sessions (e.g. cancer therapies) delivered separately to cancer patients by a cancer nurse.

Proposed outcome measures

Primary outcomes: Physical activity - IPAQ and accelerometer [8-12];

Secondary outcomes: Quality of life - EQ-5D [13;14].SF-36 [60].; Fatigue - FACT-F [52; 15; 16]; Anxiety and depression – HADS [17; 18].

Process variables: General self-efficacy [61], physical activity self-efficacy [62] and risk perception [67].

Clinical variables: Clinical factors including surgical intervention, stoma, chemotherapy.

Data collection

PHASE 1: Cardiac rehabilitation physiotherapists will firstly attend a one-day training course by a cancer-exercise specialist and complete an evaluation form about the training. Then in one research site, 12 cancer patients will be screened, recruited, and referred for rehabilitation.. The proposed outcomes will be measured using the instruments we aim to use in a larger scale trial). Patients will then attend a weekly rehabilitation programme in a cardiac rehabilitation setting. Patients will be allocated to the next available rehabilitation class, which means that all 12 cancer patients are unlikely to attend the same classes. A screening and recruitment log will be completed by a researcher to document all patients considered for the study and subsequently included or excluded at each stage of the recruitment process and reasons given. This will include information such as; when the patient was given information about the study, referred to cardiac rehabilitation, attended for clinical/risk assessment, and received an offer to attend rehabilitation classes. A researcher will also complete an intervention log to document the number of exercise classes attended by participants, type and duration of exercises, and which education classes the patient attended. On completion of rehabilitation, semi-structured face-to-face interviews will be conducted with, i) 12 cancer patients and a nominated family member, ii) 6 cancer and 6 cardiac clinicians who were involved in screening, recruitment, referral and/or delivering the intervention, and iii) 6 cardiac patients involved in the mixed cancer/cardiac patient rehabilitation classes, in order to gather responses about the acceptability of the intervention and trial procedures.

PHASE 2: In 3 research sites, cancer patients will be screened, recruited, and complete the primary and secondary outcomes measures at baseline before being randomised to the intervention or control group. Those randomised to the intervention group will be referred for rehabilitation and attend rehabilitation classes in a cardiac rehabilitation setting. Those randomised to the control group will receive 'Staying healthy after bowel cancer' booklet by Bowel Cancer UK, which includes a section on 'staying fit'. A screening and recruitment log will be completed by a researcher to document all patients considered for the study and subsequently included or excluded at each stage of the recruitment process and reasons given. A researcher will also complete an intervention record log to assess intervention fidelity. On completion of rehabilitation all participants will again complete the primary and secondary outcome measures. In addition, semi-structured face-to-face interviews will be conducted with 24 cancer patients (4 from each research site/trial arm combination) to gather responses about acceptability of the intervention and trial procedures.

Cost evaluation

Data will be collected on resource use and costs incurred or saved beyond the actual intervention. These data will inform data collection methods for a larger scale trial and also, in combination with EQ-5D data, initial modelling of the cost per QALY gained by the intervention.

Analysis

All qualitative data will be analysed in order to address Objectives 1 to 4 and 10. From quantitative data we will generate the following: estimates of eligibility, consent, recruitment and retention rates and speed of recruitment (Objective 5); estimates of completion rates of study assessment tools (Objective 7); estimates of contamination between intervention and control groups (Objective 6); estimates of intervention fidelity (Objective 9). Descriptive statistics of the proposed primary and secondary outcomes will also be made to inform a sample size calculation for a large-scale trial and decisions as to whether their inclusion would be informative in a future trial (Objective 8). Finally, comparisons between intervention sites on recruitment, retention and likely health outcomes etc. will be made to inform development of intervention and main trial components for a future large-scale trial.

Timetable

Phase 1: months 1-7		***Phase 2: months 8-21***	
Cancer-exercise training	month 1	Recruitment	months 8-13
Recruitment	months 2-3	Randomisation	months 8-13
Intervention	months 3-5	Intervention	months 9-16
Interviews	months 3-5	Interviews	months 11-19
Analysis and report	months 5-6	Analysis and report	months 18-20
Preparation for Phase 2	month 7	Outputs	months 21

3. BACKROUND AND RATIONALE

3.1 Observation studies

Observational studies have highlighted the benefit of exercise (a core component of rehabilitation) for colorectal cancer survivors. In one study, 832 people with stage iii colon cancer self-reported physical activity approximately 6 months after completion of chemotherapy [19]. Analyses adjusted for known prognostic factors, including body mass index and age, indicated that higher levels of physical activity were associated with superior disease-free, recurrence-free and

overall survival. The 3-year disease-free survival was 75.1% in patients who exercised for fewer than 18- hours metabolic equivalent task (MET) per week (walking briskly for 1 hour is approximately 4.0 METS) as compared with 84.5% in patients who exercised for more than 18 MET-hours weekly [hazard ratio: 0.57; 95% CI: 0.39 to 0.85). In a second study, 573 women diagnosed with stage i-iii colorectal cancer self-reported leisure-time physical activity before diagnosis and 1-4 years post-diagnosis [20]. Adjusted analyses indicated that compared with women who engaged in less than 3 MET-hours per week of physical activity, those engaging in at least 18 MET-hours per week had an adjusted hazard ratio for overall mortality of 0.43 (95% CI, 0.25 to 0.74) [62]. A study of 668 men diagnosed with stage i-iii colorectal cancer also found that increased physical activity was significantly associated with improved colorectal cancer specific mortality and overall mortality [21]. Adjusted analyses indicated that men who engaged in more than 27 MET hours per week of physical activity (which is equivalent to about 1 hour daily brisk walking for 7 days each week or 1 hour daily of jogging for 3.5 days each week) had an adjusted hazard ratio for colorectal cancer-specific mortality of 0.47 (95% CI; 0.24-0.92) compared with men who engaged in 3 or less MET hours per week of physical activity. Caution is required in drawing definitive conclusions from such a limited evidence-base, nevertheless it suggests that maintaining 18 MET-hours per week physical activity may reduce the risk of colorectal cancer specific and overall mortality. Thus, together, these observational studies suggest that interventions to increase physical activity in colorectal cancer survivors may improve disease outcomes. Moreover, it has been suggested that the magnitude of the associations between physical activity and disease outcomes reported in these observational studies compares favourably with the benefit observed with the use of adjuvant chemotherapy, but would likely involve lower toxicity and cost [22].

3.2 Interventions

Five recent systematic reviews indicate that physical activity interventions can address physiologic and psychosocial effects of cancer and associated treatments in adult cancer patients. A systematic review of 82 RCTs to determine the effects of physical activity concluded that interventions have a large effect on upper and lower body strength and a small to moderate effect on aerobic fitness, overall quality of life, fatigue, Insulin Growth Factors (IGF-I), and symptoms and side effects [23]. However, 83% of the studies included in the review focused exclusively on breast cancer patients. Similarly, a review of 34 RCTs indicating that physical activity has positive effects on physiology, body composition, physical functions, psychological outcomes and quality of life [24], a review of 78 RCTs indicating that exercise improves quality of life [25], a review of 15 RCTs indicating that exercise has modest positive effects on depressive symptoms [26], and a review of 44 RCTs indicating that exercise reduces fatigue [27] report from only a couple of studies featuring colorectal cancer patients. While together these reviews demonstrate the benefits of exercise interventions, a note of caution is required because the results of these studies cannot be automatically generalised to colorectal cancer patients because compared with breast cancer patients, which is the most featured group of patients in reviewed studies, they present with more advanced disease, have different treatments and symptoms, tend to be older and include equal numbers of men and women. A recent National Cancer Action Taskforce review of Allied Health Professional rehabilitation interventions found only one study where the primary tumour site was colorectal cancer and recommended more primary research to investigate the effectiveness of clinically important interventions for cancer patients and to develop a robust evidence base [28].

We are aware of two on-going large-scale trials featuring colorectal cancer patients that are yet to report results. The co.21 Colon Health and Life-Long Exercise Change trial will determine the effects of a 3-year structured physical activity intervention on disease-free survival in 962 survivors of stage ii or iii colon cancer [22]. However, the intervention is very intense and includes a mandatory behaviour support programme and supervised physical activity sessions over 3 years. The CanChange trial will determine the effects of 11 telephone-delivered sessions over a 6 month period from a health coach with 350 patients [30]. Nevertheless, a small number of pilot trials suggest that with appropriate support, colorectal cancer patients after treatment can increase physical activity levels with subsequent health-related benefits. Although only indicative findings, studies suggest that supervised exercise has a positive effect on health outcomes. Analysis of semi-structured interviews with 10 colorectal cancer survivors who immediately after treatment participated in a 12 week intervention comprising supervised exercise indicates that exercise was perceived to reduce fatigue, increase energy and confidence to do activities of daily living [31]. A pilot RCT involving 18 patients who had recently completed surgery and chemotherapy for colon cancer and randomised to either a 12-week programme of twice-weekly supervised exercise sessions for 6 weeks followed by 6 weeks home-based exercise and dietary advice or standard treatment indicates that the intervention improved dietary behaviour, fatigue, aerobic exercise tolerance, functional capacity and waist-to-hip ratio compared with standard care controls [32]. Exercise counselling and professional advice also show beneficial results. A RCT involving 46 patients who had completed treatment and randomised to either 3 months of telephone counselling to support physical activity or a contact telephone call suggests that telephone counselling increased levels of physical activity and submaximal aerobic fitness at 3, 6 and 12 months compared to controls [33]. A feasibility study of a personalised diet, exercise and weight management programme indicates that the intervention with 20 over-weight adults led to a weight change of -1.2kg overall [34]. A RCT involving 102 colorectal cancer patients randomised either to an exercise group where they were specifically advised to perform moderate-intensity exercise 3-5 times per week compared to a control group who were requested not to exercise suggests that increased cardiovascular fitness is associated with improvements in quality of life [35].

3.3 Rehabilitation for cancer patients in a cardiac rehabilitation setting

We compared the findings of studies of coronary heart disease and colorectal patients' post-treatment needs to examine if there were grounds for delivering rehabilitation to mixed classes of cardiac and cancer patients. Four qualitative studies of patients' experiences of needs after coronary artery bypass grafting [36-39] and a case note review of needs of 521 patients surgically treated for colorectal cancer [40] and a population-based cohort study including 522 patients with colorectal cancer [41] indicate that cardiac and cancer patients experience similar problems including pain, fatigue, anxiety and depression, worry, appetite loss, sexual problems, sleep disturbance, and work and financial-related difficulties and express a need for information about medication and self management. Thus, the rehabilitation needs of patients with coronary heart disease and patients with colorectal cancer are likely to be similar, suggesting that a common rehabilitation programme may be appropriate. Moreover, cardiac rehabilitation may be particularly relevant for colorectal cancer patients since the estimated prevalence of cardiovascular disease is 59 per cent at 5 months post-diagnosis and 16 per cent develop *de novo* cardiovascular disease within 36 months after treatment [42]. Pointing out the similarities in post-treatment experiences is not to deny that disease-related differences exist. Colorectal cancer patients may experience physical discomfort and bowel function problems and urinary tract infections and need advice about abdominal pain and stoma care [29]. There is a need, however, to meet the long-term survivorship needs of people affected by cancer as well as a need to identify cost-effective and sustainable models of rehabilitation. This is why researching the effectiveness of rehabilitation to mixed classes of cardiac and colorectal cancer patients with some disease-specific components delivered by experts in cardiac and cancer care respectively is justified.

4. EVIDENCE EXPLAINING WHY THIS RESEARCH IS NEEDED NOW

Over 2 million people are living with cancer in the UK, which is rising by 3% per annum [1] and includes approximately 150,000 people diagnosed with colorectal cancer [2]. Increasing incidence and survival means that there is growing demand for rehabilitation. There is a strong case for rehabilitation for colorectal cancer patients. Around 30% of colorectal cancer patients report on-going physical and psychological impairments [3; 4]. A high proportion are overweight, insufficiently active, and high risk drinkers [5], putting them at risk of poor recovery and risk of recurrence and comorbidities. Yet, colorectal cancer survivors report among the lowest physical activity participation rates of any cancer survivor group [43] and have been shown to perform considerably less physical activity after their diagnosis than they did before suggesting potential room for improvement if given appropriate support [44]. Thus, colorectal cancer has been chosen as an exemplar condition on which to focus the proposed work. However, the findings are likely to be transferable to people affected by other cancers. This is because for many cancer survivors, a healthy lifestyle, including being physically active, aimed at recovery and preventing recurrence and other chronic diseases should be a priority.

Recent policy recommends that cancer rehabilitation is specified in Service Level Agreements in commissioning contracts [45] and government cancer strategies recommend rehabilitation [46; 47]. Yet, rehabilitation is not strongly articulated in commissioning and local cancer care pathways often do not often explicitly refer to rehabilitation. Research to examine how the NHS might improve delivery of rehabilitation services to effectively and efficiently aid the recovery of cancer patients will help to address this gap. In developing this proposal particular attention has been paid to addressing a current gap in service provision: the lack of a sustainable and cost-effective cancer rehabilitation service capable of being integrated into the routine follow-up care of people affected by cancer. The proposed work is novel in that is aims to test an existing, evidence-based and theory driven cardiac rehabilitation service for colorectal cancer patients. Should this model of rehabilitation prove to be clinically and cost effective in a definitive RCT, then referral pathways could be easily adapted to ensure that the model is integrated into existing cancer service frameworks. The study is likely to be of particular interest and use to service commissioners and NHS cancer managers.

5. AIMS AND OBJECTIVES

The research question is: Is using an existing cardiac rehabilitation service delivered by a cardiac multi-disciplinary team (e.g. cardiac physiotherapist, cardiac nurse) with support from a cancer-exercise specialist, to mixed classes of cancer/cardiac patients (with some components tailored to meet cancer patients' needs and delivered by a cancer nurse), an acceptable model of rehabilitation to aid the recovery of colorectal cancer patients? Our ultimate aim is to conduct an RCT of the clinical and cost effectiveness of utilising an existing cardiac rehabilitation service versus usual care (no routine NHS rehabilitation provision) to aid the recovery of colorectal cancer patients. Given the uncertainties surrounding such an RCT, we now propose to conduct a pilot RCT with embedded feasibility study to inform the design and conduct of a larger scale trial for which separate funding would be required. In this proposed preliminary study, we seek to undertake a phased programme of work comprising of intervention testing and feasibility work (Phase 1) and a pilot trial with a process evaluation (Phase 2) within the context of planning a definitive large scale RCT. We will also pilot an economic evaluation because interventions have a cost component that needs to be considered when evaluating the effectiveness of the intervention to reduce the burden of a disease. The overall aims of this essential preliminary work are to:

1. Assess the potential of an existing cardiac rehabilitation service taking colorectal cancer patient referrals to improve health outcomes for cancer patients.
2. Refine the intervention and trial procedures for a full scale RCT.

In Phase 1, we seek to answer the following research questions: What modifications, if any, are required to be made to existing cardiac rehabilitation (the intervention) to make it more relevant and acceptable to patients and clinicians? What modifications, if any, are required to be made to the training and support provided by the cancer-exercise specialist to make it more relevant and acceptable to cardiac physiotherapists running the cardiac rehabilitation exercise classes? What modifications, if any, are required to be made to the proposed trial procedures to make the trial more feasible to conduct and to make the trial procedures more acceptable to patients and clinicians? In Phase 2, we seek to answer the following research questions: Are participating centres likely to recruit a sufficient number of patients to deliver a large-scale trial? What is the likely eligibility, consent, recruitment and retention rates and speed of recruitment for a future large scale trial and how can these be optimised? Are recruited patients likely to stay within their allocated groups? What are the likely completion rates at baseline and follow up for the proposed outcome and process measures for a future large-scale trial and how can these be optimised? What sample size is required to power a future large scale trial? Have the interventionists delivered rehabilitation as intended and in accordance with the study protocol and how can intervention fidelity be optimised for a future large scale trial? What are the enablers and barriers that clinicians experience in delivering rehabilitation for patients and in conducting the trial? What are the enablers and barriers that cancer patients experience in participating in the rehabilitation programme?

Phase 1: Feasibility study objectives

1. To assess the feasibility of delivering rehabilitation to cancer patients within a cardiac rehabilitation setting.
2. To assess the acceptability of the intervention for patients and clinicians (cancer and cardiac).
3. To assess the acceptability and adequacy of the training and support provided by a cancer-exercise specialist for cardiac physiotherapists running the rehabilitation exercise classes.
4. To assess the feasibility and acceptability of the main trial components (e.g. recruitment procedures, rehabilitation referral procedures and proposed outcomes and process measurement tools) and proposed tools for measuring impacts on outcomes and costs.

Phase 2: Pilot study objectives

5. To determine eligibility, consent, recruitment and retention rates and speed of recruitment.
6. To determine likely contamination across trial arms.
7. To determine completion rates for proposed outcomes measurement tools at baseline and follow up.
8. To provide data for sample size calculation for a definitive RCT.
9. To test intervention fidelity according to study protocol.
10. To assess the extent to which intervention and trial procedures can be integrated into routine clinical practice.
11. To conduct a preliminary economic evaluation of the cancer rehabilitation programme.

6. RESEARCH PLAN AND METHODS

6.1 Research design

This is a two-arm pilot RCT with embedded feasibility study that will be undertaken as a phased programme of work comprising of intervention testing and feasibility work (Phase 1) and a pilot trial with a process evaluation (Phase 2). In line with MRC guidance on the development and evaluation of complex interventions [6] we have included a preliminary phase, which focuses on intervention refinement and feasibility and a qualitative process evaluation of the pilot RCT in order to ensure that both the intervention and trial procedures are optimised and can be incorporated into routine clinical practice, thus increasing the likelihood that a full-scale trial will generate the desired outcomes [7]. The study will be conducted according to recommendations for good practice in pilot studies [48].

6.2 Sampling

6.2.1 Cancer patient study participants

Adults who have been, i) diagnosed with primary colorectal cancer, and ii) are in the recovery period following surgery and may or may not be receiving adjuvant chemotherapy.

6.2.2 Exclusion criteria

Adults who i) have advanced disease, or ii) fail clinical/risk assessment for rehabilitation and therefore deemed by clinicians as unsafe to participate in exercise classes, (e.g. according to recent guidance patients with severe anaemia should delay exercise and patients with compromised immune function should avoid public gyms and exercise classes [49]), or iii) have a severe cognitive impairment and therefore unable to give informed consent to participate in the study, or iv) are unable to communicate in English (N.B. if this study shows that the intervention and trial procedures are acceptable and feasible then translation service costs will be requested in a future large scale trial).

6.2.3 Sample size

As this is a pilot RCT with embedded feasibility study, a formal power calculation is not appropriate; the study is not powered to detect a clinically meaningful difference in the primary outcome between the rehabilitation and usual care groups. Rather the aim is to provide robust estimates of the likely rates of recruitment and retention, and to yield estimates of the variability of the primary and secondary outcomes to inform power calculations for a future large-scale trial. We will therefore use the pilot trial (Phase 2 of the proposed study) in order to provide a quantitative estimate of the intervention impact (relative to control) in order to inform the sample size estimation for a definitive trial. While we recognise that the number of patients to be included in a pilot study will depend on the parameters to be estimated, a general rule of thumb is to take a minimum of 30 patients to estimate a parameter [37], which we believe is achievable

in this study. For the pilot RCT (Phase 2), we believe that over 6 months across the 3 sites we will be able to approach 250 patients. From their responses we will be able to determine whether it is possible to recruit patients and also estimate eligibility, consent, participation and retention rates and speed of recruitment for a future large scale trial. We have conservatively estimated that we will recruit approximately 66 patients. Cancer clinicians estimate that approximately one third will be ineligible (e.g. have advanced disease) and based on recruitment to a RCT about physical activity with cancer patients in Scotland (27% recruitment rate) [50] and a trial involving colorectal cancer patients within 3 months of completing surgery conducted in Canada (35% recruitment rate) [51] we estimate that about a third of eligible patients will consent. Thus, we estimate that in Cardiff and Stirling 26 patients in each site will be recruited (13 intervention group and 13 control group). In Inverness, we estimate that 14 patients will be recruited (7 intervention group and 7 control group). However, a recruitment rate of 71 per cent, which was achieved in a study of a personalised lifestyle programme for colorectal cancer survivors in Scotland [34], would provide a total of 118 patients.

For the feasibility study (Phase 1) we will recruit 12 colorectal cancer patients from one site to assess the feasibility and acceptability of the intervention, recruitment processes for the trial and study instruments. Six cardiac patients and 6 clinicians will also be recruited to assess the feasibility and acceptability of the intervention and recruitment processes.

6.3 Setting

The study will be conducted in three cardiac rehabilitation facilities in NHS Highland, NHS Wales and Forth Valley: i) Highland Heartbeat Centre, Raigmore Hospital, ii) University Hospital of Wales and Maindy Sports Centre, Cardiff, iii) NHS Hub at the Peak sports and leisure complex, Stirling.

6.4 Intervention and control (usual care)

The intervention is rehabilitation for colorectal cancer patients in a cardiac rehabilitation setting. An 8/12-week (number of weeks depending on research site) post-hospital rehabilitation programme will be delivered by a member of the cardiac multi-disciplinary team (e.g. cardiac physiotherapist, cardiac nurse or dietician) to a mixed class of cancer/cardiac patients in a cardiac rehabilitation setting with some components specifically tailored for cancer patients and delivered by a cancer nurse. Rehabilitation classes will be delivered twice weekly or once a week depending on research site. The rehabilitation programme comprises 60/90 minutes (depending on research site) of exercise training (aerobic and muscle strengthening) delivered to a mixed class of cancer/cardiac patients by a cardiac physiotherapist who will receive additional training and on-going support by a cancer-exercise specialist.

Participants will set individual physical activity goals with advice and support from the physiotherapist. Cardiac physiotherapists will be pragmatically applying underpinning health behaviour theories by for instance, discussing barriers to engaging in physical activity with patients and goal setting, which is in line with current behaviour change theory [68-71] and cardiac rehabilitation guidance [72]. It is now well recognised that advice, education or information does not lead to lasting change in repetitive health behaviours. It is also universally accepted that increasing physical activity leads to a host of major health benefits, but while many individuals have the best of *intentions* to take more exercise, this does not translate into lasting change in *behaviour*. This is well-recognised as the intention-behaviour gap [73] and why action and coping planning is recommended and will be adopted [74].

The exercise class will be followed by 30/60 minutes (depending on research site) of education (e.g. stress management, diet, drug therapy, smoking cessation, benefits of exercise and relaxation). A member of the cardiac multi-disciplinary team will deliver some educational sessions to a mixed class of cancer/cardiac patients because they are relevant to both cancer and cardiac patients (e.g. smoking cessation, relaxation). A colorectal cancer nurse will deliver some educational sessions (e.g. cancer therapies) to cancer patients. These educational sessions will either be delivered to a group of cancer patients (e.g. when cardiac patients receive a session about drug therapy from a member of the cardiac multi-disciplinary team, cancer patients will receive an equivalent session about drug therapy from a cancer nurse) or one-to-one by telephone (depending on research site). To optimise intervention fidelity, interventionists will be expected to follow the cancer patient rehabilitation pathway (Appendix 1) for this study, and also their site-specific rehabilitation programme. Patients randomised to the control arm of the pilot RCT (Phase 2 of the study) will receive 'Staying healthy after bowel cancer' booklet by Bowel Cancer UK, which includes a section on 'staying fit'.

6.5 Proposed measures

A key purpose of the feasibility study (Phase 1) is to assess the acceptability of the proposed outcome measures for a large scale trial. Primary and secondary outcomes will be measured in Phase 1 before participants attend rehabilitation classes. A key purpose of the pilot study (Phase 2) is to determine completion rates of these proposed outcomes measurement tools which will be measured before participants attend rehabilitation classes (baseline) and follow up (immediately at the end of the rehabilitation programme and 3 months later).

6.5.1 Primary outcome: physical activity

The proposed primary outcome in a future large scale trial will be the difference in an objective measure of physical activity levels between the intervention and usual care (control) group. This will be the primary outcome for which data will be collected in the proposed rehearsal pilot trial to inform sample size calculations for a definitive large scale RCT.

The results of the study will allow us to make an informed judgement as to which measures we would use in a full-scale trial and which one should be the primary outcome.

Physical activity will be assessed using the Actigraph GT1M accelerometer (Actigraph LLC, Pensacola, Florida) [8-10]. Participants will be asked to wear an accelerometer for 7 days on 3 occasions (T0 - before patients are randomised to the intervention or control group; T1 - at the end of the intervention (data will be collected 12 weeks after baseline for patients in the control arm); and T2 - 3 months later). Physical activity will also be assessed subjectively using the long (self-report) version of the International Physical Activity Questionnaire (IPAQ) to ascertain the types of activities participants engaged in as this information is not provided by the accelerometers[6; 12].

6.5.2 Secondary outcomes

The proposed secondary outcomes in a future large scale trial will be the difference in measures of quality of life, anxiety and depression, and fatigue between the intervention and usual care (control) group. Data will be collected in the proposed rehearsal feasibility study and pilot trial.

Quality of life: EQ-5D, which is a parsimonious measure of health-related quality of life consisting of five dimensions: mobility, self care, usual activities, pain/discomfort, anxiety/depression, will be used to measure quality of life [13]. A recent review shows a substantial and growing body of literature using the EQ-5D in cancer, and draws the conclusion that it is a valid and reliable instrument [14]. For our pilot work, SF-36 will also be used to measure quality of life [60]. Both EQ-5D and SF-36 are used in health economics as a variable in the quality adjusted life year calculation to determine the cost-effectiveness of an intervention. SF-36 comprises eight dimensions: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health.

Anxiety and depression: The Hospital Anxiety and Depression Scale (HADS), which consists of 14 questions, 7 for anxiety and 7 for depression, will be used to measure anxiety and depression [17]. A meta-analysis suggests that it is sufficiently sensitive for identifying depression and anxiety in patients with cancer [18].

Fatigue: The Functional Assessment of Cancer Therapy Fatigue (FACT-F) [52], which is a 13-item fatigue FACT subscale, will be used to measure cancer-related fatigue. A recent systematic review of the scales used for the measurement of cancer-related fatigue show that there is no accepted definition of cancer-related fatigue and no agreement on how it should be measured [15]. Nevertheless, the review recommends the use of FACT-F. Moreover, an evaluation of a 12 week resistance exercise programme in patients with prostate cancer used FACT- F and found benefits from resistance training on cancer-related fatigue, suggesting the instrument is sensitive [16].

6.5.3 Process variables

Self-efficacy and *risk perception* will be measured to assess if these psychological constructs predict attendance at cardiac rehabilitation classes and changes in health outcomes arising from the intervention.

- General self-efficacy, which is the belief that one can perform difficult tasks or cope with adversity, will be measured using a ten-item scale [61]. Physical exercise self-efficacy, which is the belief that one can engage in, and meet physical activity goals, will also be measured [62].
- According to the behaviour motivation hypothesis [66], perceived risk is positively and directly related to health behaviour. Risk perception of suffering from diseases has been found to play an important role in the development of intentions to perform physical activity among older adults [63] and in explaining cancer-related behaviours [64;65]. Given the lack of agreement about quality of methods of measuring cancer risk perception, we will include absolute (i.e. estimation of personal risk) and comparative measures (i.e. comparison of personal risk to other people's risk). We will also include conditional (i.e. rating the probability that a certain event (e.g. cancer recurrence) will occur given their the adaptive behaviour (e.g. increasing physical activity) is, or is not, performed) and unconditional (i.e. rating the probability that a certain event will occur without specifying the adaptive behaviour) measures [67].

6.5.4 Clinical variables

In addition, clinical confounding factors will be assessed:

- Colon or rectal surgery;
- Surgical intervention (e.g. laparoscopic or open surgery);
- Temporary (a loop ileostomy) or permanent stoma or no stoma;
- Chemotherapy or no chemotherapy.

6.6 Data collection for Feasibility study (Phase 1)

The purpose of the feasibility study is to evaluate and refine the intervention and main components of the trial.
To meet Phase 1 study objectives we will carry out the following: cardiac rehabilitation physiotherapists will firstly attend a one-day training course delivered by a cancer-exercise specialist and complete an evaluation form about the

training. Then in one research site (Stirling), 12 cancer patients will be screened, recruited and referred for rehabilitation. The proposed outcomes and processes will be measured using the instruments we aim to use in a larger scale trial. Patients will be allocated to the next available rehabilitation class, which means that all 12 cancer patients are unlikely to attend the same classes . Patients will then attend a 10 week rehabilitation programme in a cardiac rehabilitation setting. A screening and recruitment log will be completed by a researcher to document all patients considered for the study and subsequently included or excluded at each stage of the recruitment process and reasons given. This will include information such as; when the patient was given information about the study, referred to cardiac rehabilitation, attended for clinical/risk assessment, and received an offer to attend rehabilitation classes. A researcher will also complete an intervention record log to document the number of classes attended by participants, type and duration of exercises, and which education classes the patient attended. On completion of rehabilitation, semi-structured face-to-face interviews will be conducted with, i) 12 cancer patients and a nominated family member, ii) 6 cancer and 6 cardiac clinicians who were involved in screening, recruitment, referral and/or delivering the intervention, and iii) 6 cardiac patients involved in the mixed cancer/cardiac patient rehabilitation classes, in order to gather responses about the acceptability of the intervention and trial procedures. Further description about data collection for Phase 1 is provided below.

6.6.1 Training

Training and on-going support is essential to promoting of intervention fidelity [53]. Cardiac physiotherapists delivering the intervention (i.e. who deliver exercise classes in a cardiac rehabilitation setting to mixed classes of cardiac/cancer patients) will attend a one-day introductory course on cancer and exercise delivered by Dr Anna Campbell, Director of Canrehab (www.canrehab.co.uk). The introductory course gives an overview of cancer types, treatments, medications and side effects. It describes the evidence-based benefits of physical activity in this population group and provides the current guidelines to physical activity and exercise management and prescription during and after treatment for cancer. A session on behaviour changes theories and practices to enhance engagement in behaviour change will also be incorporated as part of the cancer and exercise training. To meet Objective 3, those attending the training will complete an evaluation sheet about the training and will also be asked questions about the training and support in a semi-structured face-to-face interview (see Section 6.6.6).

6.6.2 Screening and recruitment of cancer patients

1. Potential recruits will be identified from existing patients at follow up. All colorectal cancer patients who have completed surgery will be screened by a colorectal cancer Clinical Nurse Specialist at the first follow up appointment following surgery (approximately 6 weeks from date of surgery) to assess if it is safe for them to engage in physical activity from a cancer clinical perspective. The clinician will assess if there are contraindications to exercise due to cancer and late effects of treatment (e.g. patients with severe anaemia or with compromised immune function). At the follow up clinic, the nurse will give eligible patients an information sheet about the study and talk them through it. If the patient agrees to participate the nurse will refer the patient to cardiac rehabilitation by email, fax or letter and advise the patient that the cardiac rehabilitation service will contact them. Patients who decline to participate having read the study information will be asked if they would be willing to complete a questionnaire about reasons for declining to participate.

2. A member of the cardiac multi-disciplinary team (e.g. cardiac physiotherapist or nurse) will contact cancer patients and invite them to attend a cardiac rehabilitation clinical /risk stratification assessment to determine whether the patient will be able to safely exercise from a cardiac clinical perspective and plan physical activity goals tailored to individual patient needs. Patients who are deemed safe to exercise will be invited to attend cardiac rehabilitation classes. Patients who decline to attend a clinical /risk stratification assessment will be asked if they would be willing to complete a questionnaire about reasons for declining to participate.

3. A researcher will contact patients who have agreed to participate and have been assessed and arrange a time for them to formally consent in writing to participate in the study and then if they have consented, have proposed outcomes measured. Consenting will be within five days of the patient being offered a place to attend the cardiac rehabilitation classes. Consenting will be carried out either in the patient's own home or at the cardiac rehabilitation facility. The researcher will confirm eligibility and consent patients to the study. If consent is declined, patients will be asked if they would be willing to complete a questionnaire concerning their reasons for non-participation.

To meet Objective 4, a screening and recruitment log will be completed by a researcher to document all patients considered for the study and subsequently included or excluded at each stage of the recruitment process and reasons given. This will also include information such as; when the patient was given information about the study, referred to cardiac rehabilitation, attended for clinical/risk assessment, received an offer to attend rehabilitation classes.

6.6.3 Intervention

All recruited cancer patients will attend post-hospital rehabilitation in a cardiac rehabilitation setting (see section 6.4 for more detail). To meet Objective 1, a researcher will contact participants each week by telephone and complete an

intervention record log to document for example, type and duration of exercises completed and content of education sessions attended.

6.6.4 Interviews with cancer patients and nominated family member

To meet Objectives 1, 2 and 4, at the end of the intervention, face-to-face semi-structured interviews [54] will be conducted with the cancer patients about the acceptability of the intervention, screening and recruitment processes and study instruments. Patients will also be consulted about what outcomes from rehabilitation are most important to them, which will inform our final choice of outcomes in the pilot trial (Phase 2) as well as in a future more definitive trial of the intervention. Patients will be invited to nominate a family member who will be interviewed separately about the intervention and ways in which they might be involved in a rehabilitation programme in the future. The interviews will last approximately 45 minutes, be audio-recorded and will take place at the hospital or cardiac rehabilitation facility. Only those who give written consent to participate in the study will be interviewed by a researcher. All researchers involved in conducting interviews will be receive guidance and support by applicants (Hubbard and Kidd) who are very experienced in conducting qualitative research and have expertise in conducting interviews with patients with cancer in a sensitive manner using good communication skills (e.g. showing empathy, interpreting body language).

6.6.5 Recruitment and interviews with cardiac patients

All cardiac patients will be informed that the study is taking place at the cardiac rehabilitation facility and that the classes that they attend may include cancer patients. To meet Objectives 1 and 2, at the end of the intervention 6 cardiac patients who attended rehabilitation classes at the same time as cancer patients will be approached by a researcher and invited to attend a semi-structured face-to-face interview [54] about their experiences of having cancer patients participate in rehabilitation. The interview will last approximately 45 minutes, be audio-recorded and will take place at the hospital or cardiac rehabilitation facility. Patients will be purposively sampled so that the study includes responses from younger and older men and women. Only those who give written consent to participate in the study will be interviewed by a researcher.

6.6.6 Recruitment and interviews with clinicians

To meet Objectives 1, 2 and 4, cancer and cardiac clinicians involved in screening and recruitment and/or delivering the intervention will be approached by a researcher and invited to attend a semi-structured face-to-face interview [54] about their experiences of the trial procedures and the intervention. The interview will last approximately 45 minutes, be audio-recorded and will take place at the hospital or cardiac rehabilitation facility. Only those who give written consent to participate in the study will be interviewed.

6.7 Data collection for pilot RCT (Phase 2)

The purpose of the pilot RCT with a process evaluation is to assess whether trial components and procedures work in practice and generate date to inform the sample size calculation for a larger scale trial of the planned intervention. To meet Phase 2 study objectives we will carry out the following: In three sites, cancer patients will be screened, recruited, have proposed outcomes measured (i.e. instruments we aim to use to measure effect in a larger scale trial) and then randomised to the intervention or control group. Those randomised to the intervention group will be referred for rehabilitation and attend rehabilitation classes in a cardiac rehabilitation setting and those randomised to the control group will receive 'Staying healthy after bowel cancer' booklet by Bowel Cancer UK, which includes a section on Staying Fit. A screening and recruitment log will be completed by a researcher to document all patients considered for the study and subsequently included or excluded at each stage of the recruitment process and reasons given. A researcher will also complete an intervention record log to assess intervention fidelity. On completion of rehabilitation, semi-structured face-to-face interviews will be conducted with 24 cancer patients with equal split between research sites and each trial to gather responses about the acceptability and the intervention and trial procedures. Twelve clinicians involved in recruitment and/or delivering the intervention split between the research sites will also be interviewed. Further description about data collection for Phase 2 is provided below.

6.7.2 Screening and recruitment of cancer patients

Screening and recruitment of cancer patients by clinicians for the pilot trial will follow the same procedures as outlined for the feasibility study (Phase 1), which are described in Section 6.6.2 above. However, we may make slight modifications to screening and recruitment procedures based on the findings of the feasibility study and these will be documented. To meet Objectives 5 and 10, a screening and recruitment log will be completed by a researcher to document all patients considered for the study and subsequently included or excluded at each stage of the recruitment process and reasons given. This will also include information such as, when the patient was given information about the study, referred to cardiac rehabilitation, attended for clinical/risk assessment, and received an offer to attend rehabilitation classes.

6.7.3 Randomisation

Patients will be randomised to the intervention or control group after they have consented to participating in the study and after baseline primary and secondary measures have been collected. Randomisation with stratification by centre will be conducted by Tayside Clinical Trials Unit.

6.7.4 Intervention and control

Participants will either receive rehabilitation (intervention group) or a 'Staying healthy after bowel cancer' booklet by Bowel Cancer UK (control group), as described in Section 6.4 above. However, we may make slight modifications to the intervention based on the findings of the feasibility study, which will be documented. To optimise intervention fidelity [53], interventionists will be expected to follow the cancer patient rehabilitation pathway (see Appendix 1) for this study and their site-specific rehabilitation programme. To meet Objectives 6 and 9, a researcher will contact participants randomised to the rehabilitation group each week by telephone in order to complete an intervention record log to document for example, type and duration of exercises completed and content of educational classes attended for participants receiving the intervention. A researcher will also contact participants randomised to the control group to record for example, any advice given about exercising.

6.7.5 Proposed outcome and process measures

Proposed outcome and process measures for a future large scale trial will be administered on three occasions: i) T0 - before patients are randomised to the intervention or control group, ii) T1 - at the end of the intervention (data will be collected 12 weeks after baseline for patients in the control arm) and iii) T2 - 3 months later. Thus, participants will be asked to wear an accelerometer for 7 days on 3 occasions (T0 - before patients are randomised to the intervention or control group; T1 - at the end of the intervention (data will be collected 12 weeks after baseline for patients in the control arm); and T2 - 3 months later). To meet Objective 7, a researcher will log missing data.

6.7.6 Semi-structured interviews

To meet Objective 10, on completion of rehabilitation, semi-structured face-to-face interviews [52] will be conducted with 24 cancer patients with equal split between research sites and each trial arm. Twelve clinicians involved in recruitment and/or delivering the intervention split between the research sites will also be interviewed. The interviews will elicit responses about the intervention and trial procedures. All researchers involved in conducting interviews will be receive guidance and support by applicants (Hubbard and Kidd) who are very experienced in conducting qualitative research and have expertise in conducting interviews with patients with cancer in a sensitive manner using good communication skills (e.g. showing empathy, interpreting body language).

6.7.7 Adverse event reporting

Although this is not a Clinical Trial of an Investigational Medicinal Product, the Investigators will adhere to Tayside Medical Science Centre (TASC) SOP 11, 'Identifying recording and reporting adverse events for clinical trials of investigational medicinal products' with expedited reporting to the Sponsor as required. This will be overseen by Tayside Clinical Trials Unit.

In particular the following Serious Adverse Event (SAE) will be reported within 24 hours of the PI or person delegated responsibility for recording SAEs becoming aware of them:

(SAE): any adverse event occurring that results in any of the following outcomes:

- Death;
- In-patient hospitalization or prolongation of existing hospitalization;
- Persistent or significant disability/incapacity;

The following protocol exclusions will apply: -

- Hospitalisation for assault or accidental injury
- Hospitalisation for pre-planned surgery

The above protocol exclusions will be recorded in the Adverse Event (AE) log for the trial and line listings will be reported annually to ethics and the Sponsor.

Note: Medical and scientific judgment should be exercised in deciding whether expedited reporting is also appropriate in situations other than those listed above. For example, important medical events may not be immediately life threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the outcomes listed in the definition above. Any adverse event is considered a serious adverse event if it is associated with clinical signs or symptoms judged by the investigator to have a significant clinical impact.

It is also worth noting that each hospital and hence cardiac rehabilitation programme will have a reporting system for adverse events (e.g. Datix) and cardiac rehabilitation programme operate incident reporting.

6.8 Analysis

All qualitative data will be analysed in order to address Objectives 1 to 4 and 10. Audio-recorded interviews will be transcribed verbatim. Transcripts will be analysed thematically using the Framework approach [55], which is a rigorous method that provides a structure within which qualitative data are organised and themes within and between groups of participants (e.g. between patients and clinicians) identified. Inter-rater reliability will be performed between the

researchers conducting analysis. From quantitative data we will generate the following: estimates of eligibility, consent, recruitment and retention rates and speed of recruitment (Objective 5); estimates of completion rates of study assessment tools (Objective 7); estimates of contamination between intervention and control groups (Objective 6); estimates of intervention fidelity (Objective 9). Descriptive presentations of the proposed primary and secondary outcomes will also be made to inform a sample size calculation for a large scale trial and decisions as to whether their inclusion would be informative in a future trial (Objective 8). Finally, comparisons between intervention sites on recruitment, retention and likely health outcomes etc. will be made to inform development of intervention and main trial components for a future large-scale trial.

6.9 Economic evaluation (Obj. 4 and 11)

Following previous research on the economics of cardiac rehabilitation [56], the economic evaluation will involve three main components: assessment of costs of the rehabilitation programme itself; estimation of further impacts on health care use; and bringing these two elements of cost together with data on outcomes described above.

6.9.1 Rehabilitation programme costs

Costs attributed to the rehabilitation programme for cancer will be borne by the NHS and by patients. NHS programme costs will be estimated on a per patient basis as the sum of costs of space rental, equipment (amortised over usual estimates of life cycles for such items), staff costs (using NHS wage rates in programme sites) and other programme consumable items (such as rehabilitation literature, again to be estimated from cost data at local programme sites). At local programme sites, we will interrogate financial records as well as interview finance and care staff, in order to assess actual impacts of providing the programme on the costs listed above – space and equipment provision, staff costs and any consumable items used. These data will also provide a basis for making further assumptions about cost impacts in other geographical locations.

Information to be obtained on patient-borne costs will be obtained by embedding questions in the data collection instrument to be administered with patients at the end of the programme about: (i.e. in a one-off schedule devised for their last interview). This will cover: distances travelled; transportation types; shoes, clothing and other equipment purchased to participate; child care expenses; and total time attending the programme. Where relevant, we will also ask patients to estimate actual monetary costs incurred by them for using or purchasing these items, but otherwise will impute data on prices of such items where respondents cannot recollect monetary amounts.

Finally, the programme involves building on a pre-existing cardiac rehabilitation programme, it will be important to assess impacts on the above NHS costs 'at the margin'; that is, in terms of what are the additional impacts on space, equipment, staff and consumables as a result of making use of a pre-existing programme. Again, this can be done by observing such impacts on the costs of such services at the local participating sites.

6.9.2 Further impacts on health care use

At each assessment with patients in both rehabilitation and usual care groups, we will ask them to report on: general practitioner visits; hospital emergency department visits and hospital admissions; visits to allied health departments such as physiotherapy and occupational therapy, nutrition, social work and vocational rehabilitation. Patients will also be asked to report on any medications used. A schedule of relevant items will be constructed about which we will ask questions on frequency of use in the previous three months (to match times of regular follow-up proposed in the main trial. Data on hospital visits and drug use will also be available through NHS records. The above items will be costed at NHS pay and prices or, where appropriate, using other (e.g. market-based) sources. Data on rehabilitation programme costs and those on further impacts will be aggregated and the statistical significance of differences in cost per patient between intervention and control group assessed by appropriate methods depending on the distributional characteristics of the data.

6.9.3 Bringing costs and outcomes together

The type and extent of economic evaluation will crucially depend upon the clinical outcome of the trial [57]:
1. If the rehabilitation outcome is at least the same as usual care, the preferred option will be that which is less costly (which will then depend on whether any reduced further health care use in the rehabilitation group offsets the costs of the programme);
2. If rehabilitation is more effective and more costly, the incremental extra cost per quality adjusted life year (QALY) gained will be estimated to aid a decision about whether the additional effectiveness gained from rehabilitation is worthwhile.

Estimation of QALYs is made possible by collection of EQ-5D and SF-36 data within the trial. The EQ-5D is a generic, preference-based measure of quality of life in which 'health' is defined in terms of five broad dimensions. In the UK, patients' assessments of their health states in the EQ-5D classification can be allocated scores derived from a survey of values by members of the general public (where 0=death and 1=full health) [58]. SF-36 has eight dimensions and is similarly scored to the EQ-5D to estimate QALYs. As this is a pilot, the above analysis will be conducted within-trial,

although we will also assess the feasibility on longer-term (lifetime horizon) modelling based on the literature on potential reduced-mortality benefits from such programmes.

7. DISSEMINATION AND PROJECTED OUTPUTS

7.1 Dissemination

The main academic outputs from our research will comprise papers in peer review journals (e.g. study design published in Trials and results published in Supportive Care in Cancer) and oral presentations at national (e.g. National Cancer Research Institute Annual Conference) and international (e.g. World Cancer Congress) conferences. To ensure that the findings from our research impact on the management of health services, knowledge mobilisation will be promoted by the production of short and concise briefings about the research and disseminated to individuals responsible for national cancer strategies (e.g. Cancer Tsar for England and Chair of the Scottish Cancer Task Force). In addition, applicants' networks (involving a range of lay, expert and voluntary sector) will be used to promote knowledge mobilisation so that the findings improve service delivery in the NHS and voluntary sector. Applicants currently hold key positions in local, national and international cancer management, policy and research organisations. Sandra Campbell, Lane and Taylor are nurse consultants in NHs Boards and clinical leads for cancer rehabilitation; Anna Campbell is physical activity consultant for Macmillan Cancer Support; Hubbard chairs the lifestyle and behaviour change subgroup of the Psychosocial Oncology National Cancer Research Institute Clinical Studies Group and is a member of EUROCHIP (a European initiative to set quality indicators for cancer rehabilitation); Adams is a member of the colorectal cancer National Cancer Research Institute Clinical Studies Group. Results of the study will also be reported to the Funder and will be available on their web site. A lay summary for patient study participants and a summary for health professionals will also be produced. To complement this activity, we will aim to publicise the study and its findings through University and study web pages, NIHR HS&DR website and appropriate forms of social media such as twitter.

7.2 Outputs

The production of a manual for the rehabilitation intervention will enable us to provide specific guidance on the training and infrastructure that would be needed and the nature of the intervention for a large scale trial. A report of the findings on acceptability and feasibility of the intervention and trial procedures will inform the design of a future large scale trial. An output of the current application will be a subsequent application for an NIHR programme grant, the aim of which will be to develop and evaluate a cost effective and sustainable model of rehabilitation for people affected by cancer. We expect the impact of this research on current practices within the health services community to be high for the following reasons. The demand for cancer rehabilitation is rising due to increasing incidence and survival. This is coupled with growing recognition for the need of rehabilitation to either deal with the late effects of treatment or the physical effects of the disease. Yet, rehabilitation is not strongly articulated in commissioning and this is partly due to lack of knowledge and evidence of what is an acceptable, effective and efficient rehabilitation model for cancer patients. The main attraction of this study is that it is testing the use of an existing and well-established rehabilitation service (i.e. cardiac rehabilitation) for use with another group of patients (i.e. cancer patients). Thus, if implemented it will not require setting up a whole new service for cancer patients. Rather, referral pathways could be easily adapted to ensure that the model is integrated into existing cancer service frameworks with additional resource to accommodate additional patients.

8. PLAN OF INVESTIGATIONS AND TIMETABLE

Key stages, milestones and outputs	-	-	-	-	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
NHS Ethics and R&D approvals (i.e. before study starts)																									
Prepare all study materials (e.g. information sheets forms and logs)																									
Appointment of Research Fellows																									
1st Steering group meeting																									
PHASE 1																									
Cancer-exercise training for cardiac physiotherapists & evaluation forms completed																									
Cancer clinicians, recruit and refer 12 cancer patients for rehabilitation																									
Researcher completes screening and recruitment logs																									
Researcher administers questionnaires and accelerometer																									
Patients attend rehabilitation (intervention)																									
Researcher telephones cancer patients and completes intervention logs																									
Researchers conducts interviews with 12 cancer patients																									
Researcher recruits 6 cardiac patients and conduct interviews																									
Researcher recruits 6 clinicians and conduct interviews																									
Researcher and Tayside CTU conducts analysis and prepares report																									
2nd steering group meeting																									
Investigators use Phase 1 report to prepare for Phase 2																									
PHASE 2																									
Cancer clinicians recruit, and refer cancer patients for rehabilitation																									
Researcher completes screening and recruitment logs																									
Researcher administers questionnaires and accelerometer (baseline – T0)																									
Tayside CTU randomises participants to intervention or control groups																									
Patients attend rehabilitation (intervention)																									
Researcher telephones cancer patients and completes intervention logs																									
Researcher administers questionnaires and accelerometer (follow up T1)																									
Researcher administers questionnaires and accelerometer (follow up T2)																									
Researcher conducts 24 interviews with patients & 12 with clinicians																									
Researcher and Tayside CTU conducts analysis and prepares report																									
3rd steering group meeting																									
Investigators produce i) manual for the rehabilitation intervention, ii) submit final report, iii) plan for developing larger trial and dissemination																									

9. PROJECT MANAGEMENT

The responsibility for obtaining NHS ethical and local R&D management approval will lie with the Chief Investigator. The Chief Investigator will be responsible for overseeing the progress of the study. The day-to-day management of the feasibility study (Phase 1) will be co-ordinated by the Chief Investigator and the day-to-day management of the pilot RCT (Phase 2) will be co-ordinated by the Trial Manager located at the Tayside Clinical Trials Unit. Responsibility for day-to-day line management of appointed researchers will be the Chief Investigator during Phase 1 and the Tayside Clinical Trials Unit Trials Manager for Phase 2. Tayside Clinical Trials Unit will be responsible for maintaining and archival of study documentation. The Chief Investigator and Trial Manager will take responsibility for ensuring that the study abides by the policies of the Research Governance Framework for Health and Community Care (Scotland), the Data Protection Act and any other relevant legislation and regulatory guidance. All co-Investigators will assist the Chief Investigator and carry out designated tasks in accordance with the study protocol. A study steering group will be responsible for advising the Chief Investigator and Trial Manager about the study. It will meet on three occasions: at the commencement of the study, at the end of Phase 1and at the end of Phase 2 to provide advice and guidance. This group includes the Chief and co-Investigators, a representative from colorectal cancer and cardiac rehabilitation clinical teams and two patient representatives and Operations Manager (Scotland) from Bowel Cancer UK. Site specific local Investigators are co-investigators (Adams, Campbell and Lane) and will be responsible for ensuring that all trial-related clinical decisions (e.g. screening for contraindications to exercise) are made and that the recruitment strategy is implemented and the research conducted in their site complies with local NHS ethics and research governance.

10. APPROVAL BY ETHICS COMMITTEE

10.1 Ethics and R&D approvals and guidance

NHS ethical approval and local R&D management approvals will be obtained before the study starts and this has been made clear in the project timetable.

10.2 Risks to participants

This is a low risk study and major risks and safety issues are not anticipated. No invasive procedures are being used in this study. The intervention includes an exercise component during the period of recovery following surgery. Moderate physical activity is recommended for colorectal cancer patients during treatment and has no contraindications for most [49]. The American College of Sports Medicine recommend that cancer patients avoid inactivity and return to normal activity as soon as possible after diagnosis and treatment and should engage in at least 150 minutes per week of moderate intensity or 75 minutes per week of vigorous intensity aerobic physical activity, or an equivalent combination of moderate and vigorous intensity aerobic physical activity [59]. Evidence suggests that it is not only feasible to exercise during the period of recovery post-surgery but that it can improve cardiovascular fitness, muscle strength, body composition, fatigue, anxiety, depression, self-esteem, and quality of life [49]. Nevertheless, effects of treatment may increase the risk of exercise-related injuries and adverse effects and so during the screening process for study participation those patients who are contraindicated for moderate intensity physical activity or who have an injury or illness which might be aggravated by exercise, will be excluded from the study:

1. The patient's cancer clinical team at a post-treatment follow up appointment will assess if there are contraindications to exercise due to cancer and late effects of treatment (e.g. patients with severe anaemia or with compromised immune function).
2. A cardiac rehabilitation clinician (e.g. cardiac nurse/cardiac physiotherapist) will conduct a clinical/risk stratification assessment to determine whether a patient can safely exercise from a cardiac clinical perspective.
3. During rehabilitation the cardiac physiotherapist running the exercise class will monitor patients for adverse events (e.g. chest pain, extreme breathlessness) and will decide whether it is safe for the patient to continue participation. An adverse events log will be kept for the duration of the study.
4. Patients will be advised and encouraged to contact their colorectal cancer Clinical Nurse Specialist if they have any questions or concerns about their health during the trial.

10.3 Consent and withdrawal

All participants will give written consent to participate in the study. Informed consent discussions will be face-to-face by appropriate staff (as previously described) with the opportunity for participants to ask any questions. Patients will be informed that they have no obligation to participate and their care will not be affected if they decline to participate. They will be made aware that the results of the study will not directly give rise to changes in rehabilitation provision; rather it will determine whether RCTs which would give rise to change in rehabilitation will be feasible. If consent to participate in the study is declined or terminated at any stage, then the patient will enter normal post treatment follow up care. Those wishing to take part will provide written informed consent by signing and dating the study consent form, which will be witnessed and dated by a member

of the research team and retained in the Investigator Site file, with a copy in the clinical notes. Participants have the right to withdraw from the study at any time for any reason, and without giving a reason. The investigator also has the right to withdraw patients from the study intervention if it is considered in the patient's best interests. There are two withdrawal options:
1. Complete withdrawal from both the study intervention (i.e. rehabilitation classes) and provision of data.
2. Partial withdrawal where the patient withdraws from participating in rehabilitation but will continue to provide data.

Consent will be sought from participants choosing option 1 to retain data collected up to the point of withdrawal. Participants will also be asked if they would be willing to give their reasons for the decision to withdraw to be recorded, which will help improve acceptability of the study in a larger scale trial. We also propose to gather data from colorectal cancer patients (through a short questionnaire) who decline to participate in the study, to explore their reasons for not giving consent and thereby helping up to make the study more acceptable to patients in a large scale trial. We will also include questions on motivation to change (risk perception) and self-efficacy so that we can assess whether there is an association between these psychological constructs and refusal to participate in the study. We recognise that non-participants do not have to provide a reason for their decision not to participate of they do not want to, however, we do propose to administer a short questionnaire to those who agree to this level of involvement in order to improve the research design of a future large scale trial.

10.4 Confidentiality and anonymity

All participants will be informed that all of the information that they provide to the research team will remain confidential and will only be accessible to members of that team. We will use the NHS Information Services Divisions Caldicott guidelines. A range of procedures will be put in place to minimise the risk of breaching confidentiality and include:

1. Only personal information that is deemed vital for running this study will be obtained and will only be used where strictly necessary. Participants will be given a unique study identifier so that their names will be filtered out of any data-sets used for analysis. The Chief Investigator will be custodian of a document that links unique study identifiers with names, which will be kept on a password-protected folder on the University of Stirling hard drive.
2. Person-identifiable data will be held by the University of Stirling (study Sponsor) with access restricted to relevant personnel only (e.g. Tayside Clinical Trials Unit).
3. The Chief Investigator will ensure that everyone with access to person-identifiable data is aware of their responsibilities and that the study complies with the law. The right to anonymity when reporting findings and the choice to withdraw from the study at any time will be emphasised to participants.
4. Collecting the minimal necessary personal information; not storing any person-identifiable data on removable media (laptops, USB flash drives, etc.); password protection of electronic files; storage of all person identifiable data at the University of Stirling on password-protected hard drives.

10.5 Data management and archival

Data management will operate in accordance with the Data Protection Act (1998). Data will be stored on a GCP-compliant data management system provided and managed by Tayside Clinical Trials Unit. Personal and primary data will be stored for 10 years according to University of Stirling regulations and afterwards destroyed.

10.6 Complaints

Participants who have concerns about the conduct of the study of wish to make a complaint will be encouraged to report these to the research Sponsor.

11. PATIENTS AND PUBLIC INVOLVEMENT

The benefits to research of the active involvement of patients and the public are well-established (see for example, an article by applicants: Hubbard, G, Kidd, L, et al. (2007), A review about involving people affected by cancer in research, policy and planning and practice, *Patient Education and Counseling*, 65, 21-33). The Chief Investigator (Hubbard) has a track record of involving patients in research and will provide support and training so that the patient advisors are confident and competent to engage in the study at this level. Patients with colorectal cancer have been and will continue to be involved in various stages of this proposed study as follows: i) members of the Cancer Patient and Carer Advisory Group of the Cancer Care Research Centre, University of Stirling identified rehabilitation, including physical activity as a research priority, which influenced the development of this proposed study, ii) the Chief Investigator (Hubbard) discussed this specific research study with Bowel Cancer UK (Scotland) Operations Manager (Emma Anderson) and members of Bowel Cancer UK (Scotland) Patient and Carer Advisory Group who each commented on drafts of the outline and full proposal, iii) in addition, co-applicants (Leslie and Thow) discussed the proposed study with patients attending cardiac rehabilitation and found that these patients were supportive of the proposed study, iv) Bowel

Cancer UK (Scotland) Operations Manager (Emma Anderson) and two members of Bowel Cancer UK (Scotland) Patient and Carer Advisory Group (Margaret Johnston and Gillian Sweetman) have agreed to contribute to the management of the research through membership of the study steering group. They will also play a key role in designing study information packs for patients recruited to the study and be involved in disseminating the research findings (e.g. presenting the research to clinical teams in NHS Boards). Thus, the minimal level of participation of the user representatives in the research project is as follows:

1. Attending all steering group meetings. In particular, they will be asked to consider the implications of any matters arising from the perspective of the patient and their families.
2. Providing feedback on all patient materials for the study. In particular, they will be asked to assess information from the perspective of the patient.
3. Commenting on findings of the study and implications for conducting a larger more definitive trial.
4. Co-facilitating dissemination of research findings by co-presenting the findings with a member of the research team.

User representatives however, will be encouraged to engage in the study to a much greater extent (e.g. co-facilitating interviews with patients) and will be supported in doing so by the CI. Thus, we hope that the user representatives through their involvement in this study will gain in skills and confidence so that they are co-applicants in any future trial of the intervention and extend their level of participation. We believe that this way of progressing PPI in research avoids tokenism and fosters genuine engagement that is empowering for user representatives.

12. EXPERTISE AND JUSTIFICATION OF SUPPORT REQUIRED

12.1 Investigators' expertise

Members of the research team have excellent university research facilities to support this project. The study will be added to the research portfolios of National Cancer Research Institute Clinical Studies Groups, thus facilitating knowledge mobilisation about the study. Hubbard (primary care, psychosocial oncology) and Adams (colorectal) are members of NCRI CSGs. The research team has proven capability for conducting robust, high quality research. It is multi-disciplinary, including researchers with relevant subject expertise (e.g. social psychology, health economics) and research method expertise (e.g. qualitative, quantitative, RCTs). It includes research clinicians as co-investigators (e.g. nurse, consultant surgeon), which will help to ensure that the clinical environment and infrastructure is in place to run the study and that the findings from the research impact on the management of health services. In addition, the study has relevant named clinical collaborators in each of the research sites.

The study will be run from a dedicated Cancer Care Research Centre based at the University of Stirling and led by **DR HUBBARD**, who is an experienced research project manager in cancer care and rehabilitation. She will be responsible for all aspects of the study, making sure that the team work collectively to achieve all milestones. She has a programme of research on cancer rehabilitation and is experienced in running feasibility and pilot studies in this substantive area. She currently has the following projects relevant to this proposed study: 1) Cancer as a catalyst for change? Extent and predictors of health behavioural change following colorectal diagnosis of patients and their families, funded by CSO; 2) Vocational rehabilitation services for patients with cancer: design of a feasibility study incorporating a pilot randomized controlled trial among women with breast cancer following surgery funded by Macmillan; 3) Family-based intervention to improve physical activity in colorectal cancer survivors and their partners, University of Stirling funding for a PhD student.

PROF HAW has expertise in public health, research methods and the evaluation of complex interventions. She will provide methodological advice and support the Lead Applicant in the conduct of the study. She has considerable experience of the coordination of large studies and is currently a grant holder on two NIHR grants – one as Principal Investigator on a national evaluation of a policy intervention; and the second as Co-investigator on a Cluster Randomised Controlled Trial of a psych-social intervention.

DR ANNA CAMPBELL is an expert in clinical exercise training and has developed an NVQ 4 qualification in exercise-based cancer rehabilitation and will provide training for the cardiac physiotherapists before they include cancer patients in rehabilitation. She is the physical activity consultant for Macmillan Cancer Support and has recently published the expert statement on exercise and cancer in the British Association of Sports and Exercise Science. She will also advise on data collection and analysis of physical activity outcome measures.

PROF MUTRIE is also a physical activity expert, leading one of the few studies investigating the long-term impact of a physical activity intervention in cancer survivors. She will advise on data collection and analysis of physical activity outcome measures.

PROF RONAN O'CARROLL, is a behavioural scientist and will advise on data collection and analysis of motivation to change behaviour and self-efficacy.

DR KIDD is an expert in self-care in cancer and qualitative research and will advise on collection of interview data and the analysis of qualitative data. She is currently Chief Investigator on a nurse-led self-care intervention for stroke patients funded by Burdett.

PROF DONALDSON is an NIHR Senior Investigator and leader in the development and application of (health) economic evaluation methods and will lead on conducting the economic evaluation.. He has been a Chief Investigator and Co-Investigator on several competitive research grants and is currently CI on two MRC-funded projects; Prevention IMPACT: developing and evaluating economic models for planning optimal cardiovascular prevention strategies and 'Is end-of-life care more valuable? Measuring societal views on health care resource allocation using the new Q2S method'.

A statistician for the study is **DR GODWIN** who will provide methodological support and verification with an emphasis on the quantitative components of the project. Godwin has provided statistical support and guidance for numerous health research projects.

PROF TREWEEK is an experienced health services researcher with expertise in trial design, the development of complex interventions and trial recruitment. He is Assistant Director of Tayside Clinical Trials Unit (TCTU), sits on the Tayside Clinical Trials Unit Management Board and is Chair of the Tayside Medical Science Centre's Data Management & Biostatistics Committee. He will be responsible for TCTU's contribution to the project. TCTU will develop a GCP-compliant data management collection system, coordinate data entry and oversee data quality assurance and data entry. It will provide a statistician to work with Dr Godwin.

A major benefit is that the study is the involvement of clinical researchers as co-investigators.

DR THOW is an Allied Health Professional, an expert in cardiac rehabilitation and physiotherapy and currently teaches cardiac physiotherapy students. **PROF LESLIE** is consultant cardiologist at Raigmore hospital, Inverness. Thow and Leslie will advise on recruitment of cardiac patients and on the implications of the study for cardiac rehabilitation service frameworks.

MS LANE, TAYLOR AND CAMPBELL are cancer nurse consultants and lead strategic development of cancer rehabilitation in their NHS Boards and will facilitate dissemination and knowledge mobilisation to ensure that the findings from our research impact on the management of cancer services. **DR ADAMS** is a Senior Lecturer and consultant in lower gastrointestinal oncology, with extensive experience in phase II and III colorectal clinical trials. He is a member of the NCRI colorectal CSG. **PROF WATSON** is consultant in colorectal and general surgery at Raigmore hospital, Inverness. He is Chief Investigator of eTHoS, an HTA sponsored UK wide RCT and co-applicant of HUBBLE a further HTA funded UK wide surgical RCT. Together, these research clinicians will be responsible for ensuring that all trial-related clinical decisions (e.g. screening for contraindications to exercise) are made and that the recruitment strategy is implemented. They will also be responsible for ensuring that adequate clinical care is provided in the event of an adverse event.

12.2 Justification of costs

Total grant requested £280,101. Total NHS cost is £17,283.

12.2.1 Research staff costs

- We are requesting 12.5% fte (£15,108) for the Chief Investigator (Hubbard) to ensure all milestones are met, maintain communication between all co-investigators and collaborators and co-ordinate the study.
- Tayside Clinical Trials Unit (TCTU) staff costs include data manager (Gr7.36, £7,174), statistician (Gr7.36, £19,168), Trial manager (Gr7.36, £27,307), Network support manager (Gr8.40, £2,403), software developer (Gr6.29, £8,718), senior statistician (Prof. grade £5,207) and co-investigator Treweek (132 hours, £6,390).
- We will appoint one 0.5 fte Research Assistant (RA) (Grade 6.26) for 21 months (£29,568) to consent participants, collect data and contribute to data analysis in Phases 1 and 2. We will also appoint two RAs for months 8-21 (£19,830 Stirling and £19,337 Cardiff) to consent participants, collect data and contribute to analysis during Phase 2.

- We will appoint a Research Assistant (Grade 6.26) for 30 days to assist Prof Donaldson in conducting the economic evaluation (£6,322).
- Co-investigators Haw (£1008), Donaldson (£1868), Godwin (£788), Kidd (£660), Thow (£660), Adams (£1296) and Mutrie (£1355) will provide 18.75 hrs each to contribute towards analysis and writing the report (N.B. their attendance at steering group meetings are not costed to the project). Anna Campbell is costed for 6 days to provide training and support (£1556). O'Carroll is costed for 40 hours commitment over the course of the project (£2,563).
- NHS co-investigators to provide advice and support for 18.75 hours each (Leslie @£66hr £1238; Watson @ £66hr £1238; Lane, Taylor and S Campbell @£35hr £1969)

12.2.2 Non-staff research costs

We are requesting non-staff research costs: i) 70 accelerometers and belts (£18,760); ii) Travel: 66 interviews (£10 per participant) = £660; iii) Transcription for 66 interviews (£70 per tape) = £4,620; iv) Travel and subsistence for Advisory Group meetings = £4000; v) printing of information sheets, etc. = £1000; vi) 3 audio recorders at £70 each RA in each research site to audio-record interviews (£210); vii) 3 laptop computers at £800 for each RA in each research site to email and complete all paperwork will conducting fieldwork (£2400); viii) TCTU non-staff costs include committee travel (£1000), equipment (£800), randomisation (£1000), archiving £1000); ix) Conference fees and subsistence for NCRI annual conference and World Cancer Congress to disseminate findings (£3500); x) Costs for three members of the team to attend NIHR 'welcome meeting'. Flights from Edinburgh to Southampton are approximately £140 return. Assuming an overnight stay (£100), travel costs to and from airports (£60) and subsistence (£20), we are requesting £1000; xi)The two patient advisors will provide 18 hrs each to contribute towards designing the information for study participants, assisting in interpreting research findings and dissemination. These are costed at Grade 6.26 (£720); xii) One patient from Cardiff has been costed for 6 days to cover costs involved with patient involvement in the project (£600); xiii) 3 cancer CNSs to screen patients to determine eligibility to participate. (total 24 hours @ £25.08, £1806).

12.2.3 Intervention costs

(NHS treatment costs (£17,283))

Backfill for attending 1 day training for 3 cardiac physiotherapists in cancer-exercise is requested (£21.29 x 7 = £447.09). To deliver the intervention we are requesting the following costs for Phase 1 in 1 research site:

- During months 2-3, Band 6 cardiac physiotherapist (hourly rate £21.29) costs for accepting 12 cancer patient referrals into cardiac rehabilitation programme which includes a) sending acknowledgement to referrer, b) recording this acknowledgement, c) recording date of successful contact with patient, d) allowing 3 x attempts for this, e) referring back to CNS on completion, f) recording referral back to CNS. This is calculated at 30 minutes per patient (£127.74).
- Costs for additional clinical /risk stratification assessment of 12 cancer patients to determine whether the patient will be able to safely exercise from a cardiac clinical perspective and plan physical activity goals tailored to individual patient needs during months 2-3 (1 hour per patient of Band 6 physiotherapist = 12 x £21.29 = £255.48).
- Band 6 physiotherapist and Band 2 physiotherapist assistant (hourly rate £10.53) providing additional 2 hour rehabilitation class each week during months 3-5 (i.e. 12 weeks) (£510.96+£252.72=763.68).

To deliver the intervention in 3 research sites during Phase 2 we are requesting the additional costs for cardiac rehabilitation taking 100 (a slight over-estimation on our target of 66 patients) colorectal cancer referrals:

- During months 8-13, Band 6 cardiac physiotherapist (£21.29) costs accepting cancer patient referrals into cardiac rehabilitation programme calculated at 30 minutes per patient (£1064 x 3 =£3193).
- Costs for additional clinical /risk stratification assessment cancer patients during months 8-13 (1 hour per patient of Band 6 physiotherapist, 100 x £21.29 = £2129 x 3 = £6387).
- Band 6 physiotherapist and Band 2 physiotherapist assistant (hourly rate £10.53) providing additional 2 hour rehabilitation class each week during months 9-16 (i.e. 32 weeks) (£1362.56 + £673.92 = £2036.48 x 3 = £6109.44)

13. REFERENCES

[1] Macmillan Cancer Support, (2008), *Two million Reasons – The cancer survivorship agenda: Why we need to support people with or beyond cancer*, Macmillan Cancer Support, London.

[2] National Cancer Intelligence Network (2006), *One, five and ten-year cancer prevalence by cancer network*, UK.

[3] Foster, C, Wright, D, Hill, et al. (2009), Psychosocial implications of living 5 years or more following a cancer diagnosis: a systematic review of the research evidence. *Eur J Cancer Care*, 18:223–247.

[4] Zabora J, Brintzenhofeszoc K, Curbow B, et al. (2001), The prevalence of psychological distress by cancer site. *Psycho-oncology*, 10:19-28.
[5] Hawkes A, Lynch BM, Owen N, et al. (2008), Health behaviours of Australian colorectal cancer survivors compared to non-cancer population controls. *Journal Supportive Care Cancer*, 16 10, 1097-104.
[6] Craig, P, Dieppe, P, MacIntyre, S et al. (2008), *Developing and evaluating complex interventions: new guidance*, London, MRC.
[7] Murray, E, Treweek, S, Pope, C, et al. (2010), Normalisation process theory: a framework for developing, evaluating and implementing complex interventions, *BMC Medicine*, 8, 63-74.
[8] Freedson, P., Melanson, E., and Sirard, J., (1998), Calibration of the Computer Science and Applications, Inc. accelerometer. *Medicine & Science in Sports & Exercise*, 30(5):777-781.
[9] Reilly JJ, Penpraze V, Hislop J, et al. (2008), Objective measurement of physical activity and sedentary behaviour: review with new data. *Arch Dis Child*, Epub Feb.
[10] Jovabnovic, J, Hughes, D, Baum, G, et al. (2011), Accelerometry and self-report in sedentary populations, *American Journal of Health Behaviour*, 35, 1, 71-80.
[11] Craig CL, Marshall AL, Sjostrom M et al. (2003), International physical activity questionnaire: 12 country reliability and validity. *Med Sci Sport Exer.* 35:1381-1395.
[12] Hagströmer M, Oja P, Sjöström M. (2006), The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. *Public Health Nutrition*; 9(06):755-62.
[13] EQ-5D <http://www.euroqol.org/eq-5d/what-is-eq-5d/eq-5d-nomenclature.html> Accessed 16 May 2011.
[14] Pickard, S, Wilke, C, Lin, H. et al. (2007), Health utilities using the EQ-5D in studies of cancer, *PharmacoEconomics*, 25, 5, 365-384 (20).
[15] Minton, O and Stone, P, (2009), A systematic review of the scales used for the measurement of cancer-related fatigue, *Annals of Oncology*, 20, 17-25.
[16] Segal, J, Reid, R, Courneya, K et al. (2003), Resistance exercise in men receiving androgen deprivation therapy for prostate cancer, *Journal of Clinical Oncology*, 21, 1653-1659.
[17] Zigmond AS, Snaith RP, (1983), The hospital anxiety and depression scale. *Acta Psychiatr Scand*. Jun, 67(6):361-70.
[18] Mitchell, A, Meader, N, Symonds, P, (2010), Diagnostic validity of the Hospital and Anxiety and Depression Scale (HADS) in cancer and palliative settings: a meta-analysis, *J Affec Disord*, 126, 3, 335-48.
[19] Meyerhardt, J, Heseltine, D, Niedzwiecki, D, et al. (2006), Impact of physical activity on cancer recurrence and survival in patients with stage iii colon cancer: findings from CALGB 89803, *Journal of Clinical Oncology*. no. 24, pp. 3535-3541.
[20] Meyerhardt, J, Giovannucci, E, Holmes, M, et al. (2006), Physical activity and survival after colorectal cancer diagnosis, *J Clin Oncol*, 24, 22, 3527-34.
[21] Meyerhardt, J, Giovannucci, E, Ogino, S, et al. (2009), Physical activity and male colorectal cancer survival, *Arch Intern Med*, 169, 22, 2102-2108.
[22] Courneya, K, Booth, C, Gill, S, et al. (2008), The Colon Health and Life-Long Exercise Change trial: a randomized trial of the National Cancer Institute of Canada Clinical Trials Group, *Current Oncology*, 15,6, 262-270.
[23] Speck, R, Courneya, K, Masse, L, et al. (2010), An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis, *Journal of Cancer Survivorship*, 4, 2, 87-100.
[24] Fong, D, Ho, J, Hui, B, et al. (2012), Physical activity for cancer survivors: meta-analysis of randomised controlled trials, *BMJ*, 344:e70
[25] Ferrer, R, Huedo-Medina, T, Johnson, B, et al. (2011), Exercise interventions for cancer survivors: A meta-analysis of quality of life outcomes, *Ann Behav Med*, 41, 32-47.
[26] Craft, L, Vanlterson, E, Helenowski, I, et al. (2011), Exercise effects on depressive symptoms in cancer survivors: A systematic review and meta-analysis, *Cancer Epidemiol Biomarkers Prev*, 21,1,3-19.
[27] Brown, J, Huedo-Medina, T, Pescatello, L, et al. (2011), Efficacy of exercise interventions in modulating cancer-related fatigue among adult cancer survivors: A meta-analysis, *Cancer Epidemiol Biomarkers Prev*, 20, 1, 123-33.
[28] National Cancer Action Team, (2009), *Cancer and palliative care rehabilitation workforce project*, NCAT, London.
[29] Andreyev, H, Davidson, S, Gillespie, C, et al. (2011), Practice guidance on the management of acute and chronic gastrointestinal problems arising, *GUT*, doi: 10.1136/gutjnl-2011-300563.
[30] Hawkes, A, Pakenham. K, Courneya, K, et al. (2009), A randomised controlled trial of a tele-based lifestyle intervention for colorectal cancer survivors ('CanChange'): study protocol, *BMC Cancer*, 9:286.
[31] Spence, R, Heesch, K, Brown, W, (2011), Colorectal cancer survivors' exercise experiences and preferences: qualitative findings from an exercise rehabilitation programme immediately after chemotherapy, *Eur J Cancer Care*, 20, 257-266.
[32] Bourke, L, Thompson, G, Gibson, D, et al. (2011), Pragmatic lifestyle intervention in patients recovering from colon cancer: A randomized controlled pilot study, Arch *Phys Med Rehabil*, 92, 749-755.
[33] Pinto, B, Papandonatos, G, Goldstein, M, et al. (2011), Home-based physical activity intervention for colorectal cancer survivors, *Psycho Oncology*, doi 10.1002/pon.2047.
[34] Anderson, A, Caswell, S, Wells, et al. (2010), "It makes you feel so full of life" LiveWell, a feasibility study of a personalised lifestyle programme for colorectal cancer survivors, *Supportive Care in Cancer*, 18,4, 409-415.
[35] Courneya K, Friedenreich C, Quinney H,et al. (2003), A randomized trial of exercise and quality of life in colorectal cancer survivors. *European Journal of Cancer Care*, 12(4):347-357.
[36] Lie, I, Bunch, E, Smeby, N, et al. (2012), Patients' experiences with symptoms and needs in the early rehabilitation pahse after coronary artery bypass grafting, *European Journal of Cardiovascular Nursing*, 11, 1, 14-24.
[37] Leegaard, M, Naden, D, Fagermoen, M, (2008), Postoperative pain and self-management: women's experiences after cardiac surgery, *Journal of Advanced Nursing*, 63, 476-485.
[38] Theobald, K and McMurray, A, (2004), Coronary artery bypass graft surgery: discharge planning for successful recoevery, *Journal of Advanced Nursing*, 47, 483-491.

[39] Goodman, H, (1997), Patients' perceptions of their education needs in the first six weeks following discharge after cardiac surgery, *Journal of Advanced Nursing*, 25, 1241-1251.
[40] Harrison, J, Young, J, Auld, S, Masya, L, Solomon, M and Butow, P, (2011), Quantifying postdischarge unmet supportive care needs of people with colorectal cancer: a clinical audit, Colorectal Disease, 13, 1400-1406.
[41] Holme, L, Hansen, D, Johansen, C, et al. (2012), Participation on cancer-rehabilitation and unmet needs: a population-based cohort study, *Support Care Cancer*, doi:10.1007/s00520-012-1420-0
[42] Hawkes et al. (2011), Lifestyle factors associated concurrently, *Eur J Cancer*, 47, 2, 267-76.
[43] Courneya, K, Katzmarzyk, P, Bacon, E, Physical activity and obesity in Canadian cancer survivors: population-based estimates from the 2005 Canadian Community Health Survey, *Cancer*, 2008, 112, 2475-82.]
[44] Lynch, B, Cerin, E, Newman, B et al. (2010), physical activity, activity change, and their correlates in a population-based sample of colorectal cancer survivors, *Annals Behav Med*, 34, 135-143.
[45] NCAT, (2009), Supporting and improving commissioning of cancer rehabilitation services guidelines, NCAT, London.
[46] Department of Health, (2011), *Improving outcomes: A strategy for cancer*, DH, London.
[47] Scottish Government, (2008), *Better Cancer Care: An Action plan*, Scottish Government, Edinburgh.
[48] Lancaster, G, Dodd, S, Williamson, P, (2004), Design and analysis of pilot studies: recommendations for good practice, *J Eval Clin Pract.* 10, 307-312.
[49] Rock, C, Doyle, C, Demark-Wahnefried, W, et al. (2012), Nutrition and physical activity guidelines for cancer survivors, *CA*: *A Cancer Journal for Clinicians*, doi: 10.3322/caaac.21142.
[50] Mutrie, N, Campbell, A, Whyte, F, et al. (2007), Benefits of supervised group exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial, *BMJ*, 339: b 3410.
[51] Courneya K, Friedenreich C, Quinney H, et al. (2003), A randomized trial of exercise and quality of life in colorectal cancer survivors. *European Journal of Cancer Care*, 12(4):347-357.
[52] Yellen, SB, Cella, DF, Webster, K, et al. (1997), Measuring fatigue and other anaemia-related symptoms with Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Sympt Manage* 13: 63–74.
[53] Dumas, J, Lynch, A, Laughlin, J, et al. (2001), Promoting intervention fidelity. Conceptual issues, methods and preliminary results from the EARLY ALLIANCE Prevention Trial, *Am J Prev Med*, 1, 20, (1S).
[54] Britten, N, Qualitative Research: Qualitative interviews in medical research, *BMJ*, 1995, 311,251-253.
[55] Ritchie, J, Spencer, L, 1993, *Analysing qualitative data. In Bryman, A, Burgess, R (eds), Qualitative data analysis for applied policy research*, London, Routledge, p. 173-94.
[56] Oldridge N, Furlong W, Feeny D, et al. (1993), Economic evaluation of cardiac rehabilitation soon after acute myocardial infarction. *American Journal of Cardiology*, 72: 154-161.
[57] Donaldson C, Hundley V, McIntosh E. Using economics alongside clinical trials: Why we cannot choose the evaluation technique in advance. *Health Economics Letters* 1996; 5:267-269.
[58] Dolan P, Gudex C, Kind P et al. (1995), *A social tariff for the EuroQol: Results from a UK general population survey.* Centre for Health Economics, Discussion Paper 138. Centre for Health Economics, University of York..
[59] Schmitz, K, Courneya, K, Matthews, C et al. (2010), American College of Sports Medicine. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors, *Med Sci Sports Exerc*, 42, 1409-1426.
[60] SF-36 <http://www.sf-36.org/tools/sf36.shtml> Accessed 17.10.12.
[61] Schwarzer, R., & Jerusalem, M. **(**1995). Generalized Self-Efficacy scale. In J. Weinman, S. Wright, & M. Johnston, *Measures in health psychology: A user's portfolio. Causal and control beliefs* (pp. 35-37). Windsor, UK: NFER-NELSON.
[62] Schwarzer, R., & Fuchs, R. (1996). Self-efficacy and health behaviors. In M. Conner & P. Norman (Eds.), *Predicting health behavior: Research and practice with social cognition models.* (pp. 163-196) Buckingham, UK: Open University Press.
[63] Stephan Y, Boiche J, Trouilloud D, Deroche T, Sarrazin P. (2011), The relation between risk perceptions and physical activity among older adults: a prospective study, Psychol Health. 2011 Jul;26(7):887-97.
[64] Katapodi M, Lee K, Facione N, Dodd M. (2004), Predictors of perceived breast cancer risk and the relation between perceived risk and breast cancer screening: a meta-analytic review. Prev Med. 38:388–402.
[65] de Vries, H., Lezwijn, J., Hol, M., & Honing, C. (2005). Skin cancer prevention: Behaviour and motives of Dutch adolescents. *European Journal of Cancer Prevention, 14*, 39–50.
[66] Rogers, R, (1975), A protection motivation theory of fear appeals and attitude change, *Journal of Psychology*, 91, 93-114.
[67] Janssen, E, van Osch, L, de Vries, H, Lechner, L, (2011), Measuring risk perceptions of skin cancer: Reliability and validity of difference operationalizations, *British Journal of Health Psychology*, 16, 92-112.
[68] Abraham, C., & Michie, S. (2008). A taxonomy of behavior change techniques used in interventions. Health Psychology, 27, 379-387.
[69] Bandura A. (1986), Social Foundations of Thought and Action. Englewood Cliffs, NJ: Prentice-Hall.
[70] Bandura A. (1989), Social Learning Theory. Englewood Cliffs, NJ: Prentice-Hall.
[71] Godin, G. (1996), The theory of planned behaviour: a review of its applications to health-related behaviours. American Journal of Health Promotion, 11: 87-98.
[72] BACPR, (2012), The BACPR Standards and Core Components for Cardiovascular Disease Prevention and Rehabilitation 2012, 2nd edition, BACPR, London.
[73] Brug, J, Oenema, A and Ferreira, I, (2005), Theory, evidence and Intervention Mapping to improve behavior nutrition and physical activity interventions, International Journal of Behavioral Nutrition and Physical Activity, 2,2.
[74] Sniehotta, F.F., U. Scholz, and R. Schwarzer, (2006), Action plans and coping plans for physical exercise: A longitudinal intervention study in cardiac rehabilitation. Br J Health Psychol. 11(Pt 1): p. 23-37.

14. APPENDIX 1: CANCER PATIENT REHABILITATION PATHWAY

Stage	Provider	Key deliverables
Stage 0 Assessment, identify and refer patient for rehabilitation and agree care plan	Cancer Clinical Nurse Specialist (CNS)/nurse consultant	1. Clinical assessment at out-patient clinic to determine if safe for cancer patient to engage in physical activity from a cancer clinical perspective. Date of assessment recorded. 2. Give cancer patient information about core components of rehabilitation as recommended in e.g. National Cancer survivorship Initiative Guidance (e.g. lifestyle, psychosocial status and quality of life, risk factor management, education, long-term management). 3. In accordance with standard cancer rehabilitation service guidance, advise and agree individual patient goals and care plan (Dr Sniehotta has kindly given us his cardiac rehabilitation action and coping planning sheets for use into the present study). 4. If patient agrees, refer patient to cardiac rehabilitation service by secure email, fax or letter (within 10 working days of assessment). Date of referral recorded. 5. Advise patient that the cardiac rehabilitation service will contact them to begin a dialogue about rehabilitation.
Stage 1 Manage referral and recruit patient to cardiac rehabilitation service	Cardiac rehabilitation provider (e.g. senior physiotherapist, cardiac CNS)	1. Send an acknowledgement of receipt of the referral back to the referrer (within 5 working days of receipt). Date of acknowledgement recorded. 2. Contact cancer patient by email, phone or letter offering them an assessment for cardiac rehabilitation class attendance (initial offer). Date of successful contact and proposed assessment date recorded. If after 3 attempts to contact patient has failed, or the patient declines offer of assessment for cardiac rehabilitation, patient referred back to Cancer CNS. Date of referral back recorded.
Stage 2 & 3 Assess patient	Cardiac rehabilitation provider (e.g. senior physiotherapist, cardiac CNS)	1. In accordance with standard cardiac rehabilitation service guidance, conduct an assessment of to determine if safe for cancer patient to participate in physical activity classes for cardiac clinical perspective. Patient referred back to Cancer CNS if deemed inappropriate for cancer patient to join exercise classes. Date of referral back recorded. 2. Give cancer patient information about rehabilitation classes. 3. Agree date when cancer patient is ready and willing to begin attendance of rehabilitation classes and book patients onto rehabilitation programme. Date recorded and sent to Cancer CNS by email or letter.
Stage 4 Deliver rehabilitation programme	Cardiac rehabilitation provider with additional input from cancer CNS/nurse consultant	1. Cancer patient attends rehabilitation classes. A record of when and which rehabilitation classes cancer patient attends recorded. 2. In accordance with standard cardiac rehabilitation service guidance, monitor physical activity component of the classes to ensure safe and effective exercise. 3. In accordance with standard cardiac rehabilitation service guidance, deliver other core components of rehabilitation (e.g. lifestyle, psychosocial status and quality of life, risk factor management, education, long-term management). 4. At end of the rehabilitation programme, refer cancer patient to colorectal CNS by email or letter. Date of referral recorded.
Stage 5 & 6 Conduct final rehabilitation assessment and discharge and transition to self management	Cancer Clinical Nurse Specialist (CNS)/nurse consultant	1. Contact cancer patient by email, phone or letter offering them a final assessment. Date of successful contact and proposed assessment date recorded. If after 3 attempts to contact patient has failed, or the patient declines offer of assessment a record of this is made. 2. Discuss and record patient achievements against original goals set out in the care plan (Stage 0). 3. Agree long-term self management plan based on individual patient goals and needs and encourage patient to take up opportunities to maintain and improve their health and well-being (e.g. join local gym).