Yet another Behaviour Change Intervention: The Feasibility of an autonomy-supportive active lifestyle intervention in older adults

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Abstract

Background: Self-Determination Theory (SDT) has been used successfully as a model for health behaviour change in weight loss programs buts its effectiveness promoting physical activity (PA) behaviour change in an elderly population at elevated risk of colon cancer has not been tested. This study investigated the feasibility of implementing an SDT approach in this population and provides preliminary evidence of its efficacy for modifying motivational regulation in the short- and long-term. Furthermore, barriers to participation, and characteristics of non-participators were explored. **Trial design:** This thesis consists of two randomized controlled feasibility trials. **Methods:** Trial A was called 'Physical Activity and Risk of Colon Cancer' (PARC) and trial B was called 'MOtiVation for Exercise- promoting an active lifestyle after Colorectal Cancer' (MOVE). Participants in PARC (n=31, mean age 69y [SD=4.9], BMI 29.3 [SD=5.1]) were patients diagnosed with polyps after a screening colonoscopy. MOVE participants (n=28, mean age 65y [SD=8.3], BMI=27.7 [SD=4.6]) were patients diagnosed with colorectal cancer after completion of treatment. In both studies, participants were randomized to either an active lifestyle programme (ALP) (PARC n=17, MOVE n=14) or the standard care group (SC) (PARC n=14, MOVE n=14). ALP received supervised exercise sessions and physical activity counselling workshops during the intervention and SC was encouraged to continue with their usual lifestyle. For PARC the intervention was 6months with a 6 months follow-up and for MOVE the intervention was 3months with 3 months follow-up. Randomization was carried out with a bespoke computer software (nQuery). The intervention facilitator was not blinded to the group allocation. Data were analysed with intention-to treat analysis. The primary outcomes were the feasibility of the intervention in these populations. Secondary outcomes were variables of behavioural regulation, physical activity behaviour, physical capacity (fitness and strength), self-efficacy, intention to exercise, and quality of life.

Results: PARC: Overall recruitment yield was 12.1% of eligible participants. Main barriers for participation for time commitment and distance to research site. Attrition post-intervention was 29% and at follow-up 43%. Attendance at the

supervised exercise sessions was 62% and at the workshops was 53%. Post-intervention, ALP had lower amotivation (P<.01), and higher levels of identification (P<.01), intrinsic regulation (P<.001), relative autonomy index (P<.01), and intention to exercise (P<0.05) compared to SC. Total leisure time activity was higher in ALP compared to SC with a mean group difference of 84 min per week (P= 0.08). At follow-up the differences in behavioural regulation were not maintained. ALP did more physical activity at follow-up than SC, with a difference in mean change for leisure-time PA of 170min (P< 0.05). There were no adverse events during the intervention.

MOVE: Overall recruitment rate was 58.3% of eligible participants. The main barriers to participation for time commitment and the travel distance to the research site. Attrition at 3months was 14% and 29% at 6months follow-up. Attendance at supervised exercise sessions was 79% and at physical activity counselling workshops 71%. Post-intervention, ALP was engaging in 98min more walking time physical activity (P< 0.05). Group differences were also observed for body composition with a reduction in body weight (-1.6kg), BMI (-0.04 kg/m^2) and body fat (-1.4%) in ALP compared to an increase in these parameters in SC (+1.1kg, +0.5 kg/m^2, +0.3%) (P< 0.05). At follow-up differences in PA and body composition were maintained (P< 0.05). No differences were observed for behavioural regulation, self-efficacy, intention to exercise, and quality of life at any time-point. Exercise was deemed safe and there were no adverse events throughout the intervention.

Conclusion: Recruitment rates of both trials were poor, but other trials have reported similar low recruitment rates in studies with an elderly population. These are the first studies based on SDT in this population to demonstrate increased physical activity behaviour post-intervention and at long-term follow-up. The findings also suggest that 6months of intervention is successful at evoking changes in behavioural regulation. These findings are comparable to other studies using this model. Larger RCTs are needed to substantiate these findings.

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Contents

Tables and figures

Appendices

List of Abbreviations

ACC	accumulated PA measured with an accelerometer
ACS	American Cancer Society
ALP	Active Lifestyle Programme
APC	Adenomatous polyposis coli
BL	Baseline
BPNT	Psychological Needs Theory
BREQ	Behavioural Regulation for Exercise Questionnaire
CC	CC
CET	Cognitive Evaluation Theory
CRC	CRC
FAP	Familial adenomatous polyposis
FITT	Frequency, Intensity, Time, Type (of exercise)
Freed	Freedson's bouts
HNPCC	Hereditary non-polyposis CC
HR	Hazard ratio
IMB	Information-Motivation Behavioural Skills Model
IMD	Index of Multiple Deprivation
IPAQ	International PA Questionnaire
ITT	Intention-to-treat analysis
Matt	Matthew bouts
MET	Metabolic equivalent task
MI	Motivational interviewing
Mod PA	Moderate intensity PA

MOVE	MOtiVation for Exercise- promoting an active lifestyle after CRC
MVPA	Moderate and vigorous PA
NBCS	National Bowel Cancer Screening
NNUH	Norfolk and Norwich University Hospital
OH	Occupational and Household PA
OIT	Organismic Integration Theory
OR	Odds ratio
PA	PA
PARC	PA and Risk of CC
RAI	Relative Autonomy Index
RR	Risk ratio
SC	Standard Care
SCT	Social Cognitive Theory
SDT	Self-determination Theory
SEE	Self-efficacy for exercise
SF-36	Short Form -36 questionnaire
TPB	Theory of Planned Behaviour
TTM	Transtheoretical model

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Chapter 1

An Introduction to the thesis

"The secret of getting ahead is getting started."

-- Agatha Christie

There are many ways to start a thesis, and the first sentence is probably the hardest. This quote above does not only resemble the difficulties inherent to writing a thesis, it is also a symbol for motivation. Without motivation one cannot get started, whether it is thesis writing, starting a diet or becoming more physically active. Motivation is the key to initiation of behaviour. Motivation is the energy that is required to make that step from contemplation to action. We require motivation in every day decision making, and without inherently valued reasons, we would have a difficult time even getting out of bed. Everything we do has to have a reason, without reason we have no motivation. In this thesis I will discuss the concept of different qualities of motivation as described by Ryan and Deci's Self-Determination Theory, rather than only presenting motivation as a quantitative variable as is often done in other motivational theories. This brief introduction to this thesis will explain the reasons for writing this thesis, and give an overview of the structure that was chosen to present the findings.

The thesis consists of two randomised controlled feasibility trials including elderly people at increased risk of developing CRC and CRC survivors. One of the trials was a 12-month and the other a 6 month PA maintenance intervention. Both trials were conducted at the University of East Anglia, Norwich and in collaboration with the Norfolk Norwich University Hospital NHS Foundation Trust. The two main goals were to 1) assess the feasibility of a theory-based lifestyle intervention in these populations, and 2) to obtain preliminary indicative evidence of the short and long-term effects of the intervention on the behavioural regulations (quality of motivation) proposed by Self-Determination Theory, PA behaviour, quality of life, cognitive variables, and body composition. As mention above, both interventions followed a different timeline in terms of the length of the intervention and the follow-up period. Thus, an ancillary goal was also to gain some knowledge of the effectiveness of different intervention durations on motivational outcomes.

Chapter structure and aims

Two introductory chapters were included in this thesis which build the foundation for the empirical chapters. **Chapter 2** introduces the reader to CRC, what is known of its causes, and the importance of lifestyle factors in the prevention of the disease.

The chapter is also aimed at providing knowledge to aid understanding why the interventions described in the thesis are warranted in these populations. It further provides the basis for practical components that were developed to inform the intervention. **Chapter 3** shows how the theoretical development of the interventions was guided by a thorough review of the current state of lifestyle behaviour change interventions in the literature, including a rationale for Self-Determination Theory (SDT) as the underpinning theory in this thesis. The tenets of SDT will be described to give the reader an understanding of the 'spirit' of SDT. In **chapter 4** the tenets of SDT will be described in a more practical manner. However, only the common methodological aspects of both feasibility trials are described here (design, participants, recruitment, randomisation, intervention, etc.). Trial specific methods are described in each empirical chapter. This seemed a logical presentation, considering the specific methods and different populations of each trial. The first empirical chapter will then present the intervention for people at increased risk of CRC (**chapter 5** henceforth referred to as the PARC trial). A brief background section will provide a rationale for conducting this trial. This is followed by a methodology section. The PARC trial was a 6-month active lifestyle intervention with supervised exercise and PA counselling workshops and included a follow-up time at 12 months. We will present the main feasibility outcomes of the trial, as well as the results for SDT variables, PA outcomes, and body composition. Finally, the chapter will end with a comprehensive discussion of the results. **Chapter 6** is structured in a similar fashion. It presents the results for the intervention with CRC survivors (henceforth referred to as the MOVE trial) and also discusses the findings in detail at the end of the chapter. This trial followed a very similar methodology to the PARC trial, but the intervention phase was only 3 months with a follow-up at 6 months. This trial was limited to this short duration because we were limited for time to complete the thesis. However, this should not be seen as a limitation, rather it provides a rare opportunity to compare two trials that were conducted under a very similar environment. Recruitment challenges are in a separate chapter (**chapter 7**). This chapter will present the methodological aspects of recruitment in more detail than was described in chapter 5 and 6. Thus, a more comprehensive consideration of the feasibility outcomes of both trials is presented

here. Furthermore, to shed light on reasons for non-participation in the trials a survey was sent to the non-responders of study invitations with the results presented in this chapter. This chapter is split into two parts. Part one will present the recruitment challenges of the PARC trial, and the second part the challenges of the MOVE trial. The findings are followed by a comprehensive discussion of each trial individually and together. Finally, the last empirical chapter is a validation study of one of the PA questionnaires used in both trials (**chapter 8**). Although, accelerometry is considered the "gold-standard" for PA measurement in the field, there is increasing scepticism over their accuracy with elderly people. Subjective PA measures (questionnaires) also have their limitations. This issue, together with a rationale for the validation of this questionnaire (International PA Questionnaire) is included in an introductory section of the chapter, then the methods are described, and results presented. The findings are discussed thereafter. In **chapter 9** the findings of the thesis are considered together in one discussion chapter. This chapter briefly summarises the findings, before discussing them in terms of their contribution to the behaviour change literature, future directions, and the strengths and limitations of the thesis. The ancillary goal of investigating the effects of duration of behaviour change interventions on SDT variables will also be discussed.

This thesis addresses some of the issues of long-term maintenance of behaviour change, in particular in PA behaviour change. The detailed description of the SDT intervention also addresses the lack of methodological detail in published studies which can hinder replication of successful interventions and thus, hamper development of the field. It is also hoped that the thesis will contribute to discussions in the field regarding accuracy of PA measurements, specifically in an elderly, morbid population by providing a validation of a widely used questionnaire against an objective measure (accelerometry).

Chapter 2

CRC: A globally growing Malady which can be reduced with more PA

"If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health"

-Hippocrates

2.1. CRC Incidence and Mortality

World-wide, colorectal cancer (CRC) is the third-most common cancer after prostate and lung cancer (GLOBOCAN), with 1.24 Million new cases in 2008 (cancerresearchUK.org). Although, it is a disease that affects people globally, incidence is highest in developed countries as opposed to developing countries. However, CRC cases are increasing in countries that are on a course of rapid 'Westernization' (CancerresearchUK.org).

In the UK, there were 39,245 new cases of CRC in 2008 (GLOBOCAN) and there are small differences in incidence rates between men and women with slightly higher numbers among men. Based on CRC data from the UK in 2011, a lifetime risk of being diagnosed with the disease is calculated to be 1 in 14 for men and 1 in 19 for women. In 2008 there were 21,215 cases in men and 18,030 cases in women (GLOBOCAN). Across all ages, the number of cases in men in Great Britain slowly increased by 1% each year from 1979 to 1999 (Cancerresearchuk.org). Since 1999, rates have slightly decreased but for women there has been very little change over this time period.

Notably, the number of cases differs by age-group with highest incidence rates in the elderly population (> 50 years of age). Ninety-five percent of all cases occur in people aged 60 and over (CancerresearchUK.org). Between the mid-1970 and 2008, an increase of 20% in cases was noted in people aged 60-69. In other words, this is a rise from 120 cases per 100,000 in 1975 to 164 cases per 100,000 in 2008 in this age group. This is a large increase in comparison to people aged 45-59 in which the incidence increased from 43 cases per 100,000 to 45 cases per 100,000 between 1975 and 2008.

Mortality data for people with a diagnosis of CRC in the UK show that there were 16,100 deaths in 2008. However, from 1999 until 2008, the mortality rate declined by 13%. It should be highlighted that there is a notable difference in the number of deaths between CC (10,164) and rectal cancer (6,095) (Cancerresearchuk.org) and there are more CC deaths amongst men compared to women. The number of deaths from CRC is highest in older individuals and lowest in younger people.

Interestingly the figures for incidence have slightly increased since 2006 in the UK. This is likely to be the result of the introduction of the NHS CRC screening programme in 2006 which aims to detect CRC before symptoms arise. Simultaneously, mortality rates decreased from 2006. This could be explained by earlier detection of localised CRC or adenomas.

2.2. A biography of CRC

The colon and the rectum are at the very distal end of the digestive system. The colon is divided into four parts; the ascending colon, transverse colon, descending colon, and the sigmoid colon. Important functions of the colon include water absorption, transportation of waste products, and the release of energy in the form of carbohydrates and fatty acids. Waste is stored in the rectum until it is ready to be passed out of the body as a bowel motion (World Cancer Research Fund and American Institute for Cancer Research, 2007).

The bowel walls are made up of several layers of tissue, and CC usually starts in the inner layer (mucosa) in the form of polyps or adenomas. These are small benign growths that can turn into a malignant growth if left untreated. Cancers that arise from adenomas are called adenocarcinomas.

2.2.1. Causes of CRC

Approximately, 88- 94% of CRCs are sporadic cancers, 1- 2% arise from inflammatory bowel disease, and 5- 10% are attributed to hereditary causes (Weitz et al., 2005). Risk factors of sporadic cancers are older age, male sex, a history of colorectal polyps, and environmental factors such as a diet rich in meat and fat, obesity, sedentary lifestyle, and smoking. People with inflammatory bowel diseases (Crohn's disease, ulcerative Colitis) are also at increased risk of CRC. However, special surveillance guidelines are in place for these patients to detect malignant cell transformation early and remove it.

Amongst the most common hereditary syndromes are hereditary non-polyposis CRC (HNPCC) and familial adenomatous polyposis (FAP). Other hereditary syndromes are known, such as Gardner's syndrome and hamartomatous polyposis syndrome, to name a few, however they are less frequent (Weitz et al., 2005). Both,

FAP and HNPCC pose a high risk for CRC development. FAP is a mutation in the tumour suppressor gene adenomatous polyposis coli (APC) which leads to augmented adenoma growth. Patients present with multiple adenomas (more than 100). This affects 50% of patients at an early age (15 years) and nearly all (95%) by the age of 35. If the patient does not receive treatment for FAP then CRC will arise most likely by the age of 40 (Weitz et al., 2005).

2.2.2. Pathogenesis

There is abundant evidence that benign tumours of the bowel, also called adenomas, are the precursors of malignant colorectal tumours or carcinomas. Adenomas are lesions in the bowel that protrude from the glandular epithelium. Important characteristics of adenomas include dysplasia and modified differentiation of the epithelial cells (Fearon, 2011).

The transformation of adenomatous polyps to a malignant growth is described by the so-called adenoma-carcinoma sequence. This model was first described by Fearon and Vogelstein (1990). During this transformation of the benign tumour to a malignant tumour, the adenoma undergoes several changes including an increase in size, a change in morphology (change in form and structure of the adenoma) and finally, dysplasia (abnormal cell differentiation). Underpinning this development are mutational processes which lead to increased expression of oncogenes, which induce tumour growth, and a loss of tumour suppressor function (Fearon and Vogelstein, 1990). This is traditionally called the 'gatekeeper' pathway. One important oncogene causing cell alterations in the colon and rectum is the *ras* gene. Approximately 50% of CRC carcinomas have been found to have *ras* gene mutations but these mutations appear to be more prevalent in adenomas of sizes larger than 1 cm. Another mechanism of carcinogenesis is the mutation of tumour-suppressor genes. Many of these tumour-suppressor genes have been identified, such as *p53*, and *APC*. A mutation in the latter is the mechanism that leads to carcinogenesis in patients with FAP. Besides the 'gatekeeper' pathway is the 'caretaker' pathway which is characterised by mutations of genes that maintain genetic stability (e.g. mismatch repair genes). Genes mutated in this pathway are e.g. *BAX* and *IGF2R*. This pathway is thought to cause 15% of sporadic CRCs.

Adenomas that are not detected and consequently removed can, over time, progress into a malignant tumour. An adenoma of approximately 10 mm in size has a 10%-15% chance of transforming into a carcinoma over a period of 10 years. This risk increases 10-fold for individuals that are suffering from severe ulcerative colitis (Fearon, 2011).

2.3. Risk factors of CRC and its precursors

The rise in CRC cases over the past decades, particularly in Westernized countries, indicates that environmental and possibly modifiable risk factors are associated with the development of the disease. Modifiable risk factors that have been identified to be associated with an increased risk of colon cancer (CC), are physical inactivity, alcohol consumption and diet (low fiber and high red meat intake). PA has also been linked to a reduced risk of adenomas, which are the pre-cursers of CRC. The following sections will provide a brief account of the lifestyle risk factors linked to an increased risk of developing CRC and adenomas and the mechanisms that are thought to be involved in this association. Lifestyle risk behaviours such as diet, alcohol, and obesity are not within the scope of this thesis and therefore, will only be briefly discussed here.

2.3.1. Diet

Consumption of red meat, diets low in fibre, high-fat diets, and high alcohol consumption have been the main focus of interest for a possible link with an increased risk of CRC. Although, the mechanisms of action are still unclear, there is convincing evidence for these dietary components to be linked to an increased risk (World Cancer Research Fund and American Institute for Cancer Research, 2007).

Findings from a meta-analysis has shown a positive association of red meat consumption of 100g daily with a 15% (RR= 1.15, 95% CI: 1.15- 1.42) increased risk of CRC (Larsson and Wolk, 2006). This may be attributed to the fat and haem content in red meat. Fat can cause excessive bile acid secretion and induce cell loss. Furthermore, haem may increase the amount of free radicals and contribute to increased cell proliferation (Corpet, 2011).

High fibre intake has been linked to a 10% (RR= 0.9, 95% CI: 0.86- 0.94) reduced risk of CRC which is thought to be linked to a decreased transit time of food through the bowel and thus, a reduction in time of exposure of the bowel lining to carcinogenic substance (Aune et al., 2011) (Peters et al., 2003).

Finally, alcohol has been shown to be perhaps the greatest contributor to CRC amongst dietary risk factors. There is a 41% increased risk of CRC in people consuming 45g of alcohol daily (World Cancer Research Fund and American Institute for Cancer Research, 2007). Alcohol consumption is linked to an increase in free radicals which are associated with an increased risk of cancer.

2.3.2. Body composition

A systematic review (Harriss et al., 2009) with 28 cohort studies from different geographical areas reported a statistically significant positive association between body mass index (BMI) and CC risk. In men the risk was 24% higher (RR=1.24, CI 1.20-1.46, P<0.001) and, in women 9% higher (RR=1.09, CI 1.04-1.14, P<0.001) for each 5kg/m_2 increase in BMI. Meta-regression analysis revealed a statistically stronger association with CC risk among men compared to women (P<0.001). An association between higher BMI (each 5kg/m_2 increase) and rectal cancer was only found in men (RR=1.09, CI 1.06-1.12, P<0.001) but not among women.

These results were similar in a former meta-analysis that included 3,128,274 men and 2,419,875 women combined from 31 articles included in the analysis (Larsson and Wolk, 2007). For each 5-unit increase in BMI, an increased risk of 30% for CC was found in men (RR=1.30, 95% CI 1.25-1.35). This association was weaker in women (RR=1.12, 95% CI 1.07-1.18). Similar to the systematic review by Hariss et al (2009), an association with rectal cancer was only statistically significant in men (RR=1.12, 95% CI 1.09-1.16) and not among women, and this was weaker than for CC. This meta-analysis included two studies that reported results on waist circumference and waist-hip ratio. Per 10 cm increase in waist circumference, a 33% increase in CC risk was observed among men (RR=1.33, 95% CI 1.19-1.49) and 16% increase among women (RR=1.16, 95% CI 1.09-1.23). A positive association between waist circumference (an indicator of "centred adiposity" and rectal cancer also existed but was weaker than for CC risk (RR=1.12, 95% CI 1.03-1.22 among men,

and RR=1.09, 95% CI 0.99-1.20 among women). The expert report (World Cancer Research Fund and American Institute for Cancer Research, 2007) also reported a meta-analysis of cohort studies on the association between waist circumference and waist-hip ratio. This revealed a significant positive association between 2.5cm increase in waist circumference and CRC risk (effect estimate=1.05, 95% CI 1.03-1.07). The association with waist-hip ratio was higher with an effect estimate of 1.03 (95% CI 1.17-1.44) per ratio increment of 0.1.

There are a number of possible mechanisms to explain the positive association between body composition and CRC risk. One possible mechanism is that a high BMI and "centred adiposity" are associated with insulin resistance, where cells are unresponsive to insulin, causing insulin levels in the blood to be elevated (Verma, 2009). Insulin has been shown to promote cell proliferation of carcinogenic cells. Furthermore, C-peptide, which is a marker of insulin secretion, has also been associated with neoplasias of the colorectal tissue. Insulin enhances the hepatic production of Insulin-Growth-Factor (IGF)-1 which additionally has been shown to stimulate neoplastic cell growth. It is difficult to pin-point one possible mechanism because perhaps an interaction of several mechanisms may contribute to CRC risk with increased body fatness.

2.3.3. PA: a definition of terms

One of the first studies to report a link between physical activity (PA) and the risk of CC was published in 1984 (Garabrant et al., 1984). A striking 80% higher risk of CC was observed for people with a sedentary occupation compared to people who were active at their jobs. Since then, a large number of studies have been published to further investigate this benefit.

PA is defined as any bodily movement produced by skeletal muscles that result in energy expenditure (Caspersen, 1988). For large cohort studies questionnaires are the most convenient method to measure PA because its low cost. However, there are limitations to questionnaires. Early studies often did not include validated questionnaires to assess PA, or only asked a single question to determine PA levels. Recent studies have addressed this limitation and developed questionnaires that define PA intensity, duration, and frequency. In addition, questionnaires distinguish

between recreational types of PA and occupational types of PA, and some measure sedentary time as well. These methods of PA measurement still have inherent limitations, such as being susceptible to recall bias which ultimately leads to measurement errors. Moreover, PA is often only assessed at one point in time, ignoring the potential for a change in PA habits throughout life. Thus, reported PA levels may not reflect usual PA habits, but only represent a 'snapshot' in time.

For ease of comparison of PA levels between studies, it is common practice to report PA as metabolic equivalent tasks (MET). METs are used to represent the intensity of PA performed and are based on the energy expenditure during this activity. A MET is the ratio of work metabolic rate to a standard resting metabolic rate of 1.0 kcal · kg^{-1} · h^{-1}, and 1 MET is considered a resting metabolic rate obtained during quiet sitting and is equivalent to 3.5 ml/kg/min of oxygen consumption (Ainsworth et al., 2000). A MET of a specific PA is a multiple of the resting MET level, e.g. during brisk walking the metabolic rate is 3.3 times that of quiet sitting, thus one expands 3.3 kcal · kg^{-1} · h^{-1} during walking (3.3 METs). In prospective and retrospective cohort studies, the likelihood of an association between PA and the risk of CC is reported as the relative risk (RR) or adjusted hazard ratio (HR). The odds ratio (OR) represent the relative measure of the association between PA on CC risk and is used in case-control studies to compare the relative risk of developing cancer compared to people without CC (Viera, 2008).

This chapter aims to give an overview of the literature exploring the relationship between PA and primary CC prevention (risk of colonic adenomas, and risk of CC), and secondary prevention (risk of recurrence and death resulting from CC). Moreover, intensity, duration, frequency, and type of PA that is associated with CC risk reduction will be investigated.

2.4. Primary prevention: The effects of PA on the prevention of adenomas and CRC

2.4.1. What is the evidence of an inverse relationship between PA and adenoma prevalence?

"Those who do not find time for exercise will have to find time for illness."

-15th Earl of Derby (1873)

Adenomas are the precursors of CRC, but not all adenomas will become malignant (Fearon and Vogelstein, 1990). Thus, understanding the lifestyle risk factors likely to increase the prevalence of adenomas is of equal importance as understanding the lifestyle risk factors associated with an increased risk of CRC.

Inverse associations between PA and adenoma risk have been found in both case-control and prospective cohort studies. For example, a case-control study with people attending a routine elective colonoscopy compared the risk of adenoma development to a group without adenomas (Hauret et al., 2004). A strength of the study was that individuals with familial adenomatous polyposis (FAP), and the presence of other bowel diseases were excluded from the analysis. A mailed questionnaire assessed PA of a typical weekday and a typical weekend day of the last month. The intensity of PA was based on METs and moderate and vigorous PA were combined for analysis and reported as quartiles. Reported PA included occupational and recreational activities. There were 177 adenoma cases identified which were matched with 228 controls. Multivariate analysis showed a 61% reduced risk of developing adenomas for individuals in the third quartile of PA compared to the least active individuals in the first quartile. There was no significant dose-response relationship.

A large cohort of the American Cancer Society's Cancer Prevention Study II with 72,868 men and 81,356 women investigated the prevalence of all polyps in active vs. inactive individuals (Kahn et al., 1998). A previous diagnosis with colorectal polyps was self-reported via a mailed questionnaire and 7,504 men and 5,111 women with colon polyps were identified. The questionnaire also assessed PA levels and classified participants as 'none/slight', 'moderate', or 'heavy' physically active.

The criteria for this classification are not clear, neither is the time-period over which PA behaviour was assessed (previous 10 years, previous year/ previous month, etc.). There was a significant inverse association with moderate PA and high PA and colon polyps in men only (OR=0.9, 95%CI 0.85-0.96, OR=0.83, 95%CI: 0.76-0.91, respectively). The relationship in women was similar but not significant (OR=0.94, 95%CI: 0.88-1.01 for moderate intensity PA, and OR=0.90, 95%CI: 0.78-1.03 for heavy intensity PA).

In contrast, the relationship between PA and adenoma risk was significant in women from the Nurse's Health Study Cohort (Giovannucci et al., 1996) but not in men from a cohort with Health Professionals (Giovannucci et al., 1995). The Nurse's Health Study Cohort included 13,057 women of which 330 had distal adenomas. Recreational PAs were reported and multiplied by their MET value according to the Compendium of Physical Activities (Ainsworth, 2002) and reported as MET-h/week. Compared to inactive women, women who exercised at least 19MET-h/week had a significant lower risk of developing adenomas (0.58, 95% CI: 0.40- 0.86). A dose-response relationship was also found. Relative to casual walking, adjusted RR for average walking pace was 0.84 (95% CI: 0.54- 1.31) and for brisk walking 0.54 (95% CI: 0.31- 0.94). In the cohort with men no significant associations were found between PA and adenoma risk, although the association was stronger with large adenomas than for small adenomas (Giovannucci et al., 1995).

Inconsistency in findings could be due to erroneous PA measurement. There is a lack of detail describing how the intensity of PA was defined, and whether PA had to be continuous to be included in the analysis. Moreover, recall bias might also be a limitation, but often the time-period to which the PA questions referred to was not reported. For studies that did report the intensity of PA in MET-h/week, there is a trend that higher PA levels have a larger effect. Enger et al. (1997) found a 30% (univariate OR= 0.7, 95% CI: 0.5- 1.0) and a 40% (univariate OR=0.6, 95% CI: 0.4-0.8) lower risk for individuals engaging in 1-13MET-h/week and more than 14MET-h/week of recreational PA, respectively, compared to individuals engaging in ≤1MET-h/week. Similarly, although recreational PA of 10-18MET-h/week showed a reduced risk of adenomas in the distal colon in women (adjusted RR=0.87, 95% CI:

0.69- 1.36), being active at least 19MET-h/week was associated with an even lower risk, and this was significant (adjusted RR=0.52, 95% CI: 0.40- 0.86) (Giovannucci et al., 1996).

2.4.2. What is the evidence of an inverse relationship between PA and CRC?

There is an abundance of studies that have investigated the association of PA and primary CRC occurrence. Studies differ greatly in their design in regards to whether PA levels have been assessed prospectively (before a CRC diagnosis) or retrospectively (after CRC diagnosis). Furthermore, measures to assess PA levels also differ between the studies and authors often do not describe the type of PA (occupational, home maintenance, recreational) that is measured with the questionnaire. This makes it difficult to identify the mode and intensity of PA that is associated with positive effects.

The following few paragraphs summarise the findings of studies investigating the association between PA and CC risk. The focus will be on the association with PA and CC, because evidence for rectal cancer is equivocal.

Findings from meta-analysis

In a recent meta-analysis with 24 case-control studies and 28 cohort studies a 24% (RR=0.76, 95% CI 0.72-0.81) lower risk for CC was reported for the most active compared to the least active individuals (Wolin et al., 2009). The inverse relationship with PA was stronger in case-control studies (RR= 0.69, 95% CI: 0.65-0.74), than in the cohort studies (RR=0.83, 95% CI: 0.78- 0.88). Further stratification of the analysis showed similar significant risk reduction in men and women. Seventeen studies also reported data separately for leisure time PA and occupational PA and both types of PA were found to be significantly associated with a reduced risk of CC (leisure PA: RR=0.77, 95% CI 0.72-0.82, occupational PA: RR=0.78, 95% CI 0.74-0.83).

Similar results were reported in another meta-analysis with 28 case-control studies and 19 cohort studies (Samad et al., 2005). Both, occupational and recreational PA were significantly inversely associated with the risk of CC in males (RR=0.79, 95% CI

0.68-0.91). However, only recreational PA was significantly associated with a reduced risk in women (RR= 0.71, 95% CI: 0.57-0.88) and no significant inverse association was found for occupational PA. Similarly to Wolin et al's meta-analysis, cohort study results were less pronounced than case-control study results. This could be partly due to the small number of studies that have been done. Moreover, it may also reflect the differences in absolute PA values between men and women, with women reporting less PA than men (Wolin et al., 2009). Perhaps higher levels of PA are needed for a risk reduction, and these higher levels may not be achieved by women. This is particularly illustrated with the inconsistency of an inverse association of occupational PA with CC risk in women. Women are less likely to have a physically demanding occupation than men, supporting the findings. Moreover, the meta-analysis included any study that measure PA at any point throughout life. The benefits of PA on a reduced risk of CRC may depend on the time-point in life that PA was frequently engaged in such that life-long PA or current PA levels might have a different effect. Moreover, these meta-analyses included all studies that reported an association between PA and CRC risk and did not stratify for different PA patterns throughout life.

In the next sections we will look at prospective cohort studies and case-control studies separately, and aim to identify the amount of PA that was necessary to yield a significant effect. Questions that will be answered are: 1. Does life-long PA have a positive effect on risk reduction of CC? 2. What types of PA are most beneficial for a risk reduction of CC? 3. What frequency, intensity and duration of PA are necessary to yield a positive effect, and does a dose-response relationship exists?

Life-long PA and the risk of CRC

Most studies that reported an inverse association between PA and CRC risk only measured PA levels at one time-point in life. PA at different periods in life, and continuous PA levels throughout life may also affect this inverse relationship and could perhaps have additional benefits. A few studies measured life-long PA and changes of PA throughout life and its association with CRC risk.

For example, the California Teacher Study is a prospective cohort study that recruited 133,479 retired female school teachers and administrative staff (Mai et

al., 2007). A total of 120,147 women were included in the analysis. Throughout the study period 395 women were diagnosed with CC. Participants were given a questionnaire to record lifetime PA levels from high school to the age of 54 and activity in the last three years before participation in the study. Lifetime PA from High school to 3 years before enrolment into the study was recorded as the average hours of moderate and strenuous intensity exercise per week. Moderate and strenuous intensity PA of at least 4h per week was significantly and inversely associated with a 25% (HR=0.75, 95% CI 0.57-1.00) lower risk for CC compared to women exercising less than 0.5 h per week. A subanalysis for PA intensity showed a significant inverse association between moderate intensity PA and CC risk (RR= 0.78; 95% CI, 0.62-0.97; P_{trend} = 0.02) but not for strenuous.

The previous study reported lifetime PA and did not define different life periods. A case-control study investigated whether different points in life had different effects on the association between PA and CC risk. This study included 98 participants with CC and 193 participants without CC who acted as the controls (Steindorf et al., 2005). In an interview, the participants reported occupational and recreational PA at different periods in their life; when participants were aged 20, 30, 40, 50, and 60 years old. Occupational PA was classified as 'light sitting', 'standing', 'moderate intensity' and 'heavy manual work'. Recreational PA was reported as MET-h per week based on METs from the Compendium of Physical activities (Ainsworth, 2002) and included activities such as walking, hiking, cycling, gardening, sports, and household activities. Total lifetime PA was associated with a 63% (OR= 0.37, 95% CI: 0.17- 0.83) reduced risk of CC. Subanalysis of PA levels by age throughout life showed the greatest benefit of PA at age 50 y and the lowest benefit at age 20 y (OR=0.21, 95% CI: 0.06-0.77, and OR= 0.52, 95% CI: 0.24- 1.13, respectively). Moreover, separate analysis for the types of PA showed a 61% (OR= 0.39, 95% CI: 0.17- 0.92) reduced risk of CC for lifetime occupational PA of ≥146.7 MET-hours per week. Recreational lifetime PA was not associated with a reduced risk of CC.

Similarly, Boyle et al. (2011a) measured lifetime occupational and recreational PA in 870 participants with CC and 996 participants without CC and found a significant inverse relationship between occupational PA and CC risk, but not with recreational

PA. Based on participants' job titles, PA intensity was classified as 'light', 'medium', or 'heavy'. Participants in the 'heavy' occupational PA category compared to the 'light' category had a 45% lower risk for proximal CC (OR= 0.55, 95% CI: 0.32- 0.95). Another case-control study by Boyle et al (2011) investigated the association between recreational PA and CC risk. PA behaviour was compared among 870 bowel cancer cases and 996 controls. Participants were aged between 40 and 79 y of age. Of these cases, 452 were diagnosed with CC and 318 with rectal cancer. Participants were asked to record the recreational PA that they performed regularly (more than 10 times) during three periods of their life: 19-34 years, 35- 50 years, and 51 years and above. Number of hours spent on each activity in each age period was calculated and each activity was assigned a MET value to present the results as MET-hours per week. The lowest risk of CC was reported for total PA at age 19- 34 years, and for 30 MET-hours per week and above (adjusted OR= 0.56, 95% CI: 0.32-0.97). For the age period 35- 50 years, a 21% lower risk of CC was reported for participants exercising 0- 30 MET-hours per week, but not for people exercising more than 30 MET-hours per week. Finally, for people aged 51 years and above, there was an inverse association between PA and CC risk only for people exercising at least 30 MET-hours per week (adjusted OR= 0.88, 95% CI: 0.49- 1.59).

All these studies do not take into account PA changes throughout life. Wolin et al. (2009) investigated the association of PA changes on the risk of CC in 156,331 men and women form the Cancer Prevention Study II Nutrition Cohort. During the study 1,863 people with CC were reported. Participants completed a questionnaire at three time-points over 15 years and participants for whom data of at least two time-points was available were included in the analysis. PA was reported as the number of hours per week spent on recreational activities. Participants exercising at least 30 MET-hours per week had a 28 % reduced risk of developing CC (HR= 0.72, 95% CI: 0.58- 0.89). Change in PA over 10 years and over 15 years was also assessed. Decreasing or increasing PA over a 10-year or 15-year period was not associated with a reduced risk of CC. However, participants who were consistently active compared to participants consistently inactive had a 13% reduced risk of CC (HR= 0.87, 95% CI: 0.69- 1.10). In this study, only 4% of participants increased their PA levels, thus, weakening any potential effects of increasing PA levels. Furthermore,

it should be noted, that PA at each time-point only represents a snapshot of time and may not represent the PA habits of the whole time-period of the study.

A limitation of the studies is recall bias because of the long time that participants had to recall PA. Findings indicate that PA levels nearer to the time of CC diagnosis are related to risk, but not PA levels much earlier in life. This could be a true relationship, but could also be due to recall bias of PA earlier in life. More studies are needed to investigate lifelong PA and its effects on the risk of CC.

2.4.3. What type, duration, frequency, and intensity of PA is associated with the lowest risk of CRC

To formulate specific guidelines to inform the development of exercise programmes, for both the prevention and after-care of cancer, it is vital to have a better understanding of the specific intensity, frequency, time, and type of exercise that will yield the desired outcomes. Although, the evidence is convincing in that PA can reduce the risk of developing CC (World Cancer Research Fund and American Institute for Cancer Research, 2007) there is still a gap in our knowledge as to what the specific ingredients for such an exercise programme are. This is partly due to the nature of the studies (retrospective studies), and the measures that were used to assess PA levels (questionnaires). The problem with retrospective studies and questionnaires is the ability to accurately remember past PA levels, espacially when life-time PA was recorded. This can lead to misclassifications of PA intensity and frequency. Furthermore, these measures of PA also only represent a snapshot in time, and may not reflect peoples' usual PA behavoiur, because follow-up data are not collected to monitor PA levels over a longer period of time to get a more accurate reflection of usual PA behaviour. However, this form of data collection is more pragmatic for studies with larger populations.

Another problem that prevents us from drawing clear conclusions about the ingredients of an exercise programme for the prevention of CC are the different methods that were used to categorise PA intensity in studies investigating the associations between PA and the risk of developing CC. Studies that were reported above, graded PA as MET-hours per week, minutes/hours of PA per week, frequency of exercise sessions per week, or duration of each exercise session per

week. Therefore, the reporting of PA is largely heterogenuous which makes it difficult to define the dose of PA (frequency, intensity, time, and type). MET-hours per week provide an estimate of intensity and duration of the PA, but this is only a relative measure. This can be explained easier by way of an example: moderate intensity walking (3mph) corresponds to 3.3MET-hours (Ainsworth et al., 1993). If one walks 6h per week, one will have done 19.8MET-hours per week. Low intensity walking (2mph) corresponds to 2MET-hours and 9h of slow walking weekly will add up to 18MET-hours per week. The result in weekly MET-hours will be very similar for both walking speeds, but the health benefits might be different because of the difference in PA intensity. Therefore, it is of importance to identifiy the exact dose of PA, including frequency, intensity, time, and type for the development of exercise programmes.

Desiging an exercise programme based on the components frequency, intensity, time, and type of PA is commonly referred to as the F.I.T.T. principle. (Walker, 2004). F.I.T.T. guides the development of exercise programmes and follows the principles of training adaptation. That is, that adaptation to training will only occur if the individual exercises at a level above the normal habitual level of activity on a frequent basis (Maughan and Gleeson, 2010). This is achieved by manipulation of the overload of the PA by a combination of training frequency, intensity, time, and type. Intensity of PA is critical as this will create a training stimulus. If the intensity of exercise is too low, no such stimulus will occur. The intensity should therefore be adjusted to create a muscle overload. Specifically, this can be achieved by increasing the workload (intensity of the activity), e.g. run faster, use more weight. Furthermore, duration (time) can be increased to increase the stimulus and improve muscle strength and endurance. The frequency of exercise is also important and should be carefully considered to allow the body to rest in between exercise because too much training can lead to injury. Lastly, the type of the exercise should be considered, based on what the goal of the exercise is. This is based on the priniciple of specificity which states that the training must match the needs of the sporting activity for fitness improvement to occur (Pollock et al., 1998).

I will now present the literature that attempted to identify the dose of PA needed to reduce the risk of developing CC. At the end I will draw conclusions of this evidence and its impact on the development of exercise interventions.

Frequency, intensity, time and type of exercise

First, I will look at the evidence of the types of PA that are associated with a reduced risk of CC. Then I will present the findings of the literature in regards to the dose of PA in terms of time, intensity, and frequency of PA needed to produce benefits to refine the ingredients for an exercise programme for the prevention of CC. An evaluation of the dose of PA was limited to studies reporting non-occupational PA. Occupational PA is less modifiable than non-occupational PA such as leisure-time PA and therefore, it is less informative about the dose of PA (Slattery, 2004). This review of dose of PA was further restricted by studies that reported on frequency, time, and intensity separately. Most studies reported PA as a total PA score, or a total amount of minutes per week, without detail about individual length and intensity. These studies were not included in this review to determine the dose of PA needed to benefit a reduced risk of CC.

Most studies have reported total PA and not specified the domains of the activities, such as occupational, home/household, and leisure-time PA, but some have presented their findings for separate PA domains. There is evidence for inverse associations between all types of PA and reduced risk of CC (Larsen et al., 2006, Boutron-Ruault et al., 2001, Friedenreich et al., 2006, Wolin et al., 2009, Chao et al., 2004). Similar risk reductions have been reported for occupational and leisure-time PA (Wolin et al., 2009). A meta-analysis reported that case-control studies showed risk reductions of 22% (RR=0.78, 95%, CI: 0.74, 0.83) for occupational PA, and 23% (RR=0.77, 95% CI: 0.72, 0.82) for leisure-time PA (Wolin et al., 2009). Although, this risk reduction was reported to be similar for men and women, it should be noted that women were less presented in the studies investigating occupational PA, espacially in early studies (Brownson et al., 1989, Dosemeci et al., 1993, Fredriksson et al., 1989). For example, a study which only reported significant associations with reduced CC risk for vigorous occupations in both men and women (OR=0.82, and 0.78), 95%CI: not reported) had a smaller number of women classified as doing

vigorous intensity activity in their occuptions (8670 men, 1671 women) and more women as having sedentary jobs (1134 men, 6511 women) (Fredriksson et al., 1989). The criteria for this classification was not described. Furthermore, PA was not self-reported, and therefore, the classification of the occupation by intensity may have been misjudged. This is a limitation of other studies investigating occupational PA and the risk of CC.

The meta-analysis (Wolin et al., 2009) did not report any findings on the association with home/household PA. Only a few studies reported on this PA domain separately, and one of them reported a 32% (HR=0.68, 95% CI 0.48-0.96) reduced risk in men, but not in women (Larsen et al., 2006). The amount of home/household PA was very high with at least 3 hours per day. Another study found no significant assocation (Johnsen et al., 2006). There are not enough studies that reported on home/household PA separtately to draw conclusions whether this type of PA is associated with a reduced risk of CC or not. But the current evidence does not support home/household PA to be associated with reduced CC risk. It is likely that only very high amounts of that type of PA are needed for a benefit based on Larsen et al's (2006) finding, but this needs to be investigated further.

More studies have reported leisure-time PA separately. One study also attempted to specify the types of leisure-time PA (sports, cycling, walking, gardening, do-it-yourself PA) (Johnsen et al., 2006). The study included 28,356 women and men of whom 297 were diagnosed with cancer after 10 years follow-up. Recreational PA was assessed with 12 questions covering the average number of hours per week spent in the past year on six types of leisure time PA (sports, cycling, walking, gardening, housework, do-it-yourself). Each activity was assigned a MET-score and PA was expressed as MET-hours per week. Interestingly, only the total number of activities was significantly associated with a reduced risk of CC (men: IRR=0.88, 95% CI: 0.78-1.00, women: IRR=0.87, 95% CI: 0.7601.00). There were no significant associations for specific types of leisure-time PA, although there was a lower risk for sports (women: IRR= 0.81, 95% CI: 0.57–1.13, men: IRR= 0.87, 95% CI: 0.63-1.21), cycling (women: IRR= 0.87, 95% CI: 0.61–1.25, men: IRR= 0.88, 95% CI: 0.66-1.28), and do-it-yourself activities (women: IRR= 0.86, 95% CI: 0.60–1.22, men: IRR=

0.68, 95% CI: 0.44- 1.06). Walking and gardening were not associated with a reduced risk of CC.

I will now turn the attention to the dose of leisure-time PA that has been associated with CC risk. As already mentioned above, it is difficult to evaluate the dose because of the different methods used for the assessment of PA. The intensity has been reported more consistently, and the evidence indicates that vigorous intensity is associated with the greatest risk reduction (Slattery, 2004, Wolin et al., 2009). For example, evidence from the Western Australian Bowel Health Study (Boyle et al., 2011b) (Boyle et al., 2011b)found an inverse association between high intensity PA and CC risk. Recreational PA behaviour was compared among 452 CC cases and 996 controls. Participants were aged between 40 and 79 years of age. The authors measured PA levels over the lifetime and reported risk of CC for PA level at different periods throughout life. To compare the results to other studies in this section, I will only report the results of the PA levels at age 51 years and above. The authors separated PA by moderate (3-6 METs) and vigorous (>6 METs) intensity PA and reported PA in MET-hours per week for each category. There was a significant trend for increasing vigorous intensity PA and decreasing CC risk. Participants exercising at least 6- 18 MET-hours per week had a 49% reduced risk of CC (adjusted OR= 0.51, 95% CI: 0.29- 0.91), and participants exercising at least 18 MET-hours per week had a 55% reduced risk (adjusted OR= 0.45, 95% CI: 0.24- 0.85). There was no benefit of exercise below 6 MET-hours per week. Six to 18 MET-hours of vigorous PA per week is equivalent to 1- 3 hours of jogging each week. The authors found no significant association with moderate intensity PA.

Other studies also reported greater associations between CC risk and vigorous intensity PA as opposed to moderate intensity PA. A case control study with 1974 CC cases and 2405 age-matched controls. PA was reported as MET-hours per week (Slattery et al., 2003). Moderate intensity PA was assigned values of 4.5 METs per minute, and vigorous intensity PA were assigned values of 6.5 METs per minute. As little as 100MET-minutes per week (equivalent to 1.6MET-hours per week) of vigorous intensity PA was associated with a 31% (OR=0.69, 95% CI: 0.49-0.99) and 33% (OR=0.67, 95% CI: 0.45-0.99) reduced risk in men and women, respectively.

Vigorous intensity for at 1,000MET-minutes per week (equivalent to 16.6MET-hours per week) was associated with the lowest risk (men: OR=0.60, 95% CI: 0.41-0.81; women: OR=0.59, 95% CI: 0.40-0.86). Moderate intensity PA was only associated with a reduced CC risk for the highest level of PA (at least 1000MET-minutes per week) with a reduced risk of 30% in men (OR=0.70, 95% CI: 0.51-0.97) and 15% in women (OR=0.85, 95% CI: 0.57-1.26). This was not significant for women. Often studies combined moderate and vigorous intensity PA and reported the amount of PA as MET-hours per week.

One study found that a minimum of 30MET-hours per week was associated with a reduced CC risk (multivariate adjusted RR= 0.65, 95% CI: 0.49- 0.87) (Chao et al., 2004). The Cancer Prevention Study II (Chao et al., 2004) included 70,403 men and 80,771 women. A self-administered PA questionnaire recorded the average number of hours per week (0, 1-3, 4-6, or ≥7) spent at moderate to vigorous intensity recreational PA (walking, jogging, running, lap swimming, tennis, bicycling, aerobics, dancing) and the results were reported as MET-hours per week. The lowest risk of CC was observed for people exercising at least 30 MET-hours per week (multivariate adjusted RR= 0.65, 95% CI: 0.49- 0.87) compared to inactive people. Although, this relationship was similar in men and women, it was not significant in women. Subanalysis of the type of recreational PA revealed that walking alone is not associated with a reduced CC risk.

Similar results were found in a Swedish population (Larsson et al., 2006). At least 30MET-hours of leisure-time PA was associated with a 41% reduced risk (HR=0.59, 95% CI: 0.43-0.81), and engaging in at 60MET hours per week and more was associated with an even lower risk of 48% (HR=0.52, 95% CI: 0.38-0.71). Another study also reported high MET-hours per week to be associated with reduced risk (Giovannucci et al., 1995). Participants in this study were 51,529 male health professionals. Moderate and vigorous intensity activities were combined and divided into quintiles. At least 46.8 MET-hours per week were associated with a reduced CC risk (RR=0.44, 95% CI: 0.27-0.71). In a large European study (the European Prospective Investigation of Cancer) associations were observed at lower levels of PA. In this study, 413,044 participants were followed up over 6.38 years,

and 1,693 people were diagnosed with CC (Friedenreich et al., 2006). The lowest risk of CC was seen in people engaging in 24.8 to 42.8 MET-hours moderate to vigorous intensity recreational PA per week compared to people engaging in less than 12 MET-hours of per week (adjusted HR= 0.83, 95% CI: 0.70- 0.98). This is equivalent of 7 to 13 hours of brisk walking per week. Moreover, exercisers at 12.0-24.8 MET-hours per week (equivalent to 3.5- 7 hours of brisk walking) had a similar risk reduction (adjusted HR= 0.85, 95% CI: 0.71- 1.00). Interestingly, there seems to be no further benefit of exercise above 42.8 MET-hours per week (adjusted HR= 0.88, 95% CI: 0.74- 1.05). Similar results were reported by Martínez et al. (1997). In this women had a reduced risk of CC if they were active for at least 21 MET-hours per week (RR=0.52, 95% CI: 0.33-0.90).

When moderate and vigorous intensity PA is combined and reported as MET-hours per week, we cannot be certain whether the association with moderate PA is only observed because it is often grouped with vigorous PA. That means, it is likely that the moderate intensity PA is only associated with a reduced CC risk, because the same people who reported moderate PA also reported vigorous PA. Furthermore, when reporting PA as grouped moderate and vigorous intensity expressed in MET-hours per week we cannot draw conclusions about the intensity, frequency and time of the PA.

Although, 30MET-hours per week (Chao et al., 2004) indicates that higher amounts of PA is associated with CC risk, MET-hours alone do not specify the intensity of the PA. MET-hours are a combination of duration and intensity of the PA. The goal of 30 MET-hours can be achieved by 10hours of walking, or 3hours of running. This illustrates that the duration of each activity performed depends on the type of the activity. But we can also not conclude whether long duration of a low intensity PA or short duration of a high intensity PA has the same benefits.

Some studies have specifically reported the duration of PA. The minimum amount of PA for a significant inverse association with CC risk was 30min per day (multivariate HR= 0.64, 95% CI: 0.47- 0.89) when compared to people exercising less than 10 min per day (Larsen et al., 2006). Men exercising more than 60min per day had the lowest risk with a 43% reduction of CC risk (multivariate HR= 0.57, 95%

CI: 0.41- 0.79). A Norwegian study reported the lowest risk of CC in women who exercised at least 31- 60min per exercise session (adjusted HR= 0.73, 95% CI: 0.53- 1.01) and at low exercise intensity (Nilsen et al., 2008). A reduced risk for men was observed for at least 60min of moderate to vigorous intensity per exercise session (adjusted HR= 0.74, 95% CI: 0.50- 1.08). It is interesting that the intensities of PA at which an association with risk reduction was observed was lower for women than for men. This does not answer the question whether long durations of low intensity or shorter durations of vigorous intensity PA is more beneficial, but indicates that at least 30min of PA are necessary for risk reduction.

It might be that lower intensity PA in longer duration does not have the same benefits as a study by Chao el al (2004) suggests. In this study walking alone was not associated with risk reduction, but walking in combination with other moderate to vigorous intensity PA was (Chao et al., 2004). Walking for at least 7 hours per week plus other activities was (including jogging, running, lap swimming, tennis, bicycling, aerobics, and dancing).

This was similar in men (multivariate adjusted RR=0.53, 95% CI: 0.36-0.78) and women (multivariate adjusted RR=0.50, 95% CI: 0.36-0.98). Another study however, reported that walking alone is sufficient to reduce risk (Wolin et al., 2007). This study only included women, and walking of at least 1-1.9 hours per week was associated with a reduced risk (RR=0.64, 95% CI: 0.43-0.94) and walking more than 4 hours per week did not show greater benefits (RR=0.66, 95% CI: 0.44-1.00). In contrast, another study only reported an association and lower risk in Japanese men, but not in women (Takahashi et al., 2007). Because an inefficient number of studies have reported on the benefits of walking separately from other PA domains (Wolin et al., 2009), we cannot evaluate the effect.

Some studies have also reported the frequency of PA and its association with reduced CC risk (Nilsen et al., 2008, Lee et al., 1997), but findings do not provide any evidence for a certain number of exercise sessions per week. In one study there no association with frequency of vigorous exercise (exercising 2-4times per week at vigorous intensity had a risk ratio of 1.2, 95% CI: 0.8-1.6) (Lee et al., 1997). In another study, there was a non-significant reduced risk for men exercising more

than 4 times per week (HR=0.77, 95% CI: 0.54-1.09), and a significant association for 2-3 weekly exercise sessions in women (HR=0.66, 95% CI: 0.47-0.92) (Nilsen et al., 2008). Not enough studies investigated this relationship and therefore, no conclusions can be drawn in regards to exercise frequency.

2.4.4. Conclusion

There is convincing evidence that PA activity is associated with a lower risk of developing adenomas, and CC (Wolin et al., 2009). Although, meta-analyses reported significant associations for men and women, after thorough examination of individual studies we conclude that the results are inconsistent for women. Notably, most studies do report a lower risk for highly active women, but this relationship is not significant. It has been hypothesised that hormone use in post-menopausal women could explain the inconsistent findings in women (Mai et al., 2007). PA over the lifetime and from the previous 3 years was measured and entered into a model to investigate the association with CC risk in pre- and post-menopausal women, and in post-menopausal women with or without hormone treatment. There was no strong evidence that lifetime recreational PA was associated with lower risk of CC among pre- and post-menopausal women. However, analysis of postmenopausal women by hormone treatment revealed a decreased CC risk among postmenopausal women who did not report hormone therapy use, but no risk reduction in postmenopausal women who had used hormone therapy. This might explain the inconsistent findings between men and women but warrants further investigation.

In regards to the type of PA, the inverse relationship between recreational PA and CC risk is consistent in the literature. Some evidence also exists for home/ household PA but evidence suggests that much longer periods of household/ gardening activities are needed on a daily basis (at least 3 hours per day) to yield a risk reduction compared to recreational PA such as walking, bicycling and other exercises (at least 1 hour per day). This could also explain why some studies which included household/ gardening PA in the recreational PA did not find a strong association with a reduced risk, especially in studies with women.

Evidence for occupational PA has been found to be somewhat inconsistent. Perhaps reporting of recreational PA is more accurate, because people are more likely to remember these types of PA than routinely performed PA such as occupational PA. Furthermore, recreational PA might be performed at higher intensities, working up a sweat over a more continuous period of time, than during occupational PA. Moreover, it should be noted that most of the studies with men only did show a significant inverse relationship between occupational PA and CC risk. Women might not have occupations that are very physically demanding, thus, weakening the relationship. Future studies should use a more comprehensive measure to assess energy expenditure during occupational PA in order to accurately categorize PA intensity into mild, moderate or strenuous. Furthermore, a definition for recreational PA should be formulated and used consistently. Here, we suggest that recreational PA should only include leisure activities such as walking, bicycling, swimming, and other exercises. Household and gardening PA should form a separate category, because these types of PA are often not continuous to achieve the minimum of 10 min continuous PA in order to count towards the daily minimum target of at least 30 to 60min of moderate intensity PA.

2.4.5. How much is enough?

In terms of intensity, the evidence is consistent that vigorous intensity PA is needed for an inverse association with CC risk. A minimum of 18MET- hours per week of vigorous intensity PA was necessary for a reduced risk in one study, which is equivalent to 3 h of vigorous intensity PA (Boyle et al., 2011b). Other studies reported walking alone to be insufficient (Larsson et al., 2006). Furthermore, only high intensity PA, for at least four times per week, and a minimum of 60min per exercise session was associated with a reduced risk in men in a Swedish sample (Nilsen et al., 2008). There might be a difference in the amount of PA needed in women. Nilsen et al (2008) reported the lowest risk of CC in women who engaged in low intensity PA, for at least 2-3 times per week at 31- 60min per exercise session.

In regards to duration, an inverse association was only reported for participants who walked at least 7 h per week and performed additional PAs such as jogging, lap swimming, and aerobics (Chao et al., 2004). Another study reported a minimum of

30min of walking, cycling or exercise per day to be associated with a reduced CC risk

This evidence suggests that PA above the current national PA guidelines of at least 150min of moderate intensity PA or 75 min of vigorous intensity PA per week might be necessary for the reduction of CC risk. The evidence of the reviewed studies suggests that durations of at least 200 min of moderate intensity PA per week, or at least 150min of vigorous intensity PA per week is needed to benefit from a reduction of CC risk. This is supported by the World Cancer Research Fund which recommended 30min of moderate PA every day of the week for people starting exercise and that this should be increased to 60min of moderate or 30min of vigorous PA daily (World Cancer Research Fund and American Institute for Cancer Research, 2007).

2.5. Secondary prevention: The effects of pre and post diagnosis PA on cancer mortality

There are only a few studies that investigated the positive effects of PA on survival after CRC and all the studies completed to date rely on observations of prospective cohorts. In these studies, overall mortality and disease-specific survival were the primary endpoints and HR estimates are based on a comparison between the most active people and inactive people. One of these cohort studies assessed cardiorespiratory fitness with HR estimates for cancer-specific death comparing people with high fitness levels to unfit people. Two of the completed prospective cohort studies assessed PA pre-diagnosis which poses a limitation because PA behaviour at that point in time may not reflect usual or current PA habits. Four other cohort studies also assessed PA pre-diagnosis of CRC but additionally assessed PA behaviour post-diagnosis. Although, these studies do not allow a conclusion on the cause-and-effect relationship, they are important to lay the ground work for RCTs. Currently, only one RCT is underway (Courneya et al., 2008). This trial randomly assigns CRC survivors into a PA intervention or a health educational intervention, and participants will be followed-up with disease-free survival as the primary endpoint.

Regardless of the time-points at which PA behaviour was assessed in these prospective cohort studies, results were consistent in that PA has a positive effect on survival after a CRC diagnosis. Nilsen et al (2008) followed people of a large Norwegian cohort (29, 295 men and 30, 074 women). At baseline assessment participants did not have a diagnosis of CRC. Recreational PA was assessed with a self-reported questionnaire. An activity score was formed based on people's frequency, intensity, and duration of the activity and people were either classified to a low or high activity group. Throughout the trial, 736 people were diagnosed with CC and 294 rectal. There were 382 CC deaths reported, and 151 deaths from rectal cancer. Overall, data showed a 44% (95% CI 0.41- 0.78) lower risk of CC specific death for people with the highest level of PA compared to people engaging in low levels of PA. However, the authors also did a sub-analysis for different anatomical cancer sites and found a 67% (95% CI 0.14- 0.76) and 71% (95% CI 0.15- 0.56) lower risk of CC mortality for cancer located in the transverse and sigmoid colon, respectively. No evidence of an inverse association between PA and mortality was found for cancer in the ascending and descending colon.

These findings are similar to the other prospective cohort where PA behaviour was assessed in healthy people at the baseline assessment (Haydon et al., 2006). In this cohort 41, 528 people (17, 049 men) without a CRC diagnosis completed a self-reported PA questionnaire collecting information on frequency, and intensity of non-occupational PA that lasted at least 20 min or more. Participants were classified as exercisers (reported exercise at least once per week) or non-exercisers (no report of exercise) or as walkers (reported walking at least once per week). After a median follow-up of 5.5 years 536 people were diagnosed with CRC and 208 all-cause deaths and 181 CRC specific deaths were recorded. Analysis revealed a 27% (95% CI 0.54- 1.00) lower risk of disease specific mortality, and a 23% (95%CI 0.58- 1.03) lower risk of all-cause mortality for exercisers compared to non-exercisers, although these findings were not statistically significant. No evidence of a positive effect of PA on mortality was found for walkers. Both studies have the limitation that PA is only reported as a score which does not allow an interpretation of the exact amount of PA need to achieve these benefits.

There are four studies that investigated the association between post diagnosis PA and cancer mortality and three of these studies assessed pre diagnosis and post diagnosis PA and results are consistent in that there is an inverse relationship between post-diagnosis PA and cancer mortality, but this relationship is inconsistent with pre-diagnosis PA. Moreover, two of these studies assessed this relationship for women and men separately allowing a comparison between genders.

The first prospective observational study to investigate the relationship between post-diagnosis PA and CRC specific death included patients diagnosed with stage III CC from the Cancer and Leukemia Group B (CALGB) adjuvant therapy trial (Meyerhardt et al., 2006b). PA was assessed with a validated lifestyle questionnaire that was administered four months after surgical resection and 6 months after completion of adjuvant therapy. Responses to the PA questions were assigned a MET score and total PA was reported in MET-h/ week. Primary endpoints were cancer and disease-free survival and overall mortality. After a median follow-up of 2.7 years 84 deaths were recorded. Hazard ratio estimates were based on the comparison to people exercising less than 3 MET-h/ week. People exercising for at least 18 MET-h/ week had a 49% (95% CI 0.26- 0.97) lower risk of dying from CRC, and exercising more than 27 MET-h/ week was associated with a 45% lower risk (95% CI 0.33- 0.91). A reduction of the risk of overall mortality was only statistically significant for high levels of PA (>27 MET-h/ week) with a 63% lower risk (95% CI 0.16- 0.82). Moreover, 3-year survival was 75.1% for people engaging in less than 18 MET-h/ week and 84.5% for people engaging in more than 18 MET-h/ week.

Another prospective cohort study assessed recreational PA in 573 women diagnosed with CRC who were identified via the Nurses' Health Study (Meyerhardt et al., 2006a). A strength of the study is that PA was assessed pre and post diagnosis which allowed and additional analysis of PA change from pre to post diagnosis. Self-reported recreational activities were assigned a MET score and reported in MET-h/ week. Change in PA from pre to post diagnosis was classified as 'decreasing', 'increasing', or 'no change' in PA. Over a median follow-up of 9.6 years 132 deaths were recorded. Compared to those exercising less than 3 MET-h/ week a 61%

statistically significant lower risk of cancer-specific mortality was observed for those exercising more than 18 MET-h/ week (adjusted HR= 0.39, 95% CI 0.18- 0.82). Overall mortality was also reduced by 57% (95% CI 0.25- 0.74) for people exercising at that intensity. No positive effects of pre-diagnostic PA were identified. Change in exercise from pre diagnostic PA level to post-diagnostic PA level was also investigated. In comparison to women who did not change PA from pre to post diagnosis, women who increased PA had a 52% (95% CI 0.24- 0.97) lower risk of cancer-specific death and a 49% (95% CI 0.30- 0.85) lower risk of all-cause death.

Meyerhardt et al (2009) did a similar study with men diagnosed with CRC. Six-hundred-sixty-eight eligible men were identified from the Health Professionals Cohort. Leisure time PA was assessed pre- and post-diagnosis and outcomes were reported in MET-h/ week. The median follow-up of the study participants was 8.6 years, and 258 deaths were recorded during this time. Similar to the Nurses Health Study, significant mortality risk reductions were found for post-diagnosis PA but not for pre-diagnostic PA. The referent for HR estimates were men engaging in less than 3 MET-h/ week. A significant lower risk of cancer-specific mortality was reported for people engaging in more than 27 MET-h/ week with a 53% lower risk (95% CI 0.24- 0.92). This was similar for overall mortality with a 41% lower risk for men engaging in at least 27 MET-h/ week. No evidence for an association was found for pre-diagnostic PA levels. A dose-response relationship was also observed for 5-year survival. Men exercising less than 3 MET-h/ week had an 85.2% chance of being alive after 5 years. This increased to 87.4% and 92.1% for men exercising 3- 27 MET-h/ week and >27 MET-h/ week, respectively. One other prospective cohort study assessed pre and post- diagnosis PA and its relationship with disease-specific and overall mortality. This study included women from the Women's Health Initiative which is a large longitudinal study consisting of clinical trials and an observational study (Kuiper et al., 2012). The study was designed to study major causes of morbidity and mortality in post-menopausal women. Median time of the pre-diagnostic PA measurement was 5.6 years and 1.5 years for the post-diagnostic measurement. Recreational PA was self-reported and frequency, duration, and intensity were recorded. Mild, moderate, and strenuous intensity were assigned a MET-score (3, 4, 7, respectively) and the weekly amount of PA was reported in MET-

h/ week. Of the 1, 339 women included in the study 265 died of after 11.9 years of median follow-up time. For post-diagnostic PA significant associations with CRC specific mortality were reported for women exercising between 3-8.9 MET-h/ week (adjusted HR= 0.3, 95% CI 0.12- 0.73), and for women exercising more than 18 MET-h/ week (adjusted HR= 0.42, 95% CI 0.11- 0.77) when compared to non-exercisers. This was similar for overall mortality with a 58% (95% CI 0.23- 0.77) and 59% (95% CI 0.21- 0.81) lower risk for women expending 3- 8.9 MET-h/ week and more than 18 MET-h/ week, respectively. For pre-diagnostic PA the HRs were only significant for overall mortality and for women exercising more than 18 MET-h/ week (adjusted HR= 0.63, 95% CI 0.42- 0.96).

As opposed to the Meyerhardt et al's studies, there was no significant trend in Kuiper's results for the association of different PA levels with cancer mortality. Moreover, risk reduction for CRC specific mortality in Kuiper et al's study was nearly 10 percentage point larger than in any of the Meyerhardt studies. This could be attributed to the low MET-scores that were assigned to the PA intensities in the latter study. Where Meyerhardt assigned MET scores to each individual activity based on the Compendium of physical activities established by Ainsworth et al (Ainsworth, 2002), Kuiper et al assigned 3, 4, and 7 METs to mild, moderate and strenuous PA, respectively. Typically, mild intensity is assigned less than 3 METs, moderate intensity 3-6 METs, and vigorous intensity above 6 METs. However, moderate bicycling and moderate swimming are assigned a MET value of 8 in the compendium. Thus, it is likely that Kuiper et al's assessment of PA intensity was underestimated having resulted in these lower HRs for cancer mortality. One study assessed cardiorespiratory fitness an indicator of PA and its association with survival of digestive cancers (Peel et al., 2009). Participants were healthy male patients examined during a preventative medical examination in Dallas, TX, United States. After a maximal treadmill fitness test patients were classified as either having low, moderate, or high fitness. Patients were followed-up for a mean of 17 years. A sub-analysis of CC deaths showed a 39% (95% CI 0.37- 1.0) lower risk of CC specific mortality compared to unfit men.

2.6. Conclusion

Although, only a few studies have been conducted to investigate the relationship between PA and survival from CRC, the current evidence is consistent that post-diagnosis PA is beneficial for survival. Risk reductions of 49- 71% and 41- 73% have been reported for disease-specific mortality and overall mortality, respectively. In general, there was a statistically significant trend for higher levels of PA to be associated with more benefit and engaging in more than 18 MET-h of PA per week was shown to be the minimum requirement to gain benefits for survival (Meyerhardt et al., 2006a, Meyerhardt et al., 2006b, Meyerhardt et al., 2009). This equates to approximately 6 hours of brisk walking per week. One study did not confirm this trend but this could be attributed to the difference in classifying PA intensity (Kuiper et al., 2012). Moreover, findings from these studies suggest that there is a difference between genders for the minimum amount of PA required with significant benefits for women exercising at least 18 MET-h per week (Meyerhardt et al., 2006a) and men at least 27 MET-h per week (Meyerhardt et al., 2009). In terms of brisk walks, this means that women would have to do at least 6 hours, and men at least 9 hours of this activity weekly. However, this difference could be attributable to PA measurement error. There might be a misconception of the definition for leisure-time PA, recreational PA, moderate, and vigorous PA among participants, which could have resulted in erroneous reporting of PA (Tudor-Locke et al., 2003). Evidence for PA pre-diagnosis was not consistent. PA was associated with 27 – 28% reduced risk of disease-specific mortality in two of the four studies investigating this relationship. Only one study reported significant findings for overall mortality with a risk reduction of 37%. Different measures of PA were used in all these studies making it difficult to compare the intensities of PA classified as high or low intensity exercisers. More studies are needed to confirm these findings and include a more detailed questionnaire to investigate PA intensity. Furthermore, to date only observational studies exist which limit the interpretation of the cause-and-effect relationship and RCTs are needed to confirm these findings. One large RCT is currently being conducted in Canada and results have not been published to date (Courneya et al., 2008)

2.7. Implications on the development of an exercise interventions and challenges of monitoring exercise behaviour to encourage changes in physical activity

The evidence points into the direction that a higher amount of weekly PA is needed to reduce the risk of developing CC, and death from the disease (World Cancer Research Fund and American Institute for Cancer Research, 2007, Meyerhardt et al, 2009). It would be unrealistic for a beginner of an exercise programme to achieve such high levels of PA, because of low levels of fitness. Therefore, the World Cancer Research Fund recommends that exercise beginners start with 30min of moderate intensity PA per day and are to increase this to 60min per day once fitness has improved.

In the light of barriers to exercise among older adults (Lees et al., 2005, Gellert et al., 2015, Schutzer and Graves, 2004, de Groot and Fagerstrom, 2011), this poses certain difficulties to achieve this PA goal. Older adults may lack motivation to exercise, have difficulties accessing exercise facilities, lack interest, or have possible health and safety concerns. Different settings of PA (home-based, individual exercise, group-exercise) could address these barriers, but also contribute to them. For example, a home-based exercise programme might be more acceptable because the barrier of 'access to exercise facilities' is eliminated with instructions for exercises provided that can be easily done at home. But it may increase concerns for safety because of a lack of supervision in a safe environment. A supervised group-based intervention might create a safe environment, but may be associated with problems of accessibility. Moreover, the intensity of PA is important to achieve the desired benefits and therefore, accurate monitoring and measurement of it is a requirement for a successful exercise programme. Intensity can be measured with heart rate monitors, or by observation of physical responses to exercise, such as elevated breathing and sweating. This can be measured with the rate of perceived exhaustion (RPE) scale (Borg, 1982), which is a rating based on physical signs, such as breathing, sweating, and heart rate. Depending on the setting of the exercise programme (home-based or supervised), some of these PA intensity measurement techniques may be more or less adequate. In a home-based setting, participants might not have access to a heart rate monitor, and therefore the RPE is more

appropriate. Whereas, in a supervised setting, technology to monitor heart rate is usually available, and will allow a more accurate measurement than RPE. However, only monitoring heart rate alone may not be appropriate in this population, because the use of beta blockers might influence the heart rate response. Therefore, a combination of measurement options should be considered.

Disregarding the adequacy of the measurement technique, most and foremost, participants need to be informed about the 'right' intensity of PA and be educated about several self-monitoring options. But before the 'right' PA intensity can be prescribed, we need to determine the workload that corresponds to moderate to vigorous intensity PA for each individual participant. This can be achieved with appropriate baseline testing which will permit training to be adopted to a participant's baseline maximal exercise capacity (VO_{2peak}) (Sasso et al., 2015), in consideration with the FITT principle earlier in this chapter. Once this baseline exercise capacity has been established, the exercise progress can be monitored throughout the group-based supervised exercise sessions, or a programme can be devised and prescribed to the participant for home-based exercise. We will now discuss some of the strengths and limitations of home-based and group-based exercises in terms of their capability to monitor exercise intensity, and thus, exercise progress.

One-to-one supervised exercise is an ideal setting to guarantee that all components of an exercise programme are met according to the recommendations (frequency, intensity, time, and type). The exercise facilitator can assess the participant's physical capabilities at the beginning of the exercise programme, and develop an individualised exercise regime suitable for the participant. The facilitator can then choose the type of exercise that is most suitable for the participants' physical capacities, and monitor the intensity of the exercise. A record can be maintained by the facilitator which will inform the participant's progress. If data is recorded at the end of each supervised exercise sessions, subsequent adjustments to the programme can be made which is determined by the participant's progress. However, such a programme may have a range of disadvantages. First, it could be costly either for the provider or the participant. Second, although, there might be a

close rapport between the facilitator and the participant, peer support which may be enhancing motivation, and thus, adherence in the long-term is lacking with such a programme (Rhodes and Nigg, 2011). There is evidence that participation at PA interventions declines the longer the duration of the intervention (van der Bij et al., 2002). But the decline seems to be less strong in group-based settings compared to educational interventions without group contact. The authors of this review also concluded that participation at home-based and group-based interventions is comparable, but that group-based interventions are better for long-term outcomes. Besides benefits in regards to adherence, and long-term outcomes, peer support resulting from group-based interventions might be important to build competence, because of social comparison. If one participant believes that they are unable to perform a certain activity, but observes another participant with similar age and medical condition, this could positively affect the participant's motivation to attempt the activity and 'believe' that they are capable of it (Jowett and Lavallee, 2007). Peer support might also benefit attendance at the programme. A survey showed that 50% of seniors related social support from friends with exercise frequency (van der Bij et al., 2002). Other participants of the supervised exercise group may be befriended, and thus, increase frequency of attendance at the group sessions.

On the other hand, group-based exercise settings are more challenging for monitoring the exercise dose. Participants in an exercise programme with people at elevated risk of CC and previously diagnosed with CC will be older, and thus are more likely to have comorbidities and physical limitations (De Bruijn et al., 2013). Although, the American College of Sports Medicine concluded that moderate intensity PA is safe for people recovering from cancer (ASCM, roundtable), cancer survivors may have cancer-related side-effects which require specific attention of the exercise facilitator, and to tailor the exercises to meet individual needs to ensure safety of the participants. Similarly, people diagnosed with CC polyps tend to be older, and may have other comorbidities and/or reduced physical functionality. This will require more engagement of the facilitator with the participant. A group-based supervised exercise programme with one facilitator could therefore be challenging to monitor exercise dose and safety of participants.

One can actively engage the participants to monitor their intensity themselves, and report these to the facilitator at the end of their exercise. However, from personal experience, participants can have difficulties reading and understanding outputs from heart rate monitors, or forget to record their intensity and report it to the facilitator. This can lead to incomplete records at the end of the exercise session.

An exercise prescription that monitors progress to adjust the regime in consideration of the principles of exercise prescriptions (FITT principle) is called a linear approach. However, there is a lack of studies in the literature that compare the efficacy of a linear approach compared to a non-linear approach (Sasso et al., 2015). This might be due to the challenges of group exercise settings, as described above.

Home-based exercise programmes are a less costly alternative to group-based supervised exercise sessions, but there might be challenges at monitoring PA intensity to ensure adequate exercise progression. There is a lack of evidence to conclude whether home-based or group-based exercise is more effective at increasing PA behaviour. A review of PA interventions found that a mixed mode (individual and group-based PA) was more effective for weight loss than individual delivery of an intervention (Greaves et al., 2011). In contrast, a COCHRANE review (Foster et al., 2008) found that home-based interventions may be superior to group-based interventions in terms of adherence, but may not be successful at increasing physical fitness as a result of the intervention. This supports the above concern, for the challenges of adequate PA intensity monitoring for exercise progression.

For the development of a PA intervention in this population, and to monitor the amount of prescribed exercise, a group-based supervised exercise programme may be more adequate. To overcome some of the difficulties of monitoring PA in a group setting with this population the format of the sessions should be carefully considered. For example, smaller groups with lower facilitator to participant ratio may reduce some of the challenges of monitoring and adjusting PA intensity. Furthermore, participants should be given a familiarisation session prior to the group exercises, so that they are comfortable with the equipment and understand how to adjust the workload. Participants should be prepared about the format and

structure of the group sessions, be provided with a rationale for keeping a record of PA intensity, and receive an explanation of how to rate their RPE and how to use heart rate monitors.

During the group-sessions participants can also be educated about the recommended levels of PA that are needed for the benefits to bowel health. Participants are able to 'learn' about their physical responses to moderate to vigorous intensity PA. This will provide a sense of safety for additional home-based exercises.

In the next chapter we will turn our attention to the theoretical underpinning of the interventions of this thesis. And in chapter 4 we will demonstrate how the theoretical underpinning will inform the components of the PA intervention, and address some of the issues described above.

Chapter 3

PA as the target in behaviour change interventions: A rationale for Self-Determination Theory

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"True enjoyment comes from activity of the mind and exercise of the body; the two are ever united."

- Wilhelm von Humboldt (1767 – 1835)

3.1. Who is meeting the PA Guidelines?

Colon cancer cases are higher in the elderly population with 86% of cases occurring in people aged 60 and over (CancerresearchUK.org). In light of the benefits of PA in terms of the inverse association with CC, this age group would benefit from higher levels of PA. The latest PA guidelines for the maintenance and improvement of health published by the Department of Health (DoH, 2011) recommend at least 150min of moderate intensity PA (aerobic exercise), or 75 min of vigorous intensity PA (or a combination of both) per week. This should be spread out over the week in bouts lasting at least 10 min. However, records from the Health survey for England 2012 show that only 58% of men and 52% of women aged 65-74 years are meeting the general PA guidelines mentioned above (Scholes and Mindell, 2013). It should be noted that according to these guidelines each activity bout has to last a minimum of 10 min to count towards the weekly goal of 150min of moderate intensity PA, and it is not required to accumulate a minimum of 30min in one day, which was a requirement for the 2004 recommendations (Craig et al., 2009). Evidence for the association of PA and a risk of CC suggests that these guidelines may not be sufficient for reducing risk. The World Cancer Research Fund recommends moderate PA of at least 30min every day of the week. And this should be increased to 60min or more of moderate intensity exercise or 30min vigorous intensity exercise every day once fitness levels improve (World Cancer Research Fund and American Institute for Cancer Research, 2007). In light of these recommendations (30min of moderated intensity PA per day) only 26% of men and 22% of women in the UK aged 65-74 years were sufficiently active in 2012 (Scholes and Mindell, 2013).

3.2. The challenges of measuring free-living PA

In 2008, the Health Survey for England (Craig et al., 2009) also measured PA behaviour using accelerometry in addition to self-reported PA which drastically reduced the number of people meeting these PA recommendations from 26% to 6% for men and from 22% to 4% for women aged 65- 74 years of age. This demonstrates a lack of agreement between subjective and objective PA measurement. Accurate assessment of PA is critically important when examining the relationship between PA exposure and a number of health related outcomes

(Freedson et al., 1998). Furthermore, accurate measurement is vital if one is to investigate the efficacy of a PA intervention to detect changes from baseline measures to follow-up. Inaccuracy can lead to reduced or eliminated strength of the relationship in question. Self-reported PA measures are susceptible to inaccuracy because these measures depend on the participant's ability to recall or report PA which can lead to biases. Subjects might also misinterpret questions, or certain types of activities might not be captured with some questionnaires (Some questionnaires only capture recreational PA, whereas others capture a variety of different PA domains). Accelerometers are alternative methods that do not rely on the subject's ability to recall PA or the quality of the self-report questionnaire. These are small devices (electronic sensors) that can be worn around the hip, arm, or ankle. They measure the quantity and intensity of movement (Berlin et al., 2006). These devices have the ability to store measurements of intensity, frequency, pattern, and duration of activity. Data are subsequently processed on a computer. Based on calibrations of the devices they have the ability to discriminate intensity into mild, moderate, and vigorous intensity PA, but also detect periods of inactivity. Thus, accelerometry is often considered to be the most accurate method of measuring PA and benefits include the reduction of recall and social desirability biases (Matthews, 2005). However, the high costs and burden on the patient due to wear time make accelerometers less desirable than self-reported measures. Additionally, because the validity of accelerometers has mostly only been tested for walking activities, potentially vigorous activities (e.g. walking uphill), activities that involve mainly the upper body (e.g. resistance exercises), and other ambulatory activities such as cycling, swimming, and gardening are very difficult to measure with accelerometry (Matthews, 2005). Moreover, most validation studies have been carried out with a healthy and younger population and measurement accuracy in an elderly population with comorbidities is still to be determined. Self-administered questionnaires are favoured for large-scale assessments because of their low cost and ease of administration. Furthermore, type of activities can easily be captured with self-reported measures, which is not possible with accelerometry unless the subject completes a PA diary concurrently with the wear time of the accelerometer. However, this further adds not only to the subject's burden but also

to the researcher's burden with a large amount of data to be analysed. Clearly, both, subjective and objective measures have their own benefits and drawbacks, but to investigate relationships between PA patterns and health outcomes, or PA intervention efficacy, accelerometers are considered to be the gold-standard. Yet, it is also clear that large-scale studies such as national surveys, and small projects with limited funding opportunities (e.g. PhD projects) will likely be reliant on self-reported PA measures because of the obvious costs of the devices (one device from Actigraph for example costs between $200 and $300). Thus, focus of research has recently been on the investigation of the validity of most commonly used self-report PA measures against accelerometry. However, a large proportion of these studies included young and middle-aged and seemingly healthy adults. Therefore, there is still a need to validate self-report measures against accelerometry in the elderly to accurately capture PA behaviours and PA intensity in this population to improve the reporting of such data.

3.3. The problem of long-term adherence to PA

As already highlighted, there is a need to not only address the low PA levels of the population but to also accurately measure PA in the population for the evaluation of intervention efficacy and the investigation of PA with health outcomes. With either type of measurement (subjective or objective) national survey data reveals that an insufficient amount of people meet the current PA recommendation, not only in the UK, but also in other European countries, and the United States (Eurobarometer, Schiller et al., 2012). With the release of the first PA recommendations for health in 1995 by the Centre for Disease Control and the American College of Sports Medicine (Pate et al., 1995) there has been a growing interest in PA interventions.

Past interventions have heavily focused on the relationships between PA and biological outcomes (e.g. cholesterol, insulin, etc.) leading to highly controlled, short-term interventions with healthy, motivated participants (Antikainen and Ellis, 2011). Certainly, those studies taught us a lot about the benefits of PA explaining mechanisms of action, and thus, drove the increasing interest in behaviour change research. A more physically active nation is certainly in the interest of the National

Health Service in the UK. The Department of Health estimates that physical inactivity costs the NHS between £1 billion and £1.8 billion annually (www.nhs.uk, accessed 01/03/2015).

Recognizing the need for a more active population, an abundance of studies has tested PA behaviour change interventions. The evidence shows that the majority of PA interventions are successful at behaviour change post-intervention (Müller-Riemenschneider et al., 2008, Fjeldsoe et al., 2011, Greaves et al., 2011). However, evidence for a lasting positive effect at a post-intervention follow-up is lacking. A Cochrane review in 2008 (Foster et al., 2008) on interventions for promoting PA concluded that studies are effective at least in the short term, but long-term effectiveness is not established. Studies were included if participants were at least 16 years of age, and free from pre-existing medical conditions that could limit participation in PA. Issues that were raised during the review were that the majority of the studies under investigation did not last beyond 12 months. In terms of design, the authors noted a marked heterogeneity in the interventions used in each study. Other systematic reviews came to similar conclusions (Müller-Riemenschneider et al., 2008, Fjeldsoe et al., 2011). Although, PA interventions may be effective in the short-term, it should be noted that PA behaviour varies substantially between studies. Müller-Riemenschneider et al (2008) found that the proportion of interventions participants meeting the PA recommendations for health post-intervention ranged between 4.6% and 81%. For maintenance the authors found a moderate decline of PA behaviour between early and late follow-up but noted that intervention effects were mostly stable. Two interventions did not find any significant effects at follow-up. The studies that found significant intervention effects at follow-up included a maintenance intervention, which is either repeating the initial intervention during the maintenance period, or the use of booster strategies such as print material and phone calls. The two studies that did not find an intervention effect at follow-up did not use such maintenance strategies. It could be argued that this is not a convincing evidence of the effectiveness of long-term PA behaviour if only long-term interventions with post-intervention interventions are able to achieve a significant positive intervention effect at follow-up. If we are to change people's PA behaviour in the long-term we need to include a 'true' follow-

up period without any participant contact to achieve a sustainable public health effect. Moreover, a continued intervention post-intervention would increase costs. There is currently a lack of interventions with maintenance of behaviour change, which might be due to a lack of research attention, or publication bias toward successful interventions, or that research funding does not allow sufficient resources or time to conduct extended post-intervention follow-up assessments (Fjeldsoe et al., 2011). However, some techniques have been associated with positive effects of PA behaviour change interventions. These include interventions that focused on the increase of self-efficacy, enjoyment of exercise, addressed barriers to exercise, setting goals, provision of feedback on performance, and the provision of pedometers for self-monitoring (Greaves et al., 2011, Bauman et al., 2002). Furthermore, centre-based interventions with supervised exercise session, and interventions targeting groups have been shown to be superior to home-based interventions, and interventions targeting individuals (Bauman et al., 2002, Antikainen and Ellis, 2011). In terms of intervention intensity, interventions were more successful in maintaining PA behaviour if they lasted at least a mean of 24 weeks, and if they had a higher number of intervention contacts (mean of 13 contacts) (Fjeldsoe et al., 2011). This review also found that trials achieving maintenance of PA outcomes more commonly included face-to-face contact than those that did not include face-to-face contact.

3.4. Are interventions based on common sense or evidence?

"He who loves practice without theory is like the sailor who boards ship without a rudder and compass and never knows where he may cast." (Leonardo Da Vinci, 1452-1519)

Despite the abundance of PA interventions aiming to increase PA levels of individuals, we are still largely in the dark about the determinants of PA behaviour change (Michie and Abraham, 2004). There are examples of trials with successful outcomes at more than 12 months but the great diversity in research design,

measurement approaches, and populations studied, theories used, variables tested, and PA outcomes make it difficult to identify the components that lead to success. It further makes it difficult to integrate the findings and summarize the status of the field, thus limiting the ability of subsequent research to build on previous findings (Bauman et al., 2002).

In 1993, Weinstein proclaimed that Health Behaviour Theory has tended to be particularly interested in understanding people's motivation to change behaviour rather than the ability to change (Weinstein, 1993). Although, this was more than 20 years ago, and one would expect that the research has addressed these shortcomings, research has still not provided a recipe for health behaviour change (Painter et al., 2008, Jeffery, 2004, Heath et al., 2012, Greaves et al., 2011). One of the main reasons why the field is not moving forward is not the lack of behaviour change theories, but rather the poor description of interventions in publications. It has been repeatedly pointed out by behaviour change researchers that detailed description of interventions is needed for replication to reduce inconsistencies in outcome data (Michie and Abraham, 2004, Hoffmann et al., 2014, Noar and Zimmerman, 2005, Marcus et al., 2006, Dombrowski et al., 2007). Furthermore, there is a lack of systematic approach for describing behaviour change interventions by using labels for similar techniques and the same labels for different techniques (Dombrowski et al., 2007).

It is recognized among behaviour change researchers that interventions should draw on theories to inform the development of interventions (Michie et al., 2014). In fact, in the UK the Medical Research Council recommends that the development of any complex intervention should be informed by theory which is likely to advance the understanding of the processes of change (Craig et al., 2008). However, a recent meta-analysis asking whether theory influences the effectiveness of health behaviour interventions did not find evidence that behaviour change interventions informed by theory are more effective than atheoretical interventions (Prestwich et al., 2014). This question has been the focus of several previous reviews and the results are mixed with some reporting positive associations with theory use, some reporting no associations, and some even negative associations (Michie et al., 2014)

(page 21). Reasons for the lack of consistency could be due to the lack of interventions actually using a behaviour change theory to inform their intervention. The majority of interventions were found to only use theory to 'inform the research', suggesting that theories are not translated into practice (Painter et al., 2008). Prestwich et al's (2014) meta-analysis identified 190 behaviour change interventions and only just over half of them (56.3%) explicitly reported that they were based on theory. And only 42% of these interventions reported measuring theoretical constructs pre-and post-intervention. Another review of behaviour interventions found that only 44% of identified randomised controlled trials (RCT) in behaviour change reported the theoretical basis for intervention development and that only one study provided a clear theoretical rationale (Dombrowski et al., 2007). The authors reported that a third of reviewed RCTs failed to provide any justification of why a particular theory had been selected and none of the trials explained 'how' theory led to development of an intervention. "This weakness in rationale often makes it impossible to determine if published interventions are based solely on common sense or on established theory and evidence". (Dombrowski et al., 2007). Dombrowski et al summarize that without stated rational and detailed description of interventions the mechanisms of behaviour change will be inconclusive. Furthermore, the use of theory will advance the science and lead to more effective interventions. Theories can provide a framework that can aid the development of interventions to inform the selection and sequence of intervention strategies (Prestwich et al., 2014).

3.5. The search for a theory

"In the context of behaviour change, theories seek to explain why, when and how a behaviour does or does not occur, and the important sources of influence to be targeted in order to alter the behaviour. They should reflect an integration of the knowledge accumulated about the relevant mechanisms of action and moderators of change." (Michie et al., 2014)

Despite the current lack of evidence for the positive effects of behaviour change interventions informed by a theoretical model, there is clearly a justification for a more rigorous use of theory because atheoretical interventions fail to build on existing knowledge (Michie and Abraham, 2004). In a recent book "ABC of behaviour change theories" the authors identified 83 different behaviour change theories (Michie et al., 2014). Yet, only a minority is frequently used to inform behaviour change interventions. Only four theories of the 83 accounted for 63% of articles found. These were the Transtheoretical Model of Change (TTM), the Theory of Planned Behaviour (TPB), Social Cognitive Theory (SCT), and the Information-Motivation-Behavioural Skills Model (IMB). The most frequently reported theories in the PA interventions are SCT, TPB, and TTM (Antikainen and Ellis, 2011).

We will only include a very brief description of these theories to guide the reader to our decision making of the theory that was used to inform the two PA interventions described in this thesis.

Social Cognitive Theory

SCT is a triadic reciprocal model in which cognitive/personal factors, behaviour, and environmental factors influence each other in a bidirectional manner (Bandura, 1988). The theory assumes that people can influence their behaviour in a goal-directed way. SCT integrates a number of concepts to understand human behaviour. The most frequently used in behaviour change include *outcome expectations*, *perceived self-efficacy*, *goal setting*, and *self-regulation*. Briefly, outcome expectations reflect peoples' beliefs about the outcome of a particular behaviour. Self-efficacy is the belief that one has the skill set and capabilities to exercise control over events to accomplish a set of goals. Goal setting provides objectives that one is trying to achieve. Goals are a cognitive representation of desired outcomes. And finally, self-regulation refers to the ability to evaluate one's modifications to their behaviour and either reward the behaviour or discontinue it. Self-efficacy is the only concept of SCT that has been used extensively and was found to be the most powerful factor when predicting behaviour. However, the model has not been used in its entirety in the PA domain (Buchan et al., 2012).

The Theory of Planned Behaviour

The TPB has been used to understand the influencing factors of adoption, motivation, and adherence to PA (Ajzen, 1991). The theory was designed to predict and explain human behaviour in specific contexts. A central factor in TPB is *intention* to perform a behaviour. The theory proposes that 'quantity' of intention is strongly associated with the likelihood of performance of the behaviour. However, an intention can only be translated into a behaviour if one has volitional control over the behaviour. Factors that influence people's intention are attitude (evaluation of behaviour), subjective norm (belief that significant others value the behaviour), and perceived behavioural control (perceive the behaviour under their control, similar to self-efficacy). Evidence has shown that the TPB performs well in explaining intentions (Buchan et al., 2012). However, evidence that intentions prediction behaviours is lacking. This is often called the "intention-behaviour-gap" (Schwarzer, 2008). The model has also found to have a high amount of unexplained variance between intention and behaviour and it has been questioned whether researchers should rely on it solely when constructing PA interventions (Buchan et al., 2012).

The Transtheoretical Model of Change

The TTM is a stage model in contrast to the cognitive models described above (Schwarzer, 2008). Stages are described as a cyclical process whereby individuals can progress into the next stage but also regress into previous stages. There are five stages (precontemplation, contemplation, preparation, action, and maintenance) (Prochaska and Velicer, 1997). Individuals are characterized by their readiness to change when moving through the stages. In addition to the stages the theory includes the concepts of self-efficacy, temptation, perceived pros and cons of changing, and ten processes of change. Because of the practicability of the model it is very appealing to behaviour change theorists. A review reported the effectiveness of PA interventions based on the TTM and found that 73% of studies showed a positive effect in the short-term (<6 months), but only 29% of studies long-term positive effects of these interventions (Adams and White, 2003). The model has also been criticised that the proposed time-frame for the progress between the stages is not conclusive (Weinstein, 1993).

All these theories have in common that they are concerned with how people make behavioural choices and that they will engage in the behaviour based on the extent to which they expect that their choices will produce results that they value (Jeffery, 2004). So for example if one values health, then they will choose to engage in exercise if they belief that this behaviour will produce the result of improved health. Jeffery (2004) further argues, that in order to advance health behaviour interventions, theory needs to address the relationships between modifiable aspects of the environment and behaviour. And currently the extent to which cognitive processes are involved in this is questionable. Another limitation of these models is that they assume that behaviour change occurs in a linear fashion where the individual considers the pros and cons of behaviour change, evaluates the effects of the behaviour on outcome expectations, and decides to engage in the behaviour when the benefits outweigh the costs (Resnicow and Vaughan, 2006). These approaches assume a "one-size-fit-all" model and do not take into account individual differences. Furthermore, these models typically only focus on the intentional phase of behaviour change but do not account for a post-intentional phase where goals are translated into action (Schwarzer, 2008). These models have been further criticised to only focus on the initiation of behaviour change and not the processes through which a person acquires the motivation for initiation of new behaviours and maintaining them over time (Buchan et al., 2012).

In summary the shortcomings of these theories include a lack of individuality, a focus on intention formation without addressing volition of the behaviour and thus, a lack of translation into action, and not addressing the relationship between modifiable aspects of the environment and behaviour. Self-determination Theory (SDT) is a model that attempts to address the limitations of these theories. SDT is a motivational theory that describes the processes that fuel or thwart motivation and has been associated with long-term adherence of newly formed health behaviours (Ryan and Deci, 2007). Moreover, it views the environment as nurturing need satisfaction and motivation, and it explains human motivation and behaviour based on individual differences (Deci and Ryan, 2000). The theory is based on the assumption that humans are innately curious and interested to succeed which fuels their motivation for action. However, some behaviours are not inherently

interesting and the theory accounts for this with different types of motivation, which stems from the interaction between the individuals inherent active nature and the social environments that either support or thwart that nature (Deci and Ryan, 2000). Specifically, SDT proposes different qualities of behavioural regulation that vary from being fully autonomous (self-determined), behaving with a full sense of volition and choice, to controlling regulation, which involves behaving to satisfy demands that are imposed on the individual from external pressures.

3.6. Self-Determination Theory to inform a PA intervention

No one would argue against the need for motivation to get one's exercise kit on and go for a run. Certain circumstances may fuel or thwart this motivation. For example, if it is raining outside with a strong wind one is likely to need more persuasion to get motivated. But if one had been sitting all day, and feels the need to expend some energy because running is seen as an activity that clears one's mind and one gets a feel-good feeling while doing it, then the person will be much more likely to be motivated, despite the rain and wind. SDT is a motivational theory comprised of sub-theories, that explain human motivation, and studies how the environment facilitates or undermines motivation.

The theory distinguishes between two qualities of behavioural regulation, intrinsic and extrinsic (Deci et al., 1999). Behaviours are intrinsically regulated when one perceives full volitional control and autonomy in their actions, whereas extrinsically regulated behaviour refers to feelings of control and thus, no perception of autonomy in their behaviour. Furthermore, intrinsic motivated tasks are inherently interesting and enjoyable, and extrinsic motivated tasks are controlled by external factors. In other words, if an activity is done for the pure joy then the activity is intrinsically motivated. If someone plays sport because they think it will lead to fame, the person is extrinsically motivated for this activity. The way the environment and social contexts effect intrinsic motivation is described with one of the sub-theories of SDT, the Cognitive Evaluation Theory (CET) (Deci et al., 1975). Furthermore, the theory holds that extrinsic motivation can vary in the quantity of perceived autonomy. It proposes a continuum of *internalization* which includes

external regulation, introjection, identification, and integration, where the perception of autonomy is least when behaviour is *externally regulated*, and greatest when behaviour is *integrated* (Deci et al., 1994). This is also summarized as a sub-theory called Organismic Integration Theory (OIT). Being on the more autonomous side of the continuum is related to better well-being. SDT proposes three psychological needs that are necessary to achieve this sense of well-being and self-determination (autonomy, relatedness, and competence). Dissatisfaction of only one of the needs will have a detrimental effect of one's well-being (Deci and Vansteenkiste, 2004). This is described as the Basic Psychological Needs Theory (BPNT).

3.6.1. Intrinsic and extrinsic motivation

> *"Intrinsically motivated activities are ones for which there is no apparent reward except the activity itself. People seem to engage in the activities for their own sake and not because they lead to an extrinsic reward."(Deci, 1975)*

Motivation to engage in behaviour can be extrinsically or intrinsically regulated. Both regulations will initially be stimulated by a stimulus and then lead to a reward or satisfaction after the behaviour is completed (Deci, 1975). Both have in common that a stimulus will cause a behaviour and the outcome will be some sort of reward or satisfaction. However, the location of the stimulus differs between intrinsic and extrinsic regulation. If the stimulus is external to the self and imposed on oneself by the external environment, then SDT speaks of extrinsic regulation. External contingencies can be rewards like money, prizes or fame (Deci and Ryan, 1985). They are instrumental for the motivation of the behaviour to occur. Intrinsic motivation is the opposite. Intrinsically motivated behaviours are engaged in for the pure enjoyment of it. The reward for the behaviour is in the activity itself and not separate from the behaviour. Deci (1975) states that intrinsically motivated behaviours are those that are engaged to feel competent and self-determined and not to satisfy an external contingency. The need to feel competent and self-

determined is the basis of intrinsically regulated behaviours. These needs are within the self and not imposed by the external environment. Intrinsically motivated activities are initiated for internal and not external reason. For example, a puzzle is placed in front of someone without further instructions. The person might just pick up the pieces of the puzzle and start trying to solve it. In this case the activity would be initiated by internal reasons such as interest/curiosity and is therefore intrinsically motivated. If the puzzle is optimally challenging to the person's skill level the person will feel satisfaction for competence. In another scenario, where the person was told to do the puzzle and have it finished in 5 minutes, the person would try to solve the puzzle to please an external factor. The external factors would be time pressure and to please the instructor and thus, the activity would be externally regulated.

3.6.2. The sub-theories of Self-Determination Theory

Psychological needs theory

Intrinsic motivation is also often explained with the natural curiosity of small children (Deci and Ryan, 1985). They pick up things, play with them, bite them, touch them, and squeeze them, all in an attempt to 'figure them out'. The activity is engaged for pure enjoyment and interest. It is fully self-determined because the reasons for engaging the activity are internal to the self and not separate from the self. A child will play with an interesting toy until it loses interest or physiological needs (hunger, thirst) may become stronger (Deci and Ryan, 1985). Eventually one may lose interest in the activity if the activity is no longer challenging and specific nutriments are absent. SDT states that intrinsically motivated behaviours need to be 'fuelled' in order to function effectively and to be maintained (Deci and Ryan, 2000). The theory proposes that three *needs* need to be satisfied to maintain intrinsic motivation. These are *autonomy, competence, relatedness* (Deci and Ryan, 2000). It is important to note that not all behaviours that meet these needs are intrinsically motivated, but that in order to maintain intrinsic motivation one needs to feel satisfaction for these needs.

Autonomy

Experiments have shown that intrinsic motivation is undermined if the person does not feel that they are the origin of that behaviour. One has to be fully volitional and a sense of choice towards the behaviour to feel intrinsically motivated. Feelings that the behaviour is controlled by external contingencies, which means the perception of choice and autonomy is undermined, will thwart the feeling of intrinsic motivation. This has been demonstrated during a variety of studies. An experimental example is a study by Deci and Cascio (1972). They exposed a study group to an extremely noxious sounding buzzer when the puzzle was not completed within a given time. Thus, the experimental group was under pressure to solve the puzzle within the time limit to avoid the sound of the buzzer. The control group did not have the threat of the buzzer. Intrinsic motivation after the experiment was lower in the experimental group compared to the control group. Other external contingencies were tested experimentally and all undermined intrinsic motivation. These findings demonstrate that external rewards undermine intrinsic motivation. People feel controlled by the reward which undermines feelings of autonomy. The activity is not completely autonomous because it is engaged to avoid punishment or satisfy and external need (e.g. monetary rewards) (Deci and Ryan, 2000). More examples will be given in the section 'Cognitive Evaluation Theory'.

Competence

Intrinsic motivation is also effected by feelings of competence. Feeling competent at an activity enhances intrinsic motivation and feeling incompetent decreases intrinsic motivation for that activity (Deci and Ryan, 1980). To illustrate this claim, imagine someone engaging in an intrinsically motivated activity such as an interesting puzzle. If the person solves the puzzle, then the success will enhance feelings of competence. The person will move on to the next puzzle and continue feeling intrinsically motivated as long as they get positive feedback, in terms of their ability to solve the puzzles. Positive feedback has been demonstrated to enhance intrinsic motivation in several studies (Deci et al., 1999). The feedback can be positive performance feedback from the activity itself, positive verbal feedback, or praise. Verbal feedback can be administered by oneself or by another person but

to enhance feelings of competence the feedback has to be positive and informational about one's performance. Harackiewicz (1979) found that intrinsic motivation was increased if students received positive verbal feedback for solving hidden figure puzzles. Furthermore, Arnold (1976) found that positive feedback from the activity itself resulted in higher perceived competence and increased intrinsic motivation for the task.

Relatedness

The role of relatedness in the maintenance of intrinsic motivation is a more distant one than that of autonomy and competence (Deci and Ryan, 2000). Autonomy and competence are strongly connected, that is a task is not truly intrinsically motivated without feeling self-determined to act. And the task will not be continued if feeling of competence is not satisfied. Therefore, both needs for autonomy and competence need to be satisfied to feel intrinsically motivated (Deci and Ryan, 1985). However, one can feel self-determined and competent to engage in a task without feeling connected to a significant other. For example, one happily plays a jigsaw puzzle by themselves. Yet, relatedness plays a role in engaging an initially extrinsic regulated behaviour. One is more likely to engage in an extrinsically motivated behaviour if a significant other that one feels connected to values that activity. A significant other can be a teacher, a family member, or a peer group. Feeling relatedness will shift the motivation regulation from a more extrinsic one to a more intrinsic one. Ryan, Stiller and Lynch (1994) showed that children expressed more perceived autonomy and control for learning if they experienced their teachers and parents as more caring.

Cognitive Evaluation Theory

Other than in drive theories, where the initiating force of behaviour can be simplified to a need to restore a biological equilibrium in the tissue, the factors that enhance intrinsically motivated behaviour according to SDT are of a psychological rather than physiological nature. Although, SDT acknowledges the existence of physiological drives, it is primarily concerned with the psychological processes that underlie intrinsically motivated behaviours (Deci and Ryan, 2000). As previously

defined, people engage in intrinsically motivated activities because the reward is inherent in the activity. The activity is interesting and there is no apparent external reward. Engagement in most activities, however, is not commonly inherently interesting and without expectation of an external reward. Often, one is doing a certain task to achieve a desirable outcome other than enjoyment and satisfaction of feelings of autonomy. People engage in activities that are not inherently interesting; for example, to avoid feelings of guilt, to please others or to get recognition. This raised questions among theorists about the determining factors of intrinsic motivation, and gave rise to a great number of empirical studies. Theorists were primarily interested in what happens to intrinsic motivation if an extrinsic reward is introduced. CET suggests that the presence of salient external rewards decreases intrinsic motivation and that the absence of external rewards increases intrinsic motivation (Ryan, 1982). Several experimental studies investigating this hypothesis found support of this. Specifically, tangible rewards (e.g. money, prices, awards) let to a decrease in intrinsic motivation (Ryan and Deci, 1985, Lepper et al., 1973, McLoyd, 1979, Deci, 1971, Deci, 1972). Verbal rewards were also investigated experimentally and generally found to increase but also to decrease intrinsic motivation (Deci et al., 1999). An important finding of the meta-analysis was that not all external events can be generalised as having a thwarting effect on intrinsic motivation. It should be distinguished between controlling and informational rewards. It was found that verbal rewards that were delivered in a controlling manner decreased intrinsic motivation, whereas informational feedback increased intrinsic motivation.

In summary, the results of these experimental studies led to three propositions on how intrinsic motivation is affected by external events (Deci, 1975). 1) External events affect the perceived locus of causality; this can be a change from either internal to external or from external to internal regulation. In the presence of external rewards, the perceived locus of causality shifts from internal to external causing a decrease in intrinsic motivation. If the external reward is absent and the person has feelings of choice, a change from external to internal perceived locus of causality is expected and will increase intrinsic motivation. 2) A change in perceived competence and self-determination will affect intrinsic motivation. If the context of

the task enhances the perceived competence and self-determination, then intrinsic motivation is increased. If the feelings of competence and self-determination are diminished, then intrinsic motivation is decreased. 3) External events can have a controlling or informational aspect. Informational aspects enhance competence, thus increasing intrinsic motivation. Controlling aspects facilitate an external perceived locus of causality, thus decreasing intrinsic motivation. A fourth aspect was added to the theory later, which is amotivation. Amotivating aspects of external events will undermine feelings of competence which promotes amotivation (Deci and Ryan, 1985).

Organismic Integration Theory

So far, two regulations of motivation were introduced in the previous paragraphs; intrinsic and extrinsic. Where intrinsically regulated motivation is characterised by feelings of self-determination, extrinsically regulated behaviours are lacking feelings of self-determination and are perceived as being controlled from the external environment. However, SDT proposes a multidimensional model of extrinsic regulation which suggests a variation in amount of perceived self-determination / autonomy. For example, a child that is doing their homework to avoid punishment from their parents is extrinsically regulated. The external contingency is to avoid punishment. A child that is doing the homework to get good grades is also extrinsically regulated. In this example the extrinsic contingency is to get good grades. Although, in both examples the child is extrinsically regulated, in the latter example the child values the behaviour to some extent and feels more self-determined in their actions to study. It values good grades because the child may want to go to University and is therefore driven to do well. However, the child that is doing the homework to avoid punishment can also become more self-determined in their regulation. The process of transforming a less self-determined extrinsic regulation into a more self-determined one, yet still extrinsic regulation, is called *internalization* (Deci et al., 1994). Organismic Integration Theory (OIT) details the different types of extrinsic regulations (Ryan and Deci, 2000). From left to right of the regulation continuum these are *external regulation*, *introjection, identification*, and *integration* (see Figure 1) (Ryan, 1995).

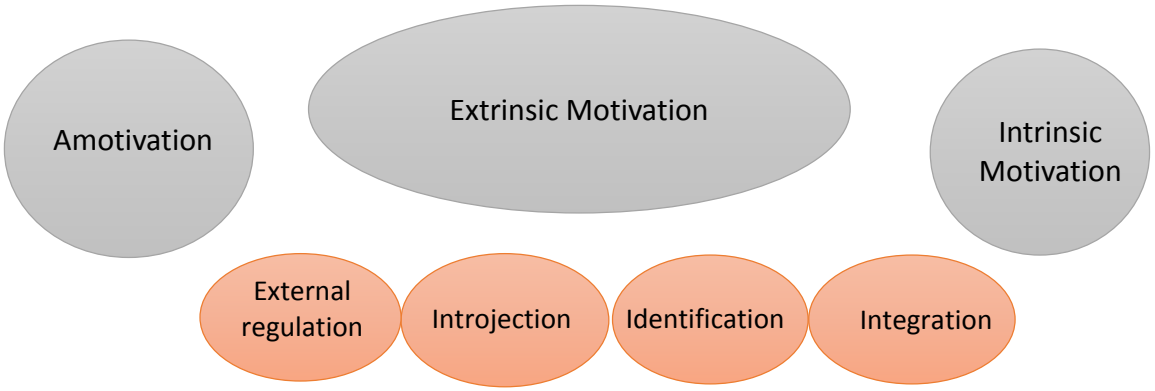


Figure 1 Continuum of human motivation (Ryan and Deci, 2000)

Amotivation is also part of the continuum, and represents a state that is lacking any intention to act (Ryan, 1995). Amotivated individuals do not value the outcomes of the behaviour, and lack competence and autonomy. To put this in an exercise context; someone who is amotivated to exercise does not believe that becoming more active will have positive health effects. Adjacent to amotivation on the regulation continuum is *external regulation* which represents the least self-determined form of extrinsic motivation (Ryan and Deci, 2000). Someone who is externally regulated performs the behaviour to satisfy a need that is external to the self. This could be someone who is seeking a reward for the behaviour or is trying to avoid punishment. The person is somewhat self-determined to act because they have a choice to do the behaviour or not. However, they do feel that the behaviour is being controlled by an external demand and the behaviour is not valued by the self. To the right of external regulation is *introjection*. This type of motivational regulation is perceived as slightly more self-determined but is still perceived to be caused by external contingencies. Integration is typically associated with feelings of pressure, anxiety or guilt. The difference to external regulation is that with introjection the controller and the controlled are the same person, whereas in external regulation the controller is a different person (Deci and Ryan, 1985). *Identification* is a more self-determined form of extrinsic motivation. The person has internalized the values of the behaviour to be part of the self and has accepted the regulation as their own (Deci and Ryan, 1985). An example from the exercise domain would be a person who regards exercising as an important activity for

improved well-being. The person makes an autonomous choice to exercise because they value the physical and mental benefits that are experienced with exercise. *Integration* is the most autonomous form of extrinsic motivation. Here the regulation is integrated into one's self and without conflict. One is completely congruent with the values of the outcomes of the behaviour. For example, a yoga teacher has integrated the values of the activity to be part of their own. It is not only a behaviour but a part of one's life. Although, integration has a lot in common with intrinsic motivation, it is still extrinsic because the outcome is separate from the behaviour itself. It is not performed for the inherent enjoyment of the activity itself. Intrinsic motivation is at the far right of the regulation continuum. This regulation is separate from extrinsic regulations because it is fully autonomous. Intrinsically motivated behaviours are engaged in for the inherent enjoyment of the activity and satisfaction lies within the activity itself.

Note that the continuum is not a stage model and one can begin at any behavioural regulation. Depending on situational factors one can shift from one to a different regulation. One can be 'identified', and under controlling contexts move to external regulation. Or one may feel tension and pressure when first exposed to an activity but if the reward is not experienced as controlling then that person could shift to a more intrinsic regulation.

3.7. Why is SDT a promising model for behaviour change in the PA domain?

SDT theory has been widely used in smoking cessation trials and medication adherence studies, but there is still a lack of intervention studies in the PA activity for health domain. Despite a lack of SDT-based PA interventions, a number of cross-sectional studies have tested the relationships between variables of SDT and exercise behaviour (Teixeira et al., 2012). A systematic review of SDT studies identified 66 studies based on SDT of which 37 used a cross-sectional design, ten a prospective design, two a mixed design, and seven an experimental design. The review found a consistent positive association between autonomous regulations for exercise and exercise behaviour disregarding the design of the study. A negative association was consistently reported between controlling regulation and exercise

behaviour. For the different types of motivational regulation, there was a consistent positive correlation between exercise behaviour and intrinsic (91% of samples) and integrated regulation (85% of samples), and identified regulation (75% of samples). This indicates that intrinsic and integrated regulations are the strongest predictors of exercise behaviour, but identified regulation also plays an important role. This seems slightly contradictory to SDT, because identified regulation is more externally regulated than integrated and intrinsic regulation. But it has been argued that at the start of an exercise programme, or the start of any new behaviour that is not inherently interesting, the reasons for taking part are predominantly external reasons (Ryan, 1995) (Vallerand and Reid, 1984). This explains why identified regulation also is positively correlated with exercise behaviour. Introjected regulation produced mixed results with 30% of the study samples showing a positive association, 5% a negative association, and 65% no association with exercise behaviour. Gender analysis found a trend for a positive association for females and a negative association for males between introjected regulation and exercise behaviour. The psychological needs for competence, autonomy, and relatedness were also reviewed. Competence was the strongest positive predictor of exercise behaviour followed by autonomy. Relatedness showed no correlation but there was a trend towards a positive correlation. This also has been discussed previously. It is argued that relatedness plays an important role in initiating a new behaviour, because often it is a friend or someone whose opinion we value, who introduces us to a new behaviour (Deci and Ryan, 2000). The authors also reviewed the association of motivational regulation with the stages of change for exercise. Findings are also coherent with the theory. Autonomous regulation increased across the stages of change being the highest in the maintenance and action stage and the lowest in the preparation stage. Controlled regulation was highest in the preparation stage and lowest in the maintenance stage.

Although, Teixeira (2012) only examined the relationships of self-determination with exercise behaviour, other benefits associated with self-determination have been reported. Higher levels of self-determination have been related to higher attendance to exercise regimes (Ryan et al., 1997), higher attendance at intervention programmes (Williams et al., 1996), higher maintenance rates of

health behaviours such as smoking cessation (Williams et al., 2009b), weight loss (Williams et al., 1996, Silva et al., 2010a), and higher levels of PA (Mullan et al., 1997, Standage et al., 2008, Milne et al., 2008) (Wilson et al., 2006a, Chatzisarantis and Hagger, 2009, Wilson et al., 2002). Furthermore, more autonomous regulation has repeatedly been related to better quality of life, more vitality, better well-being, and positive mood. Autonomous regulations and psychological needs of competence and autonomy have consistently been demonstrated to be important mediators of healthier behaviours. Perceived competence was positively related with attendance to an aerobics class throughout the term at a University gym. People with higher perceived competence were also less likely to drop out (Ryan et al., 1997) . Intrinsic and identified regulation were shown to be more strongly correlated with exercise participation at University based exercise classes (Wilson and Rodgers, 2002). A weight loss study that assessed constructs of SDT found that autonomy oriented participants displayed a higher attendance at weekly group meetings over a 6-months intervention period. Autonomous reasons for weight loss were also significant related to more exercise at a 23 months follow-up. (Williams et al., 1996) Participants who expressed controlled reasons for weight loss were more likely to drop out, and attend less group meetings. Moreover, exercise frequency has also been linked to more self-determined regulation. Duncan et al (2010) assessed gym participants for their exercise behaviours and exercise regulation. Integrated and identified regulation was a positive predictor of exercise frequency in both males and females. Duration at each exercise session was also predicted by a highly self-determined exercise regulation; integrated regulation.

3.8. Application of Self-Determination theory in PA interventions

As identified in Teixeira's systematic review of exercise studies based on SDT, there is still a lack of PA interventions in this field. Edmunds et al (2008) compared two aerobics exercise classes in terms of attendance, psychological needs and motivational regulation. One of the classes was taught in an autonomy-supportive style and the others were taught as the teacher normally does. The SDT group exhibited a significantly greater increase in competence and relatedness over the study period. Attendance was also significantly higher in the SDT group compared

to the control group. For both groups introjection increased significantly and linearly over the study period and there were no other differences between the groups in motivational regulation. An explanation for the lack of group differences could be that the students were entered into a £50 prize draw as an incentive to take part in the study. Prizes have been demonstrated to thwart intrinsic motivation. Participants could have felt pressured in attending the exercise classes, although they were told that it was voluntary. The prize draw could still have had an effect on their perceived causality of the behaviour and it may have been shifted towards a more external causality.

A 12-week PA counselling study based on SDT reported significantly differences between the control group and the autonomy-supportive counselling groups in autonomy support index and levels of PA in favour for the experimental group (Fortier et al., 2007). However, Cardinal et al (2004) found no group differences after a 2-month mail intervention. Only women increased their PA activity levels, but this was regardless of group allocation. Perhaps the intervention was not intensive enough. All the other interventions that showed positive outcomes in favour for the SDT group had personal contact with the experimenters. Maybe the need for autonomy and competence cannot be satisfied without interpersonal contact. Although, relatedness has been found to play a minor role in behaviour change, it is however considered to be important to initiate change. To date, only one long-term behaviour change intervention in the domain of exercise and health has been conducted. A randomized controlled trial of a 1-year behavioural intervention for obese women showed significant higher levels of exercise after the intervention (Silva et al., 2011) . Participants in the intervention group received 30 theory workshops aimed at increasing PA levels and energy expenditure. After one year, the intervention group achieved significantly higher levels of moderate and vigorous intensity exercise and weight loss in comparison with a control group who received general health advice only. More specifically, mean exercise levels and percentage weight loss in the intervention group were 300 min per week and -7.3%, as opposed to the control group (179min per week, -1.7%). The differences between groups were still significant after 3 years. The authors also found that maintenance of PA behaviour at 2 years was predicted by autonomous regulation

at 1 year (Silva et al., 2010a). Moderate and vigorous PA was positively related to intrinsic motivation (Silva et al., 2011).

3.9. A final comment- why Self-Determination Theory stands out from other theories

There are 83 behaviour change theories described in the literature, yet only four of these have been dominating the development of behaviour change interventions (Michie, et al, 2014). SDT was not one of the four. So why did I choose SDT over the other, more frequently used theories?

I have already provided an account of the reasons that make SDT a promising model for long-term maintenance of behaviour change, and will not repeat these here. Rather, this section will provide a personal comment on making the choice for SDT.

When I did my research to decide which theory to use, I noticed something about the other behaviour change theories- they did mention motivation as an ingredient for successful behaviour change, but they did not explain how motivation is fostered. When reading about these theories, I felt that there was a strong disconnect between the environment that the theory was attempting to alter in order for behaviour change to occur, and the processes that affect motivation and finally lead to successful behaviour change. I felt that other theories attempt to create an environment outside of the individual that is likely to produce cognitive changes in the individual, and lead to behaviour change, but they fail to explain the processes that fuel or thwart the motivation for behaviour change. SDT in contrast, attempts to change the 'environment' inside the individual to become more volitional/autonomous and describes what fuels this motivation. It also distinguishes between different qualities of motivation and acknowledges that certain environments can lead to extrinsic or intrinsic motivational regulations. If we understand what processes in the environment fuel or thwart the desired quality of motivation, then we can effectively design an intervention to allow for internalisation of motivation to occur.

For example, theories are often concerned with 'goal setting' as a facilitator for behaviour change. Goals are objectives one tries to achieve. The theories do not

take into account the nature or motives of these goals, which can be extrinsic (e.g. weight loss), or intrinsic (e.g. to enjoy oneself). Therefore, the motives of these goals can have enhancing (if they are intrinsic) or thwarting (if they are extrinsic) effects on motivation. In SDT, the contents of individuals' goals are called motives, which are classifications of outcomes that individuals approach or avoid (Ingledew and Markland, 2008). Motives such as appearance and weight management have been shown to be experienced as controlling and motives such as personal challenge and social affiliation tend to be experienced as autonomous (Ingledew and Markland, 2008). Therefore, if 'goal setting' is used purely as a means to provide the target individual with an objective that they want to achieve, it can have detrimental effects on motivational regulation and thus, likely not lead to long-term behaviour change.

Therefore, I chose SDT because I belief that the theory attempts to personalise behaviour change, by empowering the target individuals to make autonomous decisions about their desired changes. The environment that facilitates that change is not an artificial one that is only present during the intervention, or the behaviour change programme. Rather, SDT prepares the individual to identify the components that intrinsically motivate the individual to perform the desired behaviour.

3.10. Summary

An insufficient number of people are meeting the current PA guidelines. There is a national interest to motivate more people to meet these guidelines, which not only benefits the individual's health but also decreases costs to the National Health Service. Interventions have attempted to increase PA levels in different settings, and studies have targeted healthy individuals and risk populations for specific diseases at individual, local and national levels. However, the success of interventions, has only been realised in the short-term and not the long-term. Large heterogeneity among interventions make it difficult to identify the components that work and the ones that don't. As a result, the field has been slow to advance. Although, there is some evidence for interventions being successful in the long-term, these interventions continued some form of intervention during the follow-up time. If the population is to change the PA behaviour, then interventions have

to also be successful beyond the intervention period. Many behaviour change theories have been used to inform behaviour change interventions, but they have not been superior to atheoretical interventions in successfully changing PA behaviour, especially in the long-term. Although, these interventions are teaching people cognitive skills that are linked to greater PA participation (self-efficacy for example) the evidence that they bridge the intention-behaviour gap is lacking. These theories have been criticised on the basis that they are concerned with how people make behaviour choices, and do not address the relationships between modifiable aspects of the environment and behaviour. SDT was identified as a model that addresses the limitations of commonly used theories such as the TTM, TPB, and SCT. Unlike the other models, SDT regards the environment as to be nurturing need satisfaction and motivation, and explains motivation based on individual differences. Thus, this model was chosen to inform the PA intervention studies of this thesis. In the next chapter the PA intervention will be described including details of how SDT was implemented in its development.

Chapter 4

Evidence-based instead of evidence-inspired: A description of a PA intervention for people at increased risk of and recovering from CRC

4.1. Introduction

In the previous chapter it was established that poor intervention description, and lack of fidelity to purportedly used behaviour change theories have hindered the field to move forward. Thus, we cannot clearly say which techniques are effective in behaviour change and which ones are not. However, some techniques have been identified that were more likely to lead to behaviour change in the short-term and the long-term but due to a small number of studies and poor methodological detail, more research is needed.

SDT forms the underpinning theory of the PA interventions in this thesis, and this chapter will describe how the tenets of SDT were used to inform this intervention and develop the components to facilitate behaviour change. Nevertheless, since a variety of techniques may lead to more positive intervention effects, some of these techniques were integrated into the PA behaviour change interventions. We aim to describe the intervention in detail according to the Template for Intervention Description and Replication (TIDieR) which was developed by a group of researchers to guide authors with the description of interventions (Hoffmann et al., 2014). This was developed to address the poor reporting of interventions in the literature.

SDT was described in detail in the previous chapter as a motivational theory which states that humans are inherently active and self-motivated. However, people can also be passive, feel controlled and disaffected (Ryan and Deci, 1985). The difference between these motivations is explained as intrinsic and extrinsic motivation, respectively. The theory further states, that to feel intrinsically motivated (inherently active, self-motived), three basic psychological needs have to be satisfied, which are *autonomy, competence*, and *relatedness*. Autonomy is the need to feel volition and choice over one's activities, competence is the need to be competent at an activity, and relatedness is the need to feel close to others. Moreover, motivation is not described in quantitative terms, but in qualitative terms. The quality (and not quantity) of motivation is important to drive behaviour and not quantity. Thus, extrinsic regulation is split into four categories (external regulation, introjection, integration, identification) based on the amount of self-determination (autonomy) experienced. External regulation is characterised by the

least amount of autonomy, and identification by the most (Deci and Ryan, 2000). Individuals can be motivated for different reasons, and the process by which one becomes more autonomous in an activity is referred to as *internalization*.

SDT has been applied in the field of exercise and sport, and the different qualities of extrinsic regulation have been shown to explain exercise behaviour. Autonomous regulations were consistently found to be associated with exercise behaviour. Mullan and Markland (1997) investigated the relationship between behavioural regulation and the stages of change for exercise behaviour which are described in the transtheoretical model (precontemplation, contemplation, preparation, action, maintenance) (Prochaska and Velicer, 1997). Workers (n= 314) completed a set of questionnaires to assess the current stage of change and behavioural regulation. Results revealed that individuals in the maintenance stage were significantly more self-determined than individuals in the preparation stage.

Furthermore, people in the preparation stage scored higher on external regulation than exercise maintainers. Other studies have also found an association between more autonomous regulations and higher attendance and adherence to exercise programmes, and higher maintenance rates of health behaviours (Williams et al., 1996, Mullan and Markland, 1997, Standage et al., 2008, Ryan et al., 1997). Apart from exercise adherence, exercise intensity has also been predicted by more self-determined behavioural regulations (Standage et al., 2008). Autonomous motivation was shown to positively predict moderate-intensity exercise bouts of at least 10 min and 20 min. Furthermore, self-determined exercisers were also more likely to accumulate 30min of PA per day, coherent with the current PA guidelines. Another strength of the theory is that the mechanisms by which an intervention based on SDT influences PA behaviour have been tested. For example, in a sample of obese women receiving an autonomy-supportive intervention based on SDT, that in the intervention group, the treatment significantly and positively affected need support (autonomy and competence) (Silva et al., 2010a). Both, autonomy and competence, positively affected intrinsic, identified and to a lesser degree introjection. Autonomy also negatively affected external motivation. Intrinsic regulation was the strongest significant predictor of moderate and vigorous PA. This relationship has been illustrated in Figure 2.

4.2. Aim

The overarching aim of the PA intervention was to develop an intervention based on SDT, to assess the feasibility of implantation in older people at elevated risk of CC, and to obtain preliminary data of indicative effects in relation to a number of key health outcomes, including quality of life, and PA behaviour. Variables of SDT were also assessed to evaluate whether the intervention successfully can change more externally regulated motivations into more internally regulated motivations in the context of PA. In the light of these aims, two hypotheses were formulated. 1.) An autonomy-supportive intervention will lead to an increase of PA levels post-intervention, and these levels will be maintained at follow-up. 2.) Participants in the intervention group will decrease more controlled regulations (amotivation and extrinsic regulation) and increase more autonomous regulations (integrated, identified and intrinsic regulations) compared to a control group.

We conducted two randomised controlled feasibility studies, one in people with identified polyps/adenomas at colorectal screening (PARC- PA and Risk of CC) and another with CRC survivors (MOVE- MOtiVation for Exercise- promoting an active lifestyle after CRC). Essentially, both interventions were based on the same framework. The only difference is the duration of the interventions. PARC lasted 6 months, with a 6 months follow-up, and MOVE lasted 3 months with a 3 months follow-up. The follow-up time was a 'true' follow-up without contact, apart from mid-point assessments with PARC participants. All components of the interventions (PARC and MOVE) were the same. MOVE was carried out after PARC, thus, the same material was used for MOVE. Therefore, this chapter will not describe PARC and MOVE separately, rather describe one intervention protocol with specific details being described in relevant chapters (PARC in chapter 5 and MOVE in chapter 6).

A brief overview of the reasons for the two different study populations (PARC and MOVE)

As mentioned above, one intervention included patients with a pervious diagnosis of bowel polyps (PARC) and the other intervention included patients previously diagnosed with CRC (MOVE). Originally, the thesis was to only include the PARC trial, consisting of a 6 months intervention and a follow-up at 12 months. The

importance of healthy lifestyle changes in this population have been highlighted in chapter 2. While I was conducting the literature search for this study, I grew more aware of the potential benefits of PA for survivors of CRC as well. It became clear that there is a need for lifestyle behaviour change interventions in this population as well, but that there is a lack of interventions exploring the effects of PA interventions in CRC survivors (Bourke et al., 2013).

At this point, the recruitment for PARC was already underway, and the end of the research time as a PhD student drew closer. I have made very good connections with the clinical consultants, and together with my supervisor and the consultant we discussed my interest in a second intervention with people previously diagnosed with CRC. This meant that I had to complete another application to the local research and ethics committee. Because there were strict deadlines for the completion of data collection for my thesis, which was in less than 1 year from that time, I had to re-think the components of the MOVE intervention. It was not feasible to have an intervention of 6 months duration and a 12 months follow-up. Therefore, it was decided to reduce the duration to 3 months, with a follow-up at 6 months. This was also considered as an opportunity to monitor motivational regulation over similar time points as in the PARC trials, and if the data would allow, draw conclusions about the effects of different intervention durations on maintenance of changes in motivational regulation and PA behaviour (Fjeldsoe et al., 2011).

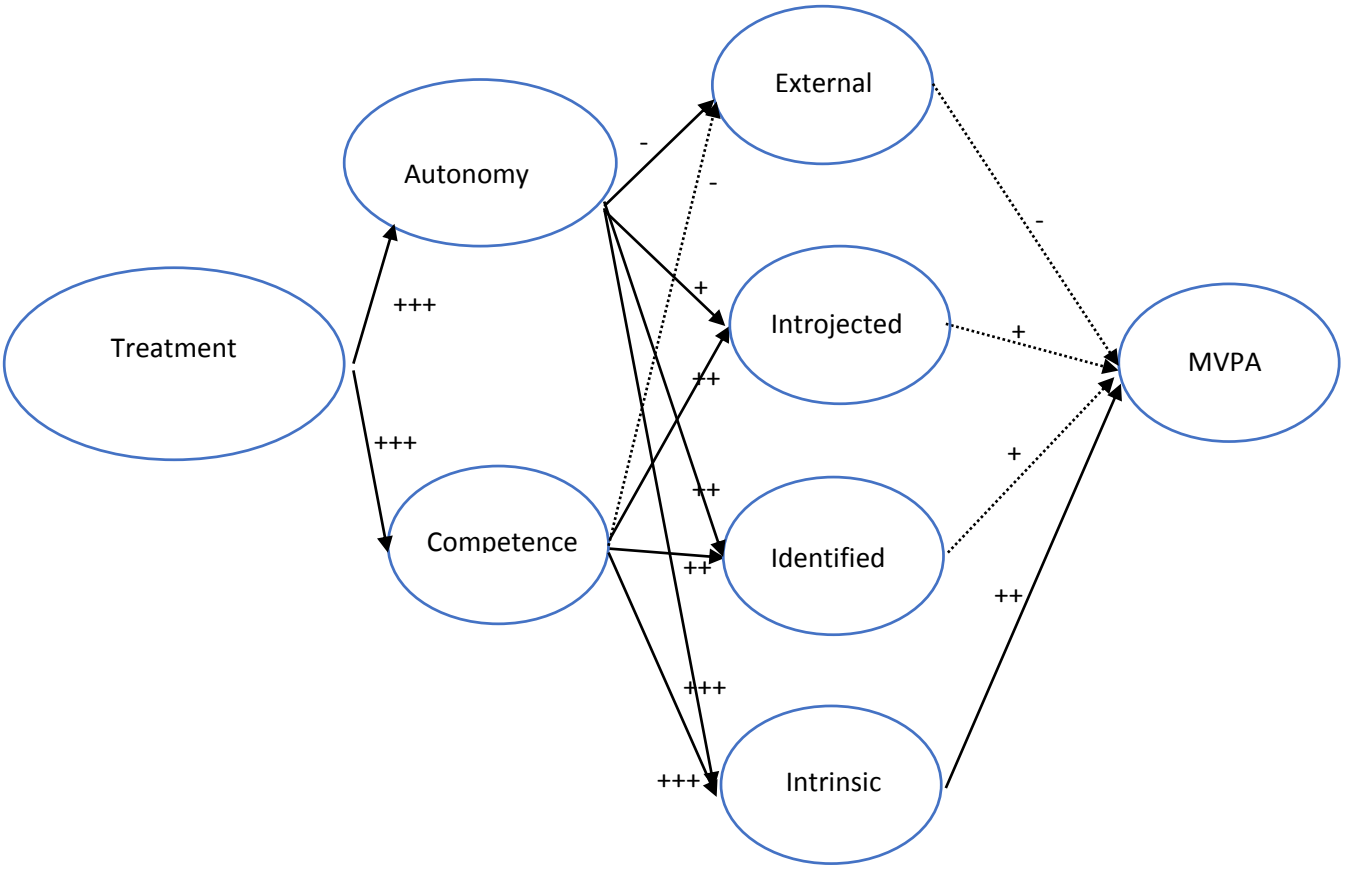


Figure 2 Treatment effects of an autonomy supportive intervention on need satisfaction and behavioural regulation.

Solid lines indicate significant effects, and dashed lines non-significant effects. Strength of positive (+) and negative (-) are indicated. MVAP=moderate to vigorous intensity PA

4.3. From theory to practice

According to SDT, if the three psychological needs for autonomy, competence, and relatedness are satisfied, one will feel more intrinsically motivated. Thus, the goal of the intervention was to support these needs to facilitate internalization of less autonomous behaviour into more autonomous behaviours. For internalization to occur Deci et al (1994) suggested three contextual events that will to promote internalization. These are: a) providing a meaningful rationale, b) acknowledging the behaver's perspective, and c) conveying choice rather than control. Furthermore, we used the proposition which were formed as part of the Cognitive Evaluation Theory which were found to facilitate intrinsic motivation. Thus,

additional strategies in this intervention included: d) Avoiding external rewards, e) supporting the feeling for competence, and f) providing informational feedback rather than controlling feedback.

Providing a meaningful rational: This can help the individual understand the personal benefits of the target activity and makes the activity personally meaningful. For example, if a patient with Type 2 Diabetes who dislikes PA is told to walk 30min daily, a meaningful rationale for doing it might be so that the patient may become less dependent on his expensive medications because of the benefits of PA. The request to do the walking activities could result in an internal conflict and result in feelings of pressure because the activity is not intrinsically motivated. Acknowledging the behaver's perspective of the conflict conveys respect for the person's reluctance to perform the activity and provide the feeling of choice. Thus, it can alleviate internal conflict and tension and the person can come to understand that the requested behaviour does not have to be in disharmony with his reluctance. In the above example, one could say "I know it is difficult to make time to walk 30min per day". This conveys to the patient that the feelings of reluctance are legitimate. This has been supported by a study where children were working on a painting task and limitations were set on being neat. When the children's inclination to being neat were acknowledged their feelings for intrinsic motivation for painting were maintained, compared to the children that were not acknowledged their feelings of not wanting to paint neatly (Koestner et al., 1984). However, it is also important how acknowledgement and rationale are presented. Specifically, it is important to convey choice rather than control when presented with a rationale or acknowledgement. This can be achieved by avoiding controlling language such as "have to", "must", and "should". If the language is not controlling the person will feel choice about the activity which further will enhance feelings of autonomy. This has also been supported by studies showing that pressuring language decreases intrinsic motivation compared to non-controlling language which increased intrinsic motivation (Ryan et al., 1983, Ryan, 1982). Likewise, avoiding external rewards is also associated with more intrinsic motivation. External rewards are instrumental for the motivation of the behaviour, thus thwart the feeling of autonomy and with it intrinsic motivation. One of the earliest studies

investigating the effects of external rewards on intrinsic motivation was a study by Deci (1971). In this study, participants were engaging in a puzzle solving activity and the experimental group received monetary rewards for each puzzle solved. Intrinsic motivation was higher in the non-rewarded group compared to the reward group. Many other studies have been conducted introducing other external rewards, such as prizes and awards, and confirmed these original findings (Ryan and Deci, 1985). Another strategy to facilitate intrinsic motivation is the support for feelings of competence. One has to feel competence for a task, or a sense of mastery for a task to be able to engage in it. This also requires that the task is 'manageable', meaning one has to feel capability to do it. If it is beyond one's capabilities, the performance feedback inherent in the task will decrease competence, and if the feedback is positive, competence will be enhanced. As an example, if a beginner to exercise starts with a marathon run, they will not be likely to complete this task and loose sense of capability, and thus, not feel competence for this task. However, if the beginner starts with a 10 min jog at any pace they choose, then they will feel a sense of competence after completion of the task because they are very likely to achieve this. Competence is facilitated when individuals have clear and realistic goals, and believe they have the capabilities of engaging in the behaviour. Finally, providing informational feedback rather than controlling feedback. Informational feedback has generally been found to increase intrinsic motivation, but if it is conveyed in a controlling way, can also decrease intrinsic motivation (Deci et al., 1999).

These strategies were incorporated into supervised exercise sessions, and into counselling workshops. Some examples of how these appear in the description of supervised exercise sessions, and workshops further along in this chapter.

Motivational Interviewing as a tool to translate SDT into action

"If you treat an individual as he is, he will stay as he is, but if you treat him as if he were what he ought to be and could be, he will become what he ought to be and could be."

—Johann Wolfgang von Goethe

The founders of MI, Miller and Rollnick, define MI as "a client-centred, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence" (Miller and Rollnick, 2012b). Person-centred means that the focus is on the concerns and perspectives of the individual. It does not aim to teach the individual new coping skills, or reshape cognitions but rather to focus on the person's present interests and concerns. The interviewer addresses ambivalence in the person by eliciting and selectively reinforcing *change talk* and then responding to resistance in a way that is intended to diminish ambivalence. This will move the person toward change. The authors emphasize that MI is a 'spirit' of communication rather than a set of techniques to be followed. The facilitator elicits knowledge, skills, information from the person, and thus, makes use of the skills that are already present within the person himself. Thus, it does not impose change through extrinsic means such as punishment, pressure, or rewards. The person will change when he is ready to change by focusing on the motivational processes within the individual that facilitate change. This way, any change the person decides to make will be consistent with the person's own values and beliefs. There are four strategies that are used to facilitate *change talk* and these are: a) the expression of empathy by the facilitator (counsellor), b) the development of discrepancy, c) rolling with resistance, and d) support for self-efficacy. The counsellor's empathy is important to make the client comfortable and provide the conditions for a successful exploration of change talk to take place (Miller and Rollnick, 2012a). The principle of developing discrepancy is based on the exploration of pros and cons of the behaviour. This will create an awareness of the discrepancy between the client's current behaviours and his goals and values. Rolling with resistance is another important strategy. This involves avoidance of countering the client's arguments against change. Argumentation will increase resistance in the client which in turn will reduce the likelihood for change. In the event of resistance, the counsellor is to accept the feelings of the client as normal and must not impose goals or strategies. The final principle is based on self-efficacy. MI recognizes that the intention to change a behaviour is not enough to engage in change. The person has to believe that they are capable of the behaviour.

This brief description of MI shows a striking resemblance to the ideas of SDT. Even in the definition of MI the authors use the concept of 'intrinsic motivation'. It has previously been pointed out that SDT can provide a theoretical framework for MI (Ginsburg et al., 2002). Markland et al. (2005) expanded on this suggestion and argued that SDT can provide a useful theoretical framework for understanding MI's efficacy. The authors contend the style and specific strategies of MI provide support for the needs for competence, autonomy, and relatedness. Change talk in the spirit of MI can foster behaviour change by promoting the internalization of new behaviours so that the motivation is self-determined. This is illustrated in Figure 2. In MI the counsellor facilitates competence by providing a clear information about behaviour and its outcomes. This enables the client to set realistic goals. Positive feedback and a non-judgemental atmosphere will further support competence. Autonomy is accommodated by exploring discrepancies of behaviour change (pros and cons of behaviour change) and thus, exploring options. This will encourage the client to makes choices over their preferred course of action. The emphatic relationship between the client and the counsellor supports the need for relatedness. This is further supported by the genuine interest in the client conveyed by the counsellor and the avoidance of criticizing choices and opinions of the client.

MI finds a lot of support in practice and from over 200 randomised controlled trials (Vansteenkiste et al., 2012). Trials have tested MI in a variety of populations and settings, including substance use, health-related behaviours, medication adherence and demonstrated its effectiveness (Lundahl et al., 2010). Because MI has been developed based on years of experience of counsellors, rather being developed based on empirical findings, it is lacking explanations for why it works (Vansteenkiste et al., 2012). SDT on the other hand is based on empirical evidence, but is lacking a 'recipe' of how to implement the model into interventions. Although, further research needs to confirm the relationships between MI and SDT variables, its availability to non-psychologically, but in MI trained counsellors, make MI an attractive tool for an autonomy-supportive intervention based on SDT.

In summary, MI and SDT appear to speak the same language. Both models differentiate between intrinsic motivation and extrinsic motivation (Miller, 1994).

This is largely agreeable with SDT, however SDT acknowledges that extrinsic forms of motivation can also be autonomous. And it was shown that new behaviours are not likely to be intrinsically motivated, but regulated by more autonomous extrinsic regulations (Mullan and Markland, 1997). Thus, from a SDT perspective MI techniques will be more likely promote autonomous extrinsic motivation for change rather than intrinsic motivation (Markland et al., 2005). Despite this, both models agree that the person is the centre of behaviour change, and that for behaviour change to occur the person's beliefs and attitudes have to become consistent with personal values. During change talk the counsellor, when expressing empathy and communicating in the 'spirit' of MI, can facilitate the three basic needs proposed by SDT (Figure 2).

Thus, we used MI as the basis for PA counselling workshops which were part of the intervention. The content of the workshops will be described in the next section.

4.4. A general overview of the intervention

This section will give a brief description of the interventions. As previously explained, this will be a general description to include both studies in the thesis. A more detailed description of each individual study will be found in relevant chapters. Here, we will only summarize the components that are the same for both studies which were informed by theory. Durations of intervention components will not be presented here because they differ for both trials. The emphasis is therefore on the theoretically informed content of the interventions.

Study design

Both studies were feasibility studies with 2-armed randomised controlled trial (RCT) design. After baseline assessment participants were randomized to either a standard care group (SC) or an active lifestyle programme (ALP). The ALP was offered supervised exercise sessions and behaviour change workshops. SC was encouraged to continue with their usual lifestyle habits and only attended the research facility for follow-up assessments.

All assessments and intervention components were delivered in a small research facility at the Medical School of the University of East Anglia.

The study was approved by the NRES Committee East of England, Norfolk, the Research & Development Office of the Norfolk and Norwich University Hospital (NNUH), and the Research and Enterprise Service at the University of East Anglia.

Participants

Participants were either patients identified via the *National Bowel Cancer Screening Programme*, the colonoscopy attendance register, or CRC register at the Norfolk and Norwich University Hospital (NNUH).

Recruitment

Potentially eligible participants were sent an invitation letter signed by the Consultant Gastroenterologist. The letters contained contact details of the specialist nurses and the researcher and it was at the patient's discretion to contact the research team. If contact was made, the patient was screened for inclusion criteria on the phone, and invited to come to the research facility for an informational meeting if they were interested in participating. Patients were also approached during colonoscopy clinics. In this case, the first person of contact was a nurse, who asked the patient whether they would like to speak to a researcher. If the patient agreed, then a researcher briefly explained the study to the patient, and provided them with a patient information sheet. The patient also signed a consent form to be contacted by the researcher, and the researcher would then contact the patient one week after initial contact to determine interest in participation and schedule an informational meeting at the University of East Anglia.

At the informational meeting the researcher obtained study consent, and carried out baseline assessments to determine final eligibility.

Randomization

Participants were randomized after all baseline measurements were completed. Randomisation was carried out with a technique called *Covariate Adaptive Randomisation*. This method is a 'minimization' method by which the decision to allocate participants to a particular group is based on trying to "balance" the particular covariates that are deemed to be important in the experiment. In these

studies, the covariates risk status, age, gender, and BMI were identified, and allocated as equal as possible between the SC and ALP. To start with, the first few volunteers were just randomly allocated, and for subsequent participants, the use of Covariate Adaptive Randomisation was applied. This minimizes the differences between the groups in terms of these covariates. This method has been deemed highly effective (Scott et al., 2002).

The randomisation was carried out by a person (JD) independent of the research team. JD emailed the allocation to the researcher who carried out the exercise sessions, the motivational workshops, and follow-up assessments (apart for fitness assessment). Thus, this researcher was not blinded to the allocation of participants. Blinding was not possible because the small number of researchers that were part of the project.

Intervention

Standard Care group

The SC was encouraged to continue with their usual lifestyle and refrain from changes to their PA habits over the study period. SC participants were not given any intervention, and received no information about PA. They were offered exercise sessions after study completion. The only contact with SC participants during the intervention was at repeated assessment appointments.

Active lifestyle group

General format

ALP was offered supervised exercise sessions twice per week for the first half of the intervention and once per week for the second half. Each session consisted of a warm-up, aerobic and resistance exercises, and cool-down stretches lasting in total 60min. Exercise took place in small groups of two to five people. The times and days of the intervention components were flexible and scheduled to suit participant's availability. Participants made a group decision and agreed on the days of the week where most people were available to schedule the supervised exercise sessions.

Participants who were unavailable for these group sessions met the exercise facilitator at a different day or time.

Behaviour change workshops to aid the uptake and maintenance of PA were delivered every fortnight throughout the whole intervention period.

The exercises and the workshops were led by the same person. This person is a trained REPs level 2 exercise specialist and a trained motivational interviewer.

Supervised Exercise sessions

Each session lasted 60min and included a 5-10 min warm-up, a 30-40 min aerobic exercise component, and a 5-10 min cool-down period. Although, aerobic exercise was the main exercise mode during the intervention, most exercise sessions included a 10-20 min resistance exercises component. Aerobic exercise was performed at an intensity of 65-85% of maximum heart rate and a RPE of 12-14 on the Borg scale (Appendix 1). Intensities were adjusted throughout the intervention once adaption to the initial workload occurred. This was achieved by increasing the exercise workload, the number of repetitions, and the duration of the exercise.

Resistance exercise was delivered in two different ways depending on the group size. In a small group size (n<3) all participants performed the resistance exercises together with the exercise leader. Each set of exercises was repeated 12-15 times and sets were repeated 2-3 times. In a bigger group (n>3) resistance exercises were set up in a circle and each participant started with a different exercise. Each exercise was performed for 1min or 12- 15 Reps, depending on the participant's preference. The circle contained 5-8 different exercises and was repeated 2-3 times. One of the two weekly supervised exercise sessions focused only on upper body muscle groups, and the second weekly sessions only on lower body muscle groups.

Support for competence during supervise exercise sessions

At the very first session each participant was given time to familiarize themselves with the exercise equipment used during the sessions. Each person received an induction on the ergometers (treadmill, rowing machine, stationary bicycle). Participants wore a heart rate monitor and were explained the reasons for its use.

A brief explanation was given about the physiological effects of exercise and the relationship between fitness and heart rate. At this point, the focus was only on familiarization and not performance. Therefore, although the participant was informed about the target heart rate they were encouraged to exercise at an intensity that was most comfortable. The facilitator frequently asked the participant how they felt, and recorded perceived rate of exhaustion with the Borg scale. The facilitator also provided positive feedback on their performance, e.g. "You are doing very well". (Providing informational feedback rather than controlling feedback) If participants struggled with or disliked one of the ergometers, the facilitator acknowledged their worries. For example, one person struggled with coordination on the rowing machine, and this discouraged her. The facilitator acknowledged this by pointing out that this exercise requires a very good coordination and that most people struggle with this exercise when they have never done it before. It will take some practice. (Acknowledging the behaver's perspective).

After the first familiarization session, more emphasis was given to exercise intensity. If participants had difficulties maintaining the targeted exercise intensity for the period of the exercise session, they were encouraged to continue the exercise at a level that was comfortable and to include short intervals where intensity was increased. This was well tolerated by participants. The time they managed to stay in the target intensity was monitored and recorded by the facilitator. These records served as feedback for the participant. Comparisons at later sessions were made to these records, which provided the participants with positive feedback based on their own personal improvements and achievements.

As soon as participants felt comfortable with a "new" level of intensity, this was further increased until the participant was able to maintain this intensity throughout the whole exercise period. To aid the facilitation of competence, the facilitator increased exercise intensity with the help of enjoyable 'exercise games' or challenges. For example, the exercise leader projected a video to the gym wall of a mountain bicycling race in the French Alps. At hill intervals the participants were encouraged to mimic the hill climb in the video by increasing the resistance on the

stationary bicycle and to maintain the resistance as long as possible, or ideally until the end of the hill-scene in the video. Similarly, at downhill scenes in the video the participants were instructed to reduce the resistance and increase their revolutions per minute. Other strategies were the inclusion of sprint intervals, or set distance targets to be achieved at the end of the session and reduce the time that it took to achieve the distance at the next session. Another challenge was to cover the distance from John 'O'Groats to Lands' End, from the furthest North East point in the UK to the furthest South West point. Seasonal challenges, like "Santa delivering packages across the whole world" were introduced to encourage enjoyment, and build competence at the same time.

Another component of the intervention was visits to a local gym with all the participants of the intervention group to join a keep-fit exercise class for older adults of the community. These sessions served to make people comfortable in an exercise environment outside the 'safe' environment of the University facility. It was a chance to meet other exercisers at their same age and demonstrate to participants that gyms are also a safe environment to exercise at. (From experience as an activity leader, participants express a 'fear' of humiliation which prevents them from going to a gym. They feel uncomfortable in an environment full of young and fit people. Taking them to the gym was thought to decrease that 'fear' if accompanied by fellow exercisers thus, increasing competence).

Support for autonomy during supervise exercise sessions

Participants could choose between three different modes of aerobic exercise; cycling, treadmill walking/running, and rowing. Participants were allowed to swap between different modes of exercise throughout an exercise session but encouraged to use the equipment for at least 10 min before changing to a different activity and to maintain their target exercise heart rate during this time.

Stationary ergometers were used in every session, sometimes only as a 10 minute warm-up, and during other sessions, these were the core of the session. If they were only a means of warm-up, participants could choose from a variety of exercise formats and types of exercises they wished to engage in for the remainder of the session. They could choose from an aerobic fit class, a step class, or a circuit class.

Resistance exercise was built into all of these choices. Participants were asked which resistance exercise they wanted to do and the activity leader planned the session according to their personal choices. Depending on the preferences of the group, the facilitator offered different times of the week at which different types of sessions would take place. And the participants could choose which they wanted to attend. For example, on a Tuesday at 9am a circuit class was on offer, and at 10am a step class. On a Friday morning participants could choose from a 9am spinning class (intensive bicycle training) or a 10am 'flexible' class which was tailored to the group preferences. So, participants had a variety of options in regards to time, day of the week, and types of exercise.

Support for relatedness

The autonomy supportive environment in which the supervised exercise sessions took place were thought to support relatedness. The exercise leader maintained an emphatic and supportive relationship with the participants. Furthermore, small group sessions provide a suitable environment to encourage social connections between the participants. Participants often turned up together, and left together, thus, engaging in personal conversations which supports relatedness.

PA Counselling Workshops

Theory workshops took place every fortnight at the University of East Anglia before one of the scheduled supervised exercise sessions to reduce travel burden. Thus, these groups were also small groups with 2-5 participants at the time. The workshops lasted between 15 and 60min depending on group size and topic. The leader of the workshops was trained in MI.

MI in a group setting is different and more difficult than with individuals (Wagner and Ingersoll, 2012)(page 9). Instead of helping one individual the facilitator has to help many people make progress which requires facilitating skills to encourage interactions between the members of the group. The facilitator's tasks are to create and maintain the group, build the group culture, and activate the interactions between members. This can be challenging with people who can differ in history, beliefs, values, and communication style. When leading a MI group, the facilitator

has to be aware of the individual differences of the members, and it is a challenge to keep moving forward as a group, without moving too fast for some members, or holding back with others. There is a danger that the focus will be with one individual, instead of the whole group. It is the leader's responsibility to involve every member of the group equally.

A major benefit of groups however, is that groups bring people together to share concerns and support one another, which increases hope and confidence (page 10) (Wagner and Ingersoll, 2012). Members can inspire one another through their progress and achievements. In a group setting members can explore a variety of issues together, learning from experiences of other group members. Even if some are not talking much, listening to others talk makes other members think about their own situations. This benefits the support for relatedness.

In general, the structure of an MI group is as follows. The facilitator establishes a topical focus for the session which will be discussed by the members. The group will do most of the talking throughout the session, and it is the facilitators task to keep the focus on the topic, elicit discussion, and to guide the conversation into a productive direction helping the members to broaden and narrow their focus (page 122) (Wagner and Ingersoll, 2012).

"Shaping group focus is like directing traffic – signalling when to go, when to stop, when to change direction, and when to wait for others." (page 122 (Wagner and Ingersoll, 2012)).

This briefly describes the challenges and the benefits of the group sessions, and gives the reader an understanding of the format of these workshops. We will now talk about the topics that were discussed.

Topical focus during the motivational interviewing guided workshops

The facilitator provided a topical focus that was discussed in the session. In this intervention, the focus was on PA behaviour. The first four workshops followed a fairly similar structure, but the following workshops depended largely on the experiences of the group. An outline of the topics of the workshops can be found in Appendix 2. Earlier workshop topics were based on increasing knowledge about the

benefits of PA, some the mechanisms of action, and understanding the association between PA and CRC risk, intensity of PA and current recommended amount of PA. Following workshops focused more on goal setting, self-monitoring techniques, setting prompts, identifying barriers and strategies to overcome them, identifying PA facilities, and relapse prevention.

The first workshop was largely built on providing a meaningful rational for PA, one of the strategies proposed to enhance intrinsic motivation which was discussed earlier. It started with a question written to a board "What do you want to get out of this PA programme?" This question forced the participants to think about their personal values, and the personal benefits they wanted to gain from this. It provided the participants with new knowledge without the facilitator falling into the trap of being the educator. Once the discussion was exhausted, the facilitator asked the participants if they would like to know more about the benefits of PA for bowel health. Asking whether more information is desired gives participants the sense of a choice, and again, does not make the facilitator the educator, thus, avoiding the development of an 'unhealthy' non-MI-spirit relationship where the facilitator is the professional. After the discussion, the facilitator summarized the benefits that were elicited by the group.

Afterwards the session took on a different shape depending on the group's interest. As long as participants did not steer away from topics that were related to PA behaviour change, and in the context of bowel health, the facilitator would encourage the discussion. Generally, every group talked about the same topics throughout all the workshops, but the order of the topics was not always the same. For example, the workshop schedule was to talk about the benefits of PA in the first session, and also provide some information about the physiological principles of improving fitness and the reasons for certain exercise intensities. But often participants had other questions or concerns that were also important to be discussed. For example, some people felt unsafe and were concerned about injuries. Thus, the facilitator talked about PA intensities, risks, safety, and warning signs that would indicate danger to the participant and warrant termination of the exercise. Other people wanted to know more about the relationship between PA

and CRC, or polyps. So the facilitator talked about the evidence of the benefits of PA for the reduction of the risk of polyps and CRC. Disregarding how the first session ended, all these topics were discussed at some stage during the intervention. Other topics that were the basis of a workshop included the mechanisms which are thought to mediate the positive effects of PA on bowel health, the intensities of PA that are beneficial with examples of types of PA, the current PA guidelines for health in general and for bowel health, ways of structuring PA to accumulate at least 10 min bouts, perceived confidence to do more PA, perceived intensities of PA, building PA into one's daily life, reminders to be active, identifying friends to be active with, identifying PA facilities in the community, identifying PA that is enjoyable, setting personal realistic goals, and the evaluation of barriers.

To facilitate discussion of these topics the facilitator made use of some MI tools, for example evaluating the pros and cons of change (Figure 3). Other tools were the exploring 'importance to change' and 'confidence to change' where people are asked to rate these on a scale from 1 to 10, 1 being least 'important / confident' and 10 being very important / confident'.

NO CHANGE	CHANGE
COSTS Stay unfit, unhealthy, less flexible	*COSTS* Have less time for other things
BENEFITS have more spare time	*BENEFITS* Less depression, sleep better, better mood, health

Figure 3 Cost-benefit grid. The responses are examples from a group session

All these topics were delivered in the 'spirit' of MI and with the strategies for enhancing intrinsic motivation in mind. The facilitator refrained from using controlling language such as "have to", "should", or "need to" and instead presented information in a supportive way that encouraged the participants to

think about their personal values. None of the topics covered was delivered in an educative style. Each topic was directed as a question to the group where they were encouraged to discuss their knowledge and experiences about the topic. The facilitator only provided new information after asking the group for permission to do so.

In summary, the structure of the workshops was rather 'loose'. Although, there was a specific set of topics that were to be discussed in the intervention, the order in which these topics were explored differed for the groups depending on their interests and knowledge brought to the workshops. This approach is called a *semistructured* approach in MI groups (page 95, (Wagner and Ingersoll, 2012)). This is defined as "focusing on an identified topic, while remaining flexible to member interests and desires, and deviating from the agenda when useful". However, later sessions were generally more structured because the facilitator was more familiar with the individual members of each group and could therefore, target the group's interests and problems. Combining different approaches (unstructured, semistructured, structured) is encouraged by the authors of "Motivational Interviewing in Groups" because it allows to openly explore interests, and then shift to a more specific task force (Wagner and Ingersoll, 2012). There is currently no literature on the effects of the type of groups, because most of the MI studies have been conducted with individual MI sessions. However, there is sufficient evidence that delivering MI in groups is effective (Wagner and Ingersoll, 2012).

Chapter 5

A Feasibility study to investigate the long-term effects of an autonomy-supportive intervention on PA Behaviour in people at increased risk of CRC: a randomized controlled trial

'Physical Activity and Risk of Colon Cancer' (PARC)

5.1. Abstract

Background: Self-Determination Theory (SDT) has been used successfully as a model for health behaviour change in weight loss programs. However, the effectiveness of SDT for promoting PA behaviour change in an elderly population at elevated risk of CRC is unknown. This study investigated the feasibility of implementing an SDT approach in this population and provides preliminary evidence of its efficacy for modifying motivational regulation. *Design:* The study was a feasibility trial with non-blinded randomised controlled design. *Methods:* Participants (n=31, mean age 69y [SD= 4.9], BMI 29.3 [SD=5.1]) were patients diagnosed with colorectal cancer after completion of treatment. Participants were randomized to either an active lifestyle programme (ALP) (n=17) or the standard care group (SC) (n=14). The intervention consisted of supervised exercise sessions and physical activity counselling. SC was encouraged to continue with their usual lifestyle for the period of study. The intervention lasted 6months. Participants were followed-up 6months post-intervention. Randomization was carried with a computer program by a statistician. The intervention facilitator was not blinded to the group allocation. Data were analysed with intention-to treat analysis. The primary outcomes were the feasibility of the intervention in these populations. Secondary outcomes were variables of behavioural regulation, physical activity behaviour, physical capacity (fitness and strength), self-efficacy, intention to exercise, and quality of life.

Results: Post-intervention, 22participants (ALP n=12, SC n=10) and at follow-up 15 participants (ALP n=8, SC n=7) were available for analysis. Overall recruitment yield was 12.1% of eligible participants. Main barriers for participation for time commitment and distance to research site. Attrition post-intervention was 29% and at follow-up 43%. Attendance at the supervised exercise sessions was 62% and at the workshops was 53%. Post-intervention, ALP had lower amotivation (P<.01), and higher levels of identification (P<.01), intrinsic regulation (P<.001), relative autonomy index (P<.01), and intention to exercise (P<0.05) compared to SC. Total leisure time activity was higher in ALP compared to SC with a mean group difference of 84 min per week (P= 0.08). At follow-up the differences in behavioural regulation were not maintained. ALP did more physical activity at follow-up than SC, with a

difference in mean change for leisure-time PA of 170min (P< 0.05). There were no adverse events during the intervention. *Conclusion:* The findings suggest that SDT could be an effective strategy for promoting long-term PA behaviour change in this population. Changes in behavioural regulation and PA are comparable other studies based on SDT. A larger randomised controlled trial is needed to further explore the utility of SDT in this context.

The study was sponsored by the University of East Anglia, Norwich, United Kingdom.

5.2. Introduction

> *"If everybody in Europe were physically active for 150min per week at moderate intensity, 21% of CC cases could be prevented by 2040"* (de Vries et al., 2010)

CRC occurrence has been on the rise and is now the third most common cancer and cause of cancer-related deaths in the UK (CancerResearchUK.org). According to the latest statistics about one in 20 people will develop CRC at some point in their life. It is a disease that mostly affects older people with 95% of all cases occurring in people aged 50 years and over. Several lifestyle factors are linked to an increased risk of developing the disease, such as a diet low in fibre and high in meat, obesity, and a sedentary lifestyle. The World Cancer Research Fund (World Cancer Research Fund and American Institute for Cancer Research, 2007) estimated that 12% of all CRC cases could be prevented if people would increase their levels of PA, a further 14% by avoiding excessive weight, and another 34% by decreasing ones alcohol intake.

The UK has rolled out a Bowel Cancer Screening Programme (www.cancerscreening.nhs.uk). The two aims of the Screening Programme are to detect CRC at an early stage and to detect polyps and adenomas. These are small obtrusions in the bowel which are the precursors of CRC and will be removed if detected during a screening colonoscopy. Recent data suggests that the risk of a new adenoma after removal during a bowel cancer screening colonoscopy is around 40% after three years (Kitahara et al., 2013). The recurrence and growth of adenomas has also been linked to lifestyle, such as a lack of PA. Thus, removing the adenomas during the procedure does not eliminate the risk factors and a recurrence is likely.

In Chapter 2 we have already presented the current evidence of the role of PA in the prevention of adenomas and CRC. After examination of the evidence we concluded that there is convincing evidence that PA is associated with a 13% lower risk of developing adenomas and a 24% lower risk of CC in both, men and women.

There was not enough evidence to support an inverse association between PA and rectal cancer risk. Furthermore, it was concluded that the negative association between CC risk was most consistent with recreational PA and inconsistent with household and occupational PA. The PA recommendation of the World Cancer Research Fund is to aim for at least 30min of moderate PA daily, and to increase this to 60min of moderate or 30min of vigorous PA every day of the week. In terms of weekly PA this would be at least 210 min to 420 min of moderate intensity PA or 210 min of vigorous PA per week. This is more than twice as much than the current general PA recommendations for health published by the Department of Health which state that a minimum of 150min moderate intensity PA or 75 min of vigorous intensity PA per week is needed for the maintenance and improvement of health (HSCIC, 2012).

In light of the PA recommendations for the prevention of CC (World Cancer Research Fund and American Institute for Cancer Research, 2007), it is a concern that only 26% of men and 22% of women aged 65-74 years were sufficiently active in 2012 as reported by the Health Survey for England (Scholes and Mindell, 2013). It is possible that people diagnosed with an adenoma may experience a 'teachable moment' where the health event (the diagnosis of the adenoma) can be a powerful motivator of health behaviour changes (McBride et al., 2008). Thus, the screening environment might be an opportunity to endorse behaviour changes. Recent findings of a lack of knowledge of the link between PA and CC risk in this population (Stead et al., 2012) further supports the need for interventions with this population in the cancer screening setting. A lack of knowledge might contribute to continued lack of PA post-screening. Providing patients with a rationale, and an intervention to learn skills how to make lifestyle changes might improve patients' lifestyle behaviours and reduces the likelihood of further polyps or a potential diagnosis of CC at follow-up screening appointments.

Depending on the outcome of the colonoscopy, patients attend a follow-up screening either one, or three years later. Because patients are not likely to feel the need to make lifestyle changes because an unawareness of the links between adenomas and cancer, they are at increased risk of a recurrence of adenomas and

at increased risk of developing CC at some point in the future. In order to evoke a teachable moment people need to be aware of the link between lifestyle and cancer risk (Lawson and Flocke, 2009). In consideration of the screening schedule (up to three years no screening) long-term behaviour change in this patient group would be desirable to yield maximum benefits in terms of a risk reduction.

Self-Determination Theory (SDT) has been used in medication adherence and smoking cessation and shown promising results for the long-term maintenance of behaviour change (Williams et al., 2009a). Although, there is still a lack of the theory's application in the field of PA interventions, a number of cross-sectional studies investigated the relationship between self-determination and exercise behaviour (Teixeira et al., 2012). Autonomous regulations have consistently been reported to be associated with higher levels of PA, and even to predict future PA behaviour (Silva et al., 2011, Teixeira et al., 2012). Furthermore, people reporting more feelings of autonomy are more likely to adhere to an intervention, are less likely to drop-out, and more likely to maintain the behaviour in the long-term (Williams et al., 1996, Ryan et al., 1997, Wilson and Rodgers, 2002). A recent lifestyle intervention with obese women was successful in achieving increased levels of PA in the intervention group compared to a control group, and the group differences were still measurable after a 2-year follow-up (Silva et al., 2011). Thus, SDT is a promising theory to support long-term PA behaviour change in people diagnosed with colonic polyps to reduce their risk of an adenoma recurrence and the development of CC.

5.3. Aims

This study aimed to investigate the feasibility of a 6-month active lifestyle programme in people at increased risk of bowel cancer. A secondary aim was to obtain preliminary data on the effects of the intervention on motivational regulation for being physically active, PA behaviour, psychosocial factors and QoL. We are also interested whether any changes post-intervention were maintained after a 6 month follow-up.

5.4. Methods

The trial was registered with ClinicalTrials.gov and given the identifier:

NCT02724306

Study design

This study was designed as a 2-armed parallel randomised controlled feasibility trial (RCT) with equal sample sizes. Changes in primary outcomes were assessed after three and six months. Participants (n=31) were recruited on a rolling basis from September 2012 to February 2014 and randomised to an active lifestyle (ALP) group or a standard care group (SC) after all baseline measures were completed. The ALP group was offered 36 exercise group sessions and 12 behaviour change workshops over a 6-months period and the SC was encouraged to continue with their usual lifestyle habits. Participants recruited before August 2013 were followed up for six months after the intervention and additional follow-up assessments took place at nine and twelve months. Participants recruited thereafter completed the intervention but were only followed-up for 6 months post-intervention. All research activities took place at the University of East Anglia, and recruitment took place at the Norfolk and Norwich University Hospital.

The study was approved by the NRES Committee East of England, Norfolk, the Research & Development Office of the Norfolk and Norwich University Hospital (NNUH), and the Research and Enterprise Service at the University of East Anglia. All documents can be found in the appendices.

Note: The study was a sub-study of a larger study. Another PhD student collected biopsies from the bowel tissue, when participants were undergoing their screening colonoscopy. The following inclusion and exclusion criteria were chosen based on the primary outcomes of the other study, as well as this study. The other study investigated the tissue for epigenetic markers, therefore, some of the inclusion criteria were chosen, to minimize negative effects on the epigenetic investigations. For example, people with inflammatory bowel syndrome were excluded, because this could have had a negative effect on bowel tissue investigations. And another student conducted qualitative research interviews with the participants at the beginning of the study.

Participants

Participants were patients with a positive diagnosis of bowel polyps and were identified either via the *National Bowel Cancer Screening Programme* or colonoscopy attendance register at the NNUH. Inclusion criteria were: i) a diagnosis of 'low' (<5 polyps of <1cm in size), 'intermediate' (>5 polyps of <1cm in size or one polyp >1cm) or 'high' (>1 polyp of >1cm in size) risk polyp as a result of the screening colonoscopy; ii) aged 60 years and above and iii) physically able to partake in regular exercise. Exclusion criteria were i) physical activity levels that meet the most recent American Cancer Society (ACS) guidelines of 150min of moderate intensity PA or 75min of vigorous intensity PA per week, ii) presence or history of other co-morbid conditions which might preclude patients from safely undertaking regular exercise, including cardiovascular or pulmonary disease or stroke; iii) presence of other colorectal conditions (e.g. inflammatory bowel disease) or known familial colorectal cancer syndrome; iv) chronic use of any treatments or alternative therapies that may affect the results of any study of colorectal tissue e.g. high corticosteroid, anticoagulant or laxative use, regular enemas, high dose vitamin or antioxidant supplements, etc.; v) previous diagnosis of cancer; vi) inability to adequately understand written and spoken English, vii) presence of drug controlled type II diabetes mellitus and viii) current involvement in other ongoing research.

The reason for these strict inclusion and exclusion criteria are based on the investigation of colorectal tissue which was part of this project, but not part of this thesis. Therefore, patients with other colorectal conditions or patients taking medication that potentially effect the colorectal tissue in any way, were excluded from the study. The age criterion was chosen, because patients on the National Bowel Cancer Screening Programme are all 60 years of age and older. We also wanted participants to not meet the current PA guidelines because potential changes in the colorectal tissue due to increased PA would have not been able to be observed if a number of participants were already active at study entry.

Note: In the original protocol the inclusion criteria were restricted to having a diagnosis of an 'intermediate' (more than 5 polyps smaller than 1cm or one large polyp of at least 1 cm) or 'high' risk (more than 1polyp of more than 1cm in size).

This was chosen, because intermediate and high risk, patients would be seen for a follow-up colonoscopy after 1 year. BS, the other student who investigated effects of PA on bowel tissue, wanted to investigate bowel tissue before the intervention and post-intervention. Due to the time-frame of the PhD programme, BS would have not been able to get bowel tissue from low risk patients. Therefore, they were initially not included. This was changed at a later stage because patients were excluded from the study if they had less than 5 small polyps of less than 1cm in size. This change was made to broaden the inclusion criteria and this change did not affect the outcome measures of this thesis. In the original protocol patients were also excluded if they were taking NSAIDS on a daily basis. This was also changed at a later stage to increase recruitment. The reason for this exclusion criteria, was that NSAIDS might have an effect on bowel tissue. In order to exclude factors other than exercise that could cause changes in biomarkers of the bowel tissue, this criterion was applied initially. Again, because it did not affect the outcome measures of this part of the project (the present thesis), it was decided to include patients taking NSAIDS to increase the number of participants.

Recruitment

Recruitment took place from September 2012 to January 2014. The recruitment strategies are described in detail in a later chapter. An additional chapter was included on recruitment to describe the process of recruitment, challenges experienced, and results of a survey to non-participators to explore reasons for non-participation. The reader may refer to chapter 7. Briefly, recruitment of patients took place via three different routes; 1) Recruitment via specialist nurses, 2) recruitment via invitation letter from a consultant, and 3) recruitment via clinics. The latter two strategies were added at a later stage, because the primary recruitment strategy did not yield the desired target number of participants. An amendment was added to implement these additional recruitment strategies. Recruitment-related amendments are shown in Figure 4. In all instances, patients were provided with a participant information sheet and a consent form to provide their contact details and give the researcher permission to contact the patient. In all recruitment strategies, the first contact with a patient was via a health professional. Participants were able to read the participant information sheet at

home in their own time, and the researcher contacted the patient within one week after first contact to provide more information about the study and to establish whether the patient was interested in study participation. If the patient was interested, a meeting was scheduled at the University of East Anglia, Norwich, UK, where the patient was screened for eligibility and the consent form was signed.

Randomization

After all baseline measurements were completed participants were randomised to one of two groups, the active lifestyle (ALP) group or a standard care (SC) group. Randomisation was carried out with a technique called *Covariate Adaptive Randomisation*. Polyp risk status, age, gender, and BMI were used as covariates (World Cancer Research Fund and American Institute for Cancer Research, 2007). (Refer to sections 2.1 to 2.3 of Chapter 2 for rationale of choosing these covariates). This method is a 'minimization' method by which the decision to allocate participants to a particular group is based on trying to "balance" the particular covariates that are deemed to be important in the experiment. In these studies, the covariates risk status, age, gender, and BMI were identified, and allocated as equal as possible between the SC and ALP. To start with, the first few volunteers were just randomly allocated, and for subsequent participants, the use of Covariate Adaptive Randomisation was applied. This minimizes the differences between the groups in terms of these covariates. This method has been deemed highly effective (Scott et al., 2002).

The randomisation was carried out by a person (JD) independent of the research team. JD emailed the allocation to the researcher who carried out the exercise sessions after all baseline assessments were completed (apart from fitness assessment). Thus, this researcher was not blinded to the allocation of participants.

The researcher carrying out the exercise sessions and the motivational workshops was not blinded to the allocation of participants.

Other considerations

Trial Steering Committee

A trial steering committee, which consisted of the researchers (LL, KL, BS), the principle investigator (JS), secondary supervisor (JH) (JH is also the clinical collaborator), and third supervisor (NB), and a specialist nurse (UM), met at least every 3 months. At this meeting, the primary focus was recruitment. Researchers reported on the progress of recruitment, and collaboratively, the members of the steering committee came to conclusions about potential amendments to the current recruitment strategies. The nurse communicated the conclusions from the meeting to other nurses at the hospital, who were involved in recruitment.

Training

Nurses who recruited into the study met with the researchers prior to commencement of the study. Researchers provided the nurses with information about the study. They were informed about the inclusion criteria and provided with a folder that contained patient information sheets, consent forms for research biopsies, and a consent form for patient details to be passed on to the research team. Another folder was provided where consent forms and patient contact details were kept, for the researchers to be collected at a later point.

Intervention

Standard Care group

The SC was encouraged to continue with their usual lifestyle and refrain from changes to their diet and PA habits over the study period. Participants of the SC were invited to follow-up appointments at three and six months.

Active lifestyle group

General format

ALP was offered to participate in supervised exercise sessions twice per week for three months and once per week for the following three months. Participants were also offered to take part in PA workshops which took place biweekly for the period of the intervention. Each session consisted of a warm-up, aerobic and resistance exercises, and cool-down stretches lasting in total 60min. Exercise took place in small groups of two to five people. Behaviour change workshops to aid the uptake

and maintenance of PA were delivered every fortnight throughout the whole intervention period totalling 12 workshops. The exercises and the workshops were led by the same person. This person is a trained REPs level 2 exercise specialist and a trained motivational interviewer. The facilitator recorded attendance at each of the supervised exercise sessions.

Details about the components of the supervised exercise sessions and the PA workshops are described in Chapter 4.

Other considerations of the intervention

In the event of a serious adverse event, the researcher would take appropriate measures ensure the safety of the participants. Serious adverse events were recorded by the researcher within 24h of becoming aware of an adverse event.

Outcome measures

All assessments took place at an exercise facility at the University of East Anglia. Participants were invited for assessments at baseline, and every 3 months, until the end of the study (baseline, 3, 6, 9, and 12 months).

Feasibility outcomes

Feasibility outcomes such as response to letters, number of eligible people, reasons for exclusion, were assessed and are reported in more detail in chapter 7. Other feasibility outcomes such as compliance (attendance at supervised exercise sessions and workshops) and attrition (reasons for drop-out) will be reported here.

Other outcomes included the motivational regulation to exercise, PA behaviour, cardiopulmonary fitness, self-efficacy for exercise, quality of life, and body composition.

All questionnaires were collected in a questionnaire booklet which the participant could complete at home. Participants were instructed to complete the whole booklet at once and not to fill in parts of the questionnaires on different days.

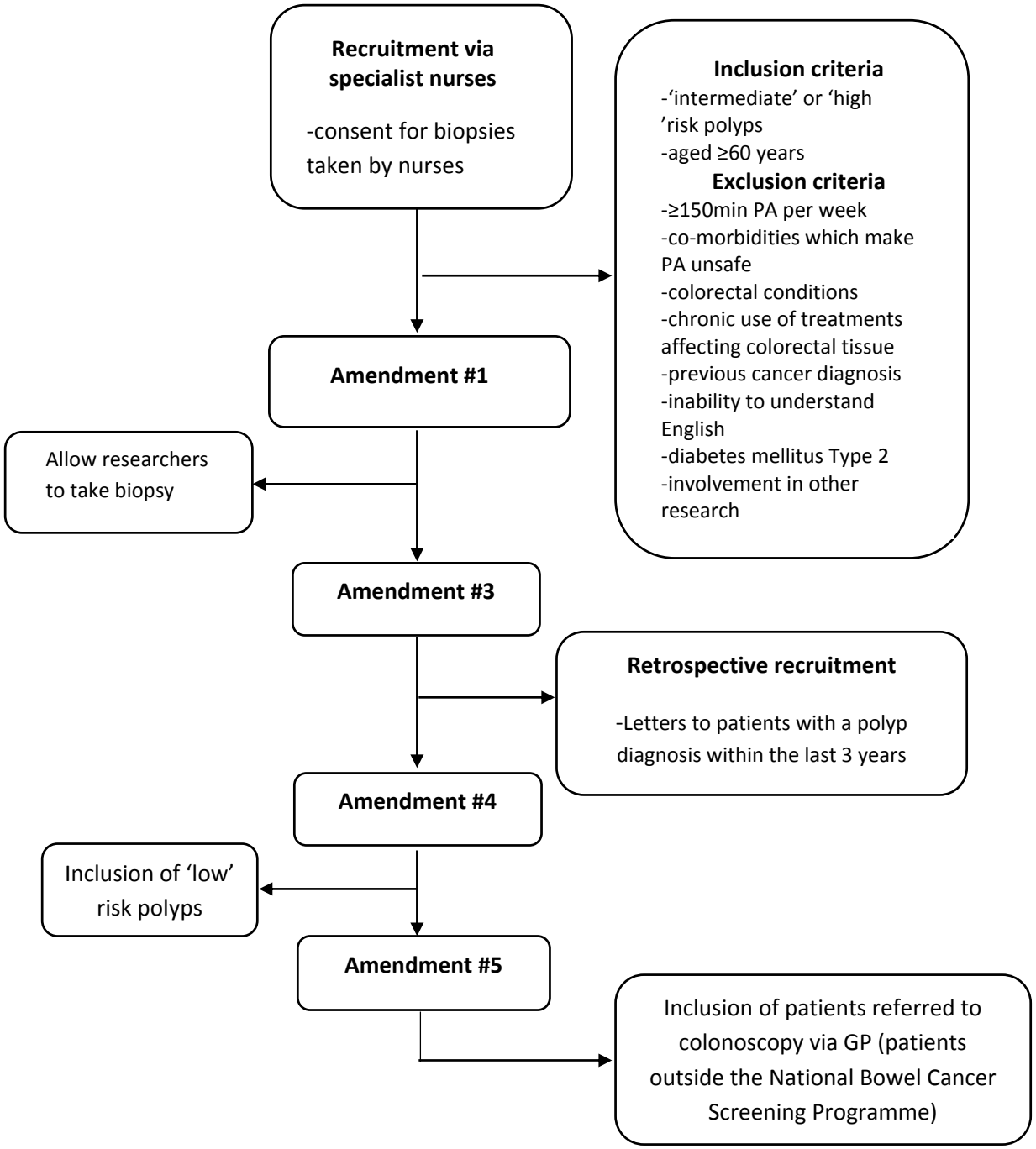


Figure 4 Flow of recruitment-related amendments that were implemented throughout the study

Behaviour Regulation for Exercise

The Behaviour *Regulation for Exercise Questionnaire* version 2 (BREQ-2) (Appendix 3) was used to assess participant's motivation regulation for exercise (Markland and Tobin, 2004). The original BREQ (Mullan et al., 1997) measured four intrinsic and extrinsic forms of regulation, namely *external, introjected, identified* and *intrinsic*. The BREQ-2 was developed to include *amotivation*. A relative autonomy index (RAI) can also be calculated and a higher score indicates more self-determination. The higher the RAI the more self-determined the person feels. Responses to the 19-item questionnaire were scored on a 5-point Likert scale ranging from 0= "Not true for me" to 4= "very true for me". Research supports the 5-factor model of the BREQ-2 and internal consistency was found to be acceptable (Cronbach's alpha ranged from 0.79 to 0.86).

Physical activity

Subjective measure

The *accelerometer ActiGraph® GT3X* was used to measure participant's free-living PA over a period of seven days. Participants were instructed on the correct wear position of the accelerometers (around the waist and above the right iliac crest). An accelerometer a small unobtrusive device that detects the acceleration produced by the movement of the body. It also allows assessment of frequency, intensity and duration of PA (Ridgers and Fairclough 2011). The ActiGraph® GT3X collects acceleration data from three planes of movement and thus, provides a more accurate assessment of PA than uniaxial devices. Accelerometry has been found to be superior over subjective measures when compared against doubly labelled water (Colbert et al. 2011). Acceleration data is collected over a set time interval, called epochs, and the total amount of accelerations is recorded as *counts*. The epoch period was set at 1 min as recommended by previous calibration studies (Freedson et al., 1998, Hendelman et al., 2000, Miller et al., 2010). PA behaviour was assessed every 3 months throughout the study, at baseline, 3, 6, 9, and 12 months.

Accelerometer data is reported as accumulated moderate to vigorous PA (MVPA) which is the sum of all movements above 1952 counts per minute (cpm) (Freedson et al., 1998) which are the most frequently used accelerometer counts. Because the PA guidelines for health recommend that PA should be carried out in bouts of at least 10 min to contribute towards the PA goals, we also reported PA in terms of 10-min of moderate intensity PA (1952-5724 cpm), and 10-min bouts of vigorous intensity PA (>5724 cpm). However, no vigorous intensity PA was recorded at any time-point (apart from one person). Thus, results are only reported as accumulated MVPA and moderate bouts. There has been criticism of the conventionally used cut-points for moderate and vigorous intensity PA developed by Freedson et al (1998) (moderate intensity: 1952-5724 cpm, vigorous intensity >5724 cpm) that lower cpms should be used for the elderly. Thus, we included an additional measure of 10-min bouts with the criteria of 760-5724 cpm for moderate intensity PA (Matthews et al., 2005) and refer to them as 'Matthews bouts' in the remainder of the chapter.

Self-assessed physical activity

The *International PA Questionnaire* (IPAQ) (appendix 7) is a self-administered questionnaire designed to measure four domains of PA: 1) job-related, 2) Transportation-related, 3) House work-related, and 4) Recreation-related (http://www.ipaq.ki.se). A benefit of the IPAQ is its tested validity across different languages and therefore, offers a comparable estimate of PA within and between countries. The validity of the IPAQ has been rated as acceptable for total PA (ρ= 0.55) and the different activity domains (Hagstromer et al., 2006).

The questionnaire was delivered in an interview-form with each participant. The questionnaire has been criticised to over-report PA and that especially the elderly population experienced difficulties in interpreting the question's meaning (Heesch et al., 2010). Our previous findings reported acceptable validity for the interview-delivered IPAQ (ρ=0.43) in this population (the reader may refer to chapter 8). Before delivering the questionnaire, the researcher explained the different domains of PA to the participant, clarified what moderate and vigorous activities meant, that only activities of a duration of 10 min or longer will be recorded, and emphasized

that only the last seven days were to be considered in the answers to the questions. Then the researcher read each question out loud to the participant and helped clarify types of activities if the participant had difficulties answering the question.

Physical activity diaries

Participants were provided with a PA diary which they were asked to complete for 7 consecutive days. These were the same 7 days that they were asked to wear the accelerometer. The diary provided space to record the type of activity, the intensity of the PA as rate of perceived exhaustion (RPE), and duration of the activity. Participants were given instructions by a researcher on how to complete the diary, and were provided with written information on how to rate the PA intensity based on the RPE scale.

Physical fitness

Participants performed a test of maximal aerobic capacity ($\dot{V}O_{2\,max}$) on an electronically braked cycle ergometer, and the tests lasted approximately 8-12 min. The test started with a 2 min freewheeling-period and thereafter the intensity increased every 2 min by 15 Watts until exhaustion. During the test, a continuous ECG trace was monitored by a medical professional to detect potential risks to the participant. Once the participant reached their $\dot{V}O_{2\,max}$ and which was determined by voluntary discontinuation of the test due to physical exhaustion, the test was stopped and the participant allowed to 'freewheel' for as long as they deemed necessary.

The person who carried out the fitness test was blinded to the group allocation of the participant.

Quality of life and other outcomes

The *Short From-36* (SF-36) (appendix 6) is a 36 item generic quality of life questionnaire that can be used across age, disease, and treatment group. It measures functional health and well-being over eight health domains: physical functioning (limitations in performing physical activities), role-physical (limitations in role activities due to physical health problems), bodily pain (level of pain and its impact on activities), general health (individual evaluation of health status), vitality

(measures subjective well-being), social functioning (impact of health on social activities), role-emotional (limitation performing role activities due to emotional problems), and general mental health (Maruish, 2011). A higher score is indicative of better QoL.

The *Intention to exercise* (Appendix 4) is a short assessment consisting of two questions: "I intend to exercise regularly over the next month" and "I intend to exercise regularly over the next 6 months". The questionnaire is based on Ajzen's model of 'Theory of Planned Behviour' (Ajzen, 1991) and has been used in PA behaviour change interventions. Intention is rated on a 7-point Likert Scale ranging from 1= "Completely Agree", to 7= "Completely disagree".

The *Self-Efficacy for Exercise* (SEE) (appendix 5) is a 9-item questionnaire and assesses self-efficacy to continue exercising under a variety of situations, such as bad weather, pain, lack of enjoyment (Resnick and Spellbring, 2000). A higher score represents higher self-efficacy. Test of validity revealed a high internal consistency (alpha=0.92).

Anthropometric measures

Body weight was measured using the *SECA 711* scale and was measured to the nearest 0.1kg. Height was measured with a stadiometer to the nearest 0.1cm. Weight (kg) and height (m) were used to calculate the Body Mass Index (BMI) (kg / m^2). Body fat was analysed using an *AKERN BIA 101*. Waist and hip circumference were also measured using a *Seca* tape measure.

Data analysis

Data preparation

Excel spreadsheets were created for every outcome measure and data was entered into the spreadsheet. Only data from the SF-36 was entered into a software (purchased from Quali Metric). Data scored with this software was then exported into an excel file. All data was examined visually for completeness and errors before being copied to the Statistical Package for the Social Sciences (SPSS) version 22 for analysis. Graphs were created with the GraphPad Prism 6 software.

The initial analysis plan

We planned to include all data in the analysis, including non-completers using an intention-to-treat model. In the event of missing data, this was to be imputed with a suitable imputation strategy after examination of the data. Primary and secondary outcome measures were to be examined with repeated measures ANOVA General Linear Model to assess change in dependent variables and to test for between-group differences. This was chosen because there are five time-points at which data is collected, BL, 3, 6, 9, and 12 months. Post-hoc tests were to be selected for the repeated measures variables to examine between group differences at each time-point.

Change of plan of analysis

The data was examined for sphericity which is an assumption for the repeated measures ANOVA. The majority of domains of the SF-36 and the IPAQ-L did not meet the assumption for sphericity. Therefore, overall sphericity did not hold for the data set which could result in a loss of power (Fields, 2005).

For normality testing in SPSS, the data were split into groups, and examined with normality plots and normality test (*Kolmogorov-Smirnov)* test of Normality). If significance values were greater than 0.05, the data were deemed normally distributed. If data was non-normally distributed, attempts were made to normalise the data by applying log-transformations. Due to the nature of the data (many zero values for PA behaviour, or zero values for amotivation), log-transformation did not normalise the data. Replacing the zero values with very small numbers, (e.g. 0.001) did also not normalise the data.

In addition to violation of sphericity and normality of some outcomes measures, the examination of the data set also revealed a large number of missing data. At primary study end-point (6 months) 32% of data, and at follow-up (12 months) 54% of data were missing.

Based on the violations of assumptions for ANOVA, in addition to the large amount of missing data, other analysis options were considered. An ANOVA is considered a

robust test, and valid even when the assumptions for normality and sphericity are not met. In regards to normality, if sample sizes are even between the groups, the test will still be valid. In regards to sphericity, SPSS offers a correction of the results with the Greenhouse Geisser test. However, the large number of missing data was the deciding factor to not continue with the repeated measures ANOVA. In SPSS, a repeated measures ANOVA only includes the number of participants for the test that were available for all time-points. Participants with missing data will be excluded from all analysis. Imputation of data is an option, but has been shown to be flawed in longitudinal studies with large amount of missing data (Lane, 2008). Therefore, it was decided to perform mixed model analysis to investigate changes over time to avoid type I errors as well as loss of power which may occur with the imputation of missing data (Armijo-Olivo et al., 2009). Mixed model analyses was shown to be more reliable and better grounded statistically for handling missing data in longitudinal trials compared with imputation methods. This approach models all the actual data with no attempt at imputation for missing values.

Mixed model analysis

For the data analysis 31 participants (all participants who entered the study) were included in the analysis. The mixed model analysis included the following number of participants at each time point: BL: n= 31, 3 months: n=27, 6 months: n=22, 9 months: n=15, 12 months: n=15. The data was prepared in SPSS for mixed model analysis. This required to re-organise the data into a transposed table. For mixed model analysis of repeated measures, we need to specify a covariance structure for each variable. In our model, we chose the 'diagonal' covariance structure. This structure assumes that variances are independent and, therefore, all of the covariance are 0. In SPSS this is the default covariance structure for repeated measures (Fields, 2005). We also tested the AR (1) structure whether it would be a better fit. It can be useful to run the model with a different covariance structure to see whether changing the structure improves the fit of the model (Fields, 2005). Depending on the covariance structure a Type I error or Type II error could occur depending on the simplicity or complexity of the covariance structure used. However, the *Akaike's information criterion* (a goodness-of-fit indicator) was similar

for both structures, therefore the diagonal structure was used. Group and Time factors were entered into the fixed effects model to examine the main effects. Type III was chosen as the sum of squares. The outcome variable was entered as the dependent variable. The time variable was entered as a covariate and group was entered as a factor. Additional statistics were chosen (descriptive statistics such as means, standard deviation, 95% confidence intervals) to be calculated. If significant p-values (<0.05) were observed for time and group effects, post-hoc tests were carried out to determine at what time-point the difference was present. The post-hoc test was also performed with the same mixed model analysis but the time-point that I wanted to investigate was specified.

All outcome measures were examined with mixed models analysis, apart from the outcome of number of participants meeting the weekly PA guidelines, which was examined with the chi square test. For this, a dummy variable was created to distinguish participants into two categories; meeting the guidelines, and not meeting the guidelines. Chi square analysis was performed with these variables to compare whether the number of participants meeting the guidelines differed between the SC and ALP groups.

The PA diaries were not included in the analysis because most participants did not report their PA in a manner that it could be analysed. Participants did not record the duration of the activity in enough detail so that the researcher could calculate a MET value. Some participants only recorded certain types of PA, such as periods during which they were engaging in exercise, but failed to record other activities such as household activities. Because the data did not seem representative of their 'true' PA the diaries were not included in the analysis.

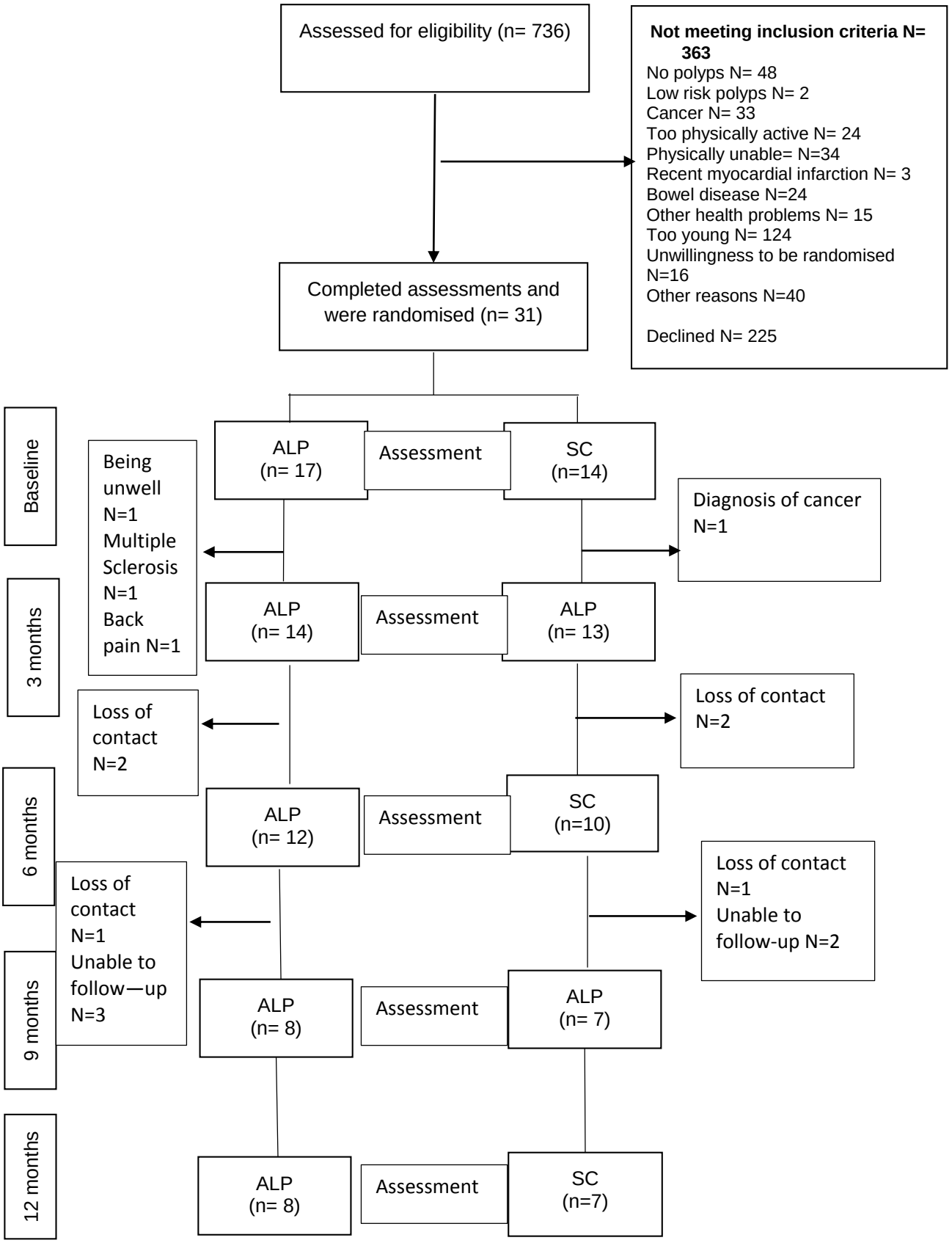


Figure 5 Flow of participants through the study

5.5. Results

Feasibility outcomes

A detailed description of all recruitment related feasibility outcomes can be found in chapter 7. Figure 5 shows the flow of participants through the study. Briefly, 363 (49%) of the potential participants approached were excluded for not meeting the inclusion criteria. A further 225 (30%) declined to take part.

After baseline assessments, 31 participants (4.2% of potential participants, 8.3% of eligible participants) were randomised to either the SC (n=14) or ALP (n=17) group. Main reasons for exclusion of ineligible patients were no diagnosis of polyps (n= 48), a previous diagnosis of CRC (n= 33), other diseases of the bowel (n= 24), not being physically able to take part in the intervention (n= 34), and already meeting the current PA guidelines of 150min of moderate to vigorous intensity PA per week (n= 26). The primary reasons for declining to take part were travel distance to the research site (n= 68), time commitment (n= 44), and not willing to be randomised (n= 15).

At the primary end-point (6 months, post-intervention) 71% (n=22) of randomised participants were still available for post-intervention assessments. Reasons for drop-out were primarily loss of contact (SC: n= 3, ALP: n= 2). Three people were known to have moved away and failed to provide the researchers with updated contact details, and two participants did answer their phone after several attempts of contact. A further four participants withdrew from the study because of health problems that were not a result of the intervention, e.g. Multiple Sclerosis, cancer, general unwell-being (SC: n=1, ALP: n= 3). There were no adverse events of the intervention.

As previously described, not all participants were able to be followed-up because of a tight study deadline. Seven participants were recruited after August 2012 and thus, were not in followed-up at 12 months. Thus, after accounting for drop-outs, 16 participants were available post-intervention to complete the follow-up period of 6 months. Two participants were lost to follow-up during this time (SC: n= 1, ALP:

n=1). Reasons were the inability to contact these participants after several attempts. This is a 67% retention rate of the participants.

Attendance at the exercise sessions was average with 380 of 612 supervised exercise sessions attended, yielding a compliance of 62%. This low attendance was partially a result of drop-outs (n= 3) immediately after randomisation. The three participants who dropped-out from ALP because of health reasons attended 0 - 1 supervised exercise sessions before drop-out. Nearly half of ALP participants (n=8) attended more than 80% of supervised exercise sessions and only the drop-outs attended less than 50% of sessions. The compliance for workshop attendance was 53% (110 out of 204 workshops) and eight participants attended more than 75% of the offered workshops.

Reasons for non-attendance were work commitments, illness, or holidays. There are no records of participants not attending supervised exercise sessions or workshops without providing a valid reason for their non-attendance. Participants always made an effort to inform the exercise leader about non-attendance prior to the session that would be missed, unless their non-attendance was unexpected, such as in the case of illness.

Secondary outcomes

A summary of the baseline characteristics of both groups can be seen in

Table 1. There were no substantial group differences in any outcome measures at baseline. Outcomes of all measures (means and SD) from baseline to post-intervention are displayed in Table 2, and results for post-hoc tests in table 3. Follow-up results are displayed in Table 4 and Table 5.

Characteristics	SC (n=14)	ALP (n=17)
Sex (M/F)	9/5	11/6
Risk profile*		
Low	3	6
Intermediate	8	10
High	3	4
Age	69.4 ± 6.3	68.1 ± 3.4
Body weight (kg)	81.8 ± 16.3	90.1 ± 19.6
Body height (m)	1.71 ± 0.1	1.71 ± 0.1
BMI	27.7 ± 4.8	30.6 ± 5.2
Body fat (%)	26.4 ± 7.4	30.7 ± 5.2
Waist-hip-ratio	0.94 ± 0.1	0.93 ± 0.1

Table 1 Baseline characteristics of Intervention and Control Arms of the Study,

Note: Values are means ± SD unless otherwise indicated. SC= Standard Care, ALP= Active Lifestyle Programme, * Low risk= ≤5 polyps sized <1cm, intermediate risk= >5polyps sized <1cm, or one polyp >1cm in size, high risk= >1 polyp sized >1cm

Motivational regulation

Mid- and Post-intervention

There was a *group x time* effect (Table 2) over the course of the intervention in amotivation ($F= 9.86$, $p< 0.01$), identification ($F= 6.29$, $p< 0.05$), intrinsic regulation ($F= 13.75$, $p< 0.001$), and RAI ($F= 9.49$, $p< 0.01$) (Figure 6). The group difference for amotivation was only observed at 6 months ($p= 0.002$). Although, *group x time* effects were significant for identification, post hoc tests did not show a significant group difference in mean change. However, an examination of the mean changes shows higher levels in ALP at all time-points vs SC. Both groups increased in

identification but the intervention condition increased more than four times as much as the control condition post-intervention at 6 month. The difference in mean change between the groups for intrinsic motivation was only significant at 6 months (p= 0.004) with ALP increasing by 1.59 and SC decreasing by 0.11 compared to baseline measurements. Both groups increased similarly in extrinsic and introjected regulation and there were no differences between the groups. Similarly, the mean change in RAI was only different between the groups at 6 months (p= 0.005) but not at 3 months (p= 0.092). At 3 month there is only a slight increase in both groups with a slightly larger increase in ALP than SC (3.70 vs 0.14) but a large difference at 6 months (7.77 vs -1.73).

Follow-up

Group-specific changes in autonomous self-regulation over time were also assessed over the follow-up period to assess the maintenance of motivational change. *Group x time* effects were still observed for amotivation (F= 7.89, p< 0.01), intrinsic motivation (F= 4.70, p< 0.05), and RAI (F= 4.75, p< 0.05). Amotivation remained close to baseline values at 12 months in the control condition but decreased in the intervention condition, but this was not significant (p= 0.081) at post hoc analysis. Despite significant *group x time* effects for intrinsic regulation, post hoc tests revealed no significant group difference at 9 and 12 months between SC and ALP. However, post-intervention levels of intrinsic regulation were maintained throughout the follow-up period in ALP, but also increased slightly in SC with a mean difference between the groups of 0.9 (95% CI: -0.7 – 2.6, p= 0.24) at 9 months and 1.4 (95% CI: -0.2 – 3.1, p= 0.08) at 12 months. This was similar for RAI with post hoc tests not showing a significant group difference in mean change at 9 and 12 months (p= 0.23, and p= 0.08).

Cardiopulmonary fitness (VO2max)

Mid- and Post-intervention

Although, ALP increased fitness by 1.56 ml · kg^{-1} · min^{-1} post-intervention and SC decreased fitness by 0.1 ml · kg^{-1} · min^{-1} there was no significant *group x time* effect (F= 3.93, p> 0.05).

Follow-up

The improved fitness levels of ALP remained elevated at follow-up and did not change in the control condition. The group differences were not significant.

Accelerometry

No significant *group x time* effects were observed for any of the accelerometer outcomes, either post-intervention or at follow-up.

Self-assessed physical activity

Mid- and Post-intervention

Only leisure-time PA showed a significant *group x time* effect ($F= 5.27$, $p< 0.05$) over the course of the intervention. At 3 month and at 6 months ALP increased leisure-time PA and SC decreased the minutes of leisure-time PA, although this was not significant during the post hoc analysis ($p= 0.058$ and $p= 0.088$). Compared to SC, at 3 months ALP engaged in 273 ± 282 min vs 111 ± 139 min and at 6 months in 228 ± 204 min vs 41 ± 62 min of leisure-time PA.

No other differences were observed for any of the IPAQ domains. Although, changes in IPAQ measures show a slight increase in walking PA at 3 and 6 months in ALP and a decrease in SC, this was not significant.

Follow-up

Mixed model analysis revealed *group x time* effects for leisure time PA during the follow-up period. At 12 months the intervention condition engaged in 266 min more leisure-time PA than the control condition ($p= 0.04$).

Meeting the current PA recommendations

General guidelines of 150min of moderate intensity PA or 75 min vigorous intensity PA

With accelerometer criteria of 10-min moderate bouts, which is PA performed for at least 10 min at a time, at baseline 11.8% of ALP versus 0% ($P=0.18$) of SC met the guidelines. This was unchanged post-intervention. At follow-up, 21.4% of ALP and

7.1% in SC were meeting the guidelines with the 10-min bout criteria (P=0.56). No group differences in meeting the recommendations were observed for all other accelerometer criteria.

For self-assessed leisure-time PA, post-intervention 28.6% in ALP compared to 4.2% in SC were meeting the general PA guidelines (P=0.03). At follow-up, this difference became large, with 36.4% in ALP and 0% in SC meeting the recommendations (P=0.01).

World Cancer Research Fund Recommendations of 210- 240 min of moderate intensity or 210 min of vigorous intensity PA per week

As previously discussed, the evidence that PA is inversely associated with a decreased risk of developing CC is consistent with recreational PA but inconsistent with occupational and household PA. In the light of this, we will only consider leisure-time and walking PA here. None of the participants in the control condition met the PA guidelines at any time-point with the 10-min bouts accelerometer criteria. In ALP, 4.8%, and 7.1% participants were meeting the PA recommendations with the 10-min bouts accelerometer criteria post-intervention, and at 12 months follow-up, respectively. (P=0.59).

For self-assessed leisure-time PA, post-intervention 19% in ALP and 0% in SC were meeting these recommendations (P=0.05). At follow-up, 28.6% in ALP vs 0% in SC were meeting these recommendation (P=0.02).

Body composition

There was no significant difference between the groups for any variable of body composition at any time-point. However, there was a trend for a decrease in body weight and BMI in ALP and an increase in SC.

Quality of life

There were no significant differences between the groups in any of the QoL domains of the SF-36. The physical summary component increased in both groups. Results for the mental summary component showed a decrease during the

intervention period in SC and no change in ALP. At 9 and 12 months the mental component increased in ALP but not in SC.

Self-efficacy to exercise and intention to exercise

Mid- and Post-intervention

There was a significant *group x time* effect in intention to exercise during the intervention period (F= 6.10, p< 0.05). ALP increased intention to exercise from baseline to 3 and 6 months compared to a decrease in the control condition which decreased slightly over the study period, and this group difference was significant at 6 months (mean change difference= 2.3, p= 0.023).

There were no significant *group x time* effects for SEE but there is a trend for an increase in both groups.

Follow-up

There were no significant *group x time* effects for intention to exercise and for SEE over the follow-up period, but the intervention group showed a larger increase than the control condition for both measures.

Table 2 Changes during the intervention at 3 and 6 months in all outcome measures. Values are means (SD) unless stated otherwise

Variable		**Baseline**		**3 months**		**6 months**	**Group x time F**
	N	**Mean (SD)**	**N**	**Δ Mean (SD)**	**N**	**Δ Mean (SD)**	
Body composition							
Body weight							
SC	14	81.8 (16.3)	13	0.35 (2.2)	13	0.17 (2.3)	0.19
ALP	17	90.1 (19.6)	12	-0.40 (2.0)	12	-1.12 (2.2)	
BMI							
SC	14	27.7 (4.8)	13	0.04 (1.0)	13	0.02 (0.8)	0.28
ALP	17	30.6 (5.2)	13	-0.14 (0.6)	12	-0.36 (0.7)	
Body fat							
SC	14	26.4 (7.5)	13	0.6 (2.9)	13	1.28 (2.5)	0.28
ALP	17	30.7 (8.5)	13	2.89 (7.0)	12	0.77 (5.8)	
Waist-hip-ratio							
SC	14	0.94 (0.10)	13	-0.01 (0.05)	13	0.00 (0.1)	0.01
ALP	17	0.92 (0.09)	13	-0.01 (0.1)	12	-0.01 (0.1)	
Self-regulation							
Amotivation							
SC	14	0.18 (0.35)	12	0.06 (0.4)	11	0.23 (0.4)	9.86**
ALP	17	0.65 (0.65)	11	-0.41 (0.7)	10	-0.70 (0.7)	
Extrinsic regulation							
SC	14	0.14 (0.29)	12	0.08 (0.3)	11	0.14 (0.4)	0.42
ALP	17	0.38 (0.70)	12	0.42 (0.8)	11	0.18 (1.1)	
Introjection							
SC	14	0.60 (0.83)	12	0.53 (0.8)	11	0.55 (0.9)	0.09
ALP	17	1.11 (1.52)	12	0.58 (1.2)	11	0.14 (0.9)	

Variable		**Baseline**		**3 months**		**6 months**	**Group x time F**
	N	**Mean (SD)**	**N**	**Δ Mean (SD)**	**N**	**Δ Mean (SD)**	
Identification							
SC	14	2.16 (1.11)	12	0.40 (1.4)	11	0.20 (0.9)	6.30*
ALP	17	1.87 (1.14)	12	0.69 (0.6)	11	0.98 (1.0)	
Intrinsic regulation							
SC	14	1.96 (1.41)	12	0.65 (1.7)	11	-0.11 (0.8)	13.74***
ALP	17	1.38 (1.22)	12	0.94 (1.3)	11	1.59 (1.4)	
RAI							
SC	14	8.63 (6.98)	12	0.14 (2.5)	11	-1.73 (4.0)	9.50**
ALP	17	4.14 (7.66)	12	3.70 (6.5)	11	7.77 (8.7)	
Self-efficacy							
SC	14	5.8 (3.1)	12	-0.14 (2.3)	11	0.46 (2.2)	0.59
ALP	17	4.9 (2.2)	13	1.83 (2.2)	11	1.35 (3.1)	
Intention							
SC	14	5.1 (1.9)	12	-0.08 (2.0)	10	-0.50 (2.1)	6.10*
ALP	17	4.9 (1.8)	13	1.03 (1.7)	11	1.77 (2.0)	
Quality of Life							
Physical Function							
SC	14	50.5 (5.9)	12	-0.16 (2.1)	10	1.14 (3.4)	0.57
ALP	17	44.5 (7.7)	13	2.80 (7.4)	11	3.52 (6.9)	
Role-Physical							
SC	14	51.7 (6.6)	12	-0.00 (5.4)	10	0.45 (7.3)	0.35
ALP	17	47.1 (10.6)	13	0.69 (13.0)	11	2.65 (7.7)	
Bodily Pain							
SC	14	50.3 (8.5)	12	3.69 (9.4)	10	2.91 (10.3)	1.31
ALP	17	48.5 (9.6)	13	1.64 (9.1)	11	-1.0 (11.4)	

Variable		Baseline		3 months		6 months	Group x time F
	N	Mean (SD)	N	Δ Mean (SD)	N	Δ Mean (SD)	
General Health							
SC	14	53.2 (6.7)	12	-0.24 (5.20)	10	0.10 (6.6)	1.34
ALP	17	49.5 (8.1)	13	2.08 (9.6)	11	5.92 (7.2)	
Vitality							
SC	14	56.0 (10.5)	12	-0.50 (5.8)	10	-2.38 (8.4)	1.96
ALP	17	51.3 (10.7)	13	1.37 (5.1)	11	4.05 (6.4)	
Social Functioning							
SC	14	54.8 (5.8)	12	-0.42 (1.4)	10	-1.50 (6.3	1.37
ALP	17	52.9 (9.0)	13	1.54 (8.0)	11	-1.37 (6.8)	
Role-Emotional							
SC	14	54.2 (4.8)	12	-0.87 (3.96)	10	-2.79 (8.2)	0.95
ALP	17	50.6 (7.6)	13	-0.27 (5.0)	11	0.63 (4.1)	
Mental Health							
SC	14	56.1 (5.8)	12	-0.65 (4.5)	10	-1.57 (7.1)	0.15
ALP	17	53.6 (9.9)	13	-0.20 (7.0)	11	0.72 (5.1)	
Physical Summary							
SC	14	49.7 (5.9)	12	1.35 (4.6)	10	2.42 (4.2)	0.02
ALP	17	45.1 (7.9)	13	2.60 (8.3)	11	3.45 (6.1)	
Mental Summary							
SC	14	57.1 (4.7)	12	-1.24 (3.4)	10	-3.54 (7.2)	0.56
ALP	17	54.9 (8.2)	13	-0.40 (4.9)	11	0.07 (3.5)	

Variable		**Baseline**		**3 months**		**6 months**	**Group x time F**
	N	**Mean (SD)**	**N**	**Δ Mean (SD)**	**N**	**Δ Mean (SD)**	
Fitness							
VO_{2max} (ml · kg^{-1})							
SC	14	24.6 (4.0)		N/A	11	-1.00 (1.8)	0.34
ALP	17	22.2 (6.5)		N/A	11	1.56 (2.6)	
Accelerometry							
VM (counts · min^{-1})							0.02
SC	14	519 (185)	11	90 (87)	9	0 (131)	
ALP	17	567 (120)	12	35 (191)	11	9 (179)	
Sitting (min · wk^{-1})							
SC	14	6675 (637)	11	133 (875)	9	-527 (911)	0.03
ALP	17	6586 (1534)	12	-198 (1192)	11	-981 (881)	
10-min bouts (moderate)							
SC	14	32.4 (33.5)	11	26 (63)	9	-5 (23)	0.194
ALP	17	63 (83)	12	-2 (62)	11	-24 (43)	
Matt bouts (min · wk^{-1})							
SC	14	192 (184)		42 (139)	9	-53 (176)	0.01
ALP	17	204 (159)		56 (273)	11	-13 (241)	
Accumulated MVPA (min · wk^{-1})							
SC	14	112 (83)	11	21 (94)	9	-20 (60)	0.13
ALP	17	156 (125)	12	23 (151)	11	-10 (126)	
Steps · day^{-1}							
SC	14	6110 (1436)	6	216 (1313)	4	946 (1253)	1.89
ALP	17	5639 (1985)	5	1075 (1690)	5	731 (2325)	

Variable		Baseline		3 months		6 months	Group x time F
	N	Mean (SD)	N	Δ Mean (SD)	N	Δ Mean (SD)	
IPAQ measures							
Sitting (min · wk^{-1})							
SC	14	2533 (1296)	13	-109 (1259)	10	174 (1228)	3.50
ALP	17	2987 (1067)	13	-705 (1017)	11	-905 (1353)	
OCC (min · wk^{-1})							
SC	14	284 (279)	13	196 (366)	10	178 (455)	0.11
ALP	17	213 (214)	13	-38 (300)	11	90 (535)	
Walking (min · wk^{-1})							
SC	14	158 (205)	13	-82 (104)	10	-30 (107)	2.43
ALP	17	185 (207)	13	33 (155)	11	102 (237)	
Leisure (min · wk^{-1})							
SC	14	112 (167)	13	-10 (105)	10	-48 (91)	5.27*
ALP	17	108 (148)	13	151 (260)	11	84 (204)	
Moderate (min·wk^{-1})							
SC	14	303 (260)	13	228 (374)	10	187 (487)	0.30
ALP	17	278 (208)	13	21 (345)	11	90 (537)	
Vigorous (min · wk^{-1})							
SC	14	4 (6)	13	0 (24)	10	-4 (21)	0.64
ALP	17	21 (67)	13	32 (63)	11	9 (103)	
MVPA (min · wk^{-1})							
SC	14	466 (331)	13	146 (341)	10	153 (440)	0.28
ALP	17	485 (376)	13	86 (451)	11	200 (624)	

Note: *p≤ 0.05, **p≤ 0.01, ***p≤ 0.001, SC= Standard Care, ALP= Active Lifestyle Programme

Table 3 Group Differences in changes from Baseline to 3-months and Baseline to 6 months, SC= Standard Care, ALP= Active Lifestyle Programme

	3- months			6- months		
Variable	Mean Difference (ALP – SC)	95% CI	P-Value	Mean Difference (ALP – SC)	95% CI	P-Value
Amotivation	-0.47	-1.0-0.0	0.062	-1.0	-1.4 -0.4	0.002
Identification	0.3	-0.6-1.2	0.515	0.7	-0.2- 1.6	0.103
Intrinsic	0.3	0.1- 1.6	0.640	1.7	0.6 - 2.8	0.004
RAI	3.5	-0.6-7.8	0.092	9.6	3.3 - 16.0	0.005
Intention to exercise	1.1	-0.4 - 2.6	0.142	2.3	0.36 - 4.30	0.023
IPAQ Leisure (min · wk^{-1})	161	-6 - 329	0.058	74	-22 - 289	0.088

Note: SC= Standard Care, ALP= Active Lifestyle Programme

Table 4 Changes during follow-up at 9 and 12 months in all outcome measures from baseline to primary endpoint. Values are means (SD) unless stated otherwise.

Variable		9 months		12 months	Group x time F
	N	Δ Mean (SD)	N	Δ Mean (SD)	
Body composition					
Body weight					
SC	7	1.76 (2.1)	7	0.00 (1.7)	0.13
ALP	9	0.19 (1.9)	9	-1.26 (2.1)	
BMI					
SC	7	0.58 (0.7)	7	0.02 (0.6)	0.02
ALP	9	0.04 (0.7)	9	-0.42 (0.7)	
Body fat					
SC	7	0.74 (2.8)	7	3.28 (1.7)	0.10
ALP	9	2.03 (6.3)	9	0.76 (2.2)	
Waist-hip-ratio					
SC	7	0.04 (0.1)	7	-0.01 (0.02)	0.11
ALP	9	0.00 (0.1)	9	0.01 (0.03)	
Self-regulation					
Amotivation					
SC	7	-0.04 (0.4)	7	0 (0)	7.89**
ALP	9	-0.39 (0.8)	8	-0.56 (0.7)	
Extrinsic regulation					
SC	7	0.29 (0.5)	7	0.21 (0.4)	0.31
ALP	9	0.11 (1.2)	8	-0.19 (1.0)	
Introjection					
SC	7	0.19 (0.7)	7	0.47 (0.8)	0.01
ALP	9	0.10 (1.2)	8	0.41 (1.7)	
Identification					
SC	7	0.04 (1.0)	7	0.47 (0.8)	1.22
ALP	9	1.20 (1.2)	8	1.13 (1.0)	
SC	7	0.46 (1.3)	7	0.04 (1.4)	4.70*
ALP	9	1.61 (1.6)	8	1.66 (1.4)	
RAI					
SC	7	1.03 (5.5)	7	0.54 (5.2)	4.75*
ALP	9	8.08 (10.8)	8	8.87 (10.8)	

Variable		**9 months**		**12 months**	**Group x time F**
	N	Δ Mean (SD)	N	Δ Mean (SD)	
SEE					
SC	7	-0.47 (2.7)	7	0.71 (3.0)	1.93
ALP	9	2.50 (3.2)	8	2.34 (3.0)	
Intention					
SC	7	-0.79 (0.8)	7	0.25 (1.4)	1.83
ALP	9	1.70 (2.2)	8	1.39 (2.0)	
Quality of Life					
Physical Function					
SC	7	1.38 (2.1)	7	0.01 (2.5)	0.47
ALP	9	1.75 (9.8)	8	1.01 (8.0)	
Role-Physical					
SC	7	1.92 (6.9)	7	2.57 (6.1)	0.47
ALP	9	-3.99 (11.8)	8	-1.97 (11.4)	
Bodily Pain					
SC	7	2.82 (9.9)	7	1.21 (10.7)	1.30
ALP	9	-2.64 (9.5)	8	-2.26 (10.0)	
General Health					
SC	7	0.95 (7.9)	7	0.82 (10.6)	0.09
ALP	9	1.37 (7.7)	8	4.10 (10.6)	
Vitality					
SC	7	0.42 (3.6)	7	-2.12 (2.2)	0.60
ALP	9	5.28 (9.6)	8	2.97 (10.4)	
Social Functioning					
SC	7	3.58 (7.5)	7	3.58 (7.5)	1.85
ALP	9	-0.01 (10.9)	8	-0.63 (12.4)	
Role-Emotional					
SC	7	0.00 (0.0)	7	0.00 (0.0)	0.51
ALP	9	0.39 (5.9)	8	0.44 (7.8)	
Mental Health					
SC	7	0.37 (5.1)	7	0.00 (7.2)	0.00
ALP	9	0.29 (7.5)	8	0.65 (9.2)	
Physical Summary					
SC	7	2.29 (5.3)	7	1.40 (6.2)	0.55
ALP	9	-1.14 (10.1)	8	-0.10 (8.9)	

Variable		**9 months**		**12 months**	**Group x time F**
	N	Δ Mean (SD)	N	Δ Mean (SD)	
Mental Summary					
SC	7	0.40 (2.9)	7	0.02 (2.3)	0.01
ALP	9	1.9 (6.7)	8	1.2 (9.3)	
Fitness VO_{2max} (ml · kg^{-1})					
SC	7	N/A	7	-0.24 (2.2)	0.00
ALP	9	N/A	8	1.71 (4.4)	
Accelerometry					
VM (counts · min^{-1})					0.63
SC	7	45.9 (127.4)	6	53.5 (94.5)	
ALP	9	-33.3 (135.8)	8	3.5 (141.7)	
Sitting (min · wk^{-1})					
SC	7	-19 (317)	6	-126 (934)	0.19
ALP	9	-265 (1463)	8	-193 (1192)	
10-min bouts (moderate)					
SC	7	24 (49)	6	18 (65)	0.24
ALP	9	9 (78)	8	22 (71)	
Matt bouts (min · wk^{-1})					
SC	7	20 (144)	6	-4 (109)	0.65
ALP	9	-49 (172)	8	-59 (164)	
Accumulated MVPA (min · wk^{-1})					
SC	7	22 (61)	6	7 (74)	0.35
ALP	9	-26 (118)	8	-1 (87)	

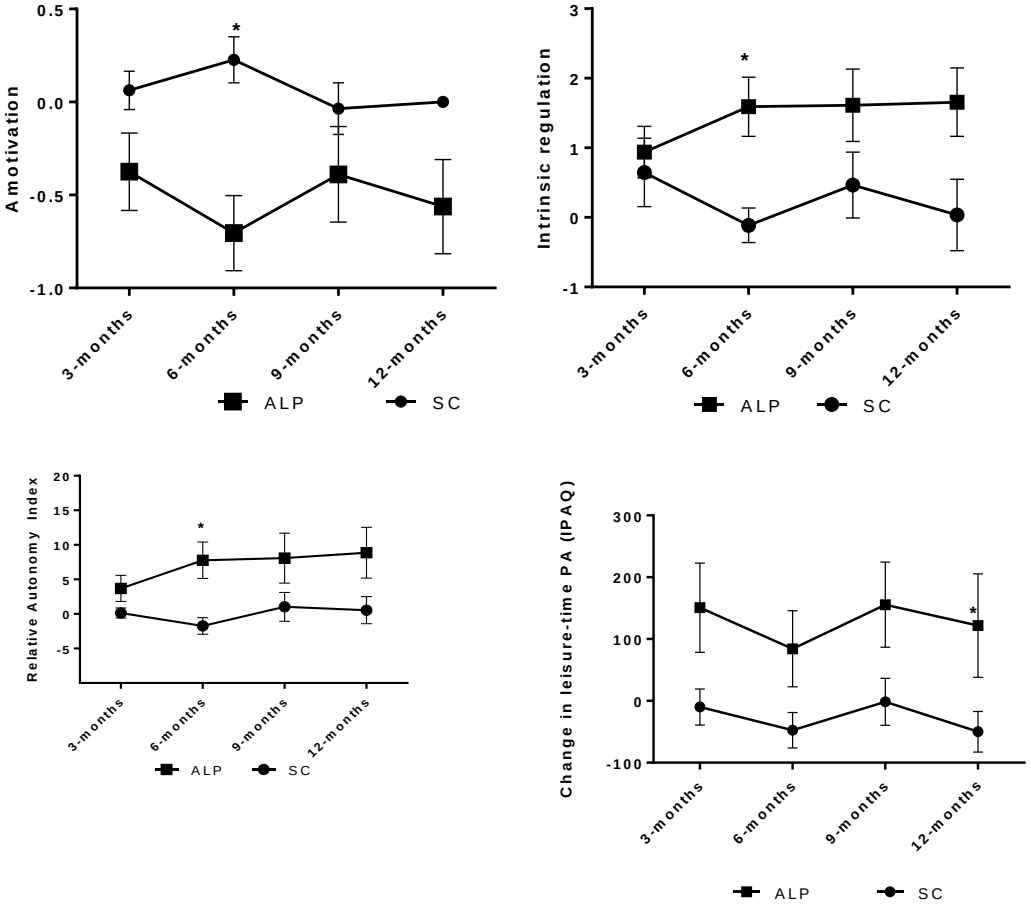
Variable		**9 months**		**12 months**	**Group x time F**
	N	Δ Mean (SD)	N	Δ Mean (SD)	
Steps · day^{-1}					
SC	4	46 (972)	6	-2244 (3644)	0.82
ALP	5	179 (1029)	4	83 (1485)	
Self-assessed PA IPAQ measures					
Sitting (min · wk^{-1})					
SC	7	-101 (1044)	7	-292 (1238)	0.15
ALP	9	-49 (1056)	8	-1000 (1412)	
OCC (min · wk^{-1})					
SC	7	66 (310)	6	65 (205)	0.00
ALP	9	-11 (329)	8	-65 (455)	
Walking (min · wk^{-1})					
SC	7	-21 (105)	7	-60 (105)	1.81
ALP	9	-4 (184)	8	-21 (233)	
Leisure (min · wk^{-1})					
SC	7	-1 (111)	7	-50 (80)	7.63**
ALP	9	156 (206)	8	122 (187)	
Moderate (min·wk^{-1})					
SC	7	56 (324)	7	26 (193)	0.03
ALP	9	17 (240)	8	5 (365)	
Vigorous (min · wk^{-1})					
SC	7	9 (23)	7	21 (27)	0.47
ALP	9	104 (143)	8	45 (72)	
MVPA (min · wk^{-1})					
SC	7	44 (387)	7	-13 (184)	1.12
ALP	9	-103 (497)	8	29 (514)	

Note: *p≤ 0.05, **p≤ 0.01, ***p≤ 0.001, SC= Standard Care, ALP= Active Lifestyle Programme

Table 5 Group Differences in changes from Baseline to 9-months and Baseline to 12 months

	9- months			12- months		
Variable	Mean Difference (ALP – SC)	95% CI	P-Value	Mean Difference (ALP – SC)	95% CI	P-Value
Amotivation	-0.3	-1.1 – 0.4	0.332	-0.6	-0.1 – 1.2	0.081
Intrinsic	0.9	-0.7 – 2.6	0.237	1.4	-0.2 – 3.1	0.078
RAI	6.1	-4.3 – 16.5	0.228	7.5	-1.1 – 16.1	0.081
IPAQ Leisure (min · wk^{-1})	146	-53 – 344	0.138	170	5 - 338	0.044

Note: *p≤ 0.05, **p≤ 0.01, ***p≤ 0.001, SC= Standard Care, ALP= Active Lifestyle Programme



ALP= Active Lifestyle Programm, SC= Standard Care Group

Figure 6 Overview of the key findings in motivational regulation and leisure time physical activity. Data points are means of the change at each time-point, error bars present the standard error of the means

5.6. Discussion

The primary aim of this study was to investigate the feasibility of an active lifestyle intervention in people diagnosed with colonic polyps. Secondary aims were to obtain preliminary data on the ability to change people's motivation to exercise, and to investigate the impact of the intervention on other health outcomes.

The recruitment rate was very poor (4.2%) compared to other studies reporting recruitment rates from 32% (Treweek et al., 2013b) to 61% (Emmons et al., 2005). However, these trials were home-based and thus, required less time commitment from the participants. Participants in this trial, if randomised to the intervention condition, were expected to visit the research site twice per week for 3 months, and once weekly for another 3 months. With travel time, each visit could have taken 2-3h of the participants' time. To improve recruitment rates, future trials should be multi-centred and offer programmes nearer to where people live. Reimbursement of travel costs should also be considered as an incentive to participate. The retention rate of 71% at the primary end-point was comparable to other trials with this population. Retention rates between 64% and 93% were reported in other CRC prevention interventions with a lifestyle component (Robb et al., 2010, Caswell et al., 2009, Emmons et al., 2005, Anderson et al., 2014). A more detailed discussion of recruitment and the different strategies used can be found in chapter 7.

Adherence to the supervised exercise sessions was 65%. We are unable to compare this to other studies with this population because no other lifestyle intervention with polyp patients included supervised exercise and workshops. However, a review of PA interventions with older adults reported an average adherence of 75% (King et al., 1998). Thus, adherence to the PA programme in this trial was below average. However, King et al (1998) also noted that the majority of trials did not include drop-outs in their analysis. If we only consider the completers of this intervention, then adherence to supervised exercise was 82%. Reasons for not attending sessions were work commitments, family commitments, illness, and holidays. Although, every effort was made to offer a flexible schedule for supervised exercise sessions and workshops, participants preferred to stick to certain times of the week. In an intervention that lasts for 6 months, it is not to be expected that

every session will be attended, because life gets in the way. Main reasons for missing out a supervised exercise session were illness, holidays or family commitments. These cannot be prevented over a 6 months period. Thus, we are of the opinion that 65 % attendance (and 82 % if drop-outs were not considered) is very good.

Almost half of the total number of withdrawals (n=4) occurred within the first two weeks of randomisation. Reasons for drop-out were health problems that made participants either ineligible to participate or deemed them physically unable to participate in an exercise programme. Thus, these participants should have possibly not been included in the trial, but the severity of their health problems was not apparent until their first attendance at the supervised exercise sessions. For example, one participant was diagnosed with CRC shortly after he was randomised. Another participant had back problems and despite assurance from his physiotherapist that participation in exercise is safe, he withdrew because of painful symptoms. Yet, another participant with multiple sclerosis had to be hospitalised only one week after her randomisation to ALP. Adherence to exercise interventions with elderly people might be lower than with younger participants, because older people are more likely to have health problems over a long-term intervention period. Thus, findings from this intervention might provide a rather realistic picture of what adherence to an exercise intervention with elderly people in a community setting would be like. It has been reported that often highly motivated and healthy people participate in such trials, not reflecting the general population (Harris et al., 2008, van Heuvelen et al., 2005). There were no adverse events during the intervention, unless people had existing health conditions. Based on the findings of attrition, attendance, and 'safety' of the intervention, we conclude that the intervention is feasible but multi-centre approaches should be considered in future studies to reduce the travel burden to the intervention site. Intervention design (self-selection to group allocation, frequency of supervised exercise sessions) needs to be carefully considered to maximise recruitment but to not jeopardise behaviour change.

Besides feasibility outcomes, an important aim of the study was to collect preliminary indicative outcome data to provide early evidence of whether an autonomy supportive intervention based on SDT is effective at transforming people's motivational regulation to be physically active from a more external regulation to a more internal regulation. The preliminary outcome data suggests that the intervention was effective at transforming motivational regulation from an external to an internal regulation. Participants in the intervention condition reported lower levels of amotivation and higher levels of identification, intrinsic motivation and the overall RAI. Moreover, the intervention effects remained significant at follow-up for amotivation, intrinsic regulation, and the RAI. This provides early evidence to confirm the internalization process of moving along the autonomy continuum from a more extrinsic regulation to an internal regulation if the environment is autonomy- supportive (Ryan and Deci, 2000). If the behaviour is internalized the person identifies with the value of an activity and accepts full responsibility for doing it. Thus, the behaviour emanates from one's self; it is self-determined (Deci et al., 1994). Similar results were reported in a lifestyle intervention with obese women in Portugal (Silva et al., 2010b). The intervention was also based on SDT and measured SDT-related outcomes at 4 months and 12 months. The authors reported significant *group x time* effects for intrinsic regulation and identification. Silva et al's study and the present study both show an elevation of identification and intrinsic regulation during the intervention, and a maintenance of this elevation post-intervention. It is interesting to note that in Silva's study participants received face-to-face contact on a regular basis throughout the 12 months intervention whereas, in our study face-to-face contact ceased after 6 months and there was no contact with the participant post-intervention until the follow-up assessment at 12 month. Yet, identification and intrinsic regulation remained at similar levels as at the 6 months assessment, although the group difference in change only remained significant for intrinsic regulation at follow-up. This suggests a maintenance effect of the intervention on behavioural regulations. Silva et al (2011) also reported significant higher levels of autonomous regulation (identification and intrinsic regulation) at 2 years (year 1 of follow-up). This indicates that motivational transformation can also be maintained

beyond 6 months. Further studies are needed to assess this maintenance in the long-term beyond 1 year of follow-up.

Another critical outcome of the study was PA behaviour. The study found a significant difference in self-assessed leisure-time PA only, with an increase in the intervention condition compared to a decrease in the control condition at all time-points. The intervention condition engaged in 228 min and 302 min of leisure-time PA post-intervention and at follow-up, compared to 41 min and 36 min in the control condition. The ALP was also meeting the PA recommendations for the prevention of CC at all follow-up time-points. Currently, there are only four trials of PA interventions with this population (Emmons et al., 2005, Robb et al., 2010, Anderson et al., 2014, Caswell et al., 2009) and only two found improvements in PA levels post-intervention. Two of these studies did not report any improvement in PA levels (Emmons et al., 2005, Robb et al., 2010), but one reported less regression of PA levels over the intervention period (Emmons et al., 2005). Both studies were leaflet based interventions without face-to-face contact. The other two studies however, did find improvements in PA levels post-intervention. Participants in the BeWEL trial received three face-to-face counselling sessions and 9 phone calls spread over a 12 month period. PA was measured with an accelerometer worn around the arm (Sensewear) (Anderson et al., 2014). The authors found a mean group difference of 619 steps per day post-intervention in favour of the intervention condition. In this present study, at post-intervention we found a mean group difference of 1143 steps per day, and at follow-up a mean difference of 782 steps per day in favour of the intervention condition (differences were not significant). All other outcomes are only reported as daily PA and not as weekly PA and the device of measuring PA is different making it difficult to compare the results to our findings.

The only other published lifestyle intervention based on SDT also found increased levels of PA at post-intervention, and at 1 year follow-up (Silva et al., 2011, Silva et al., 2010b). Self-assessed MVPA was 138 min and 93 min per week higher in the intervention group compared to a control group post-intervention and at 1 year follow-up, respectively. The mean group differences in our study for self-assessed

MVPA post-intervention and follow-up was 192 min and 219 min per week. These results demonstrate that an autonomous-supportive intervention has the capability to not only transform motivational regulation but also to maintain a newly learned PA behaviour beyond the intervention. Autonomous forms of motivational regulation have been associated with maintenance of PA behaviour, confirming the findings of this study (Thogersen-Ntoumani and Ntoumanis, 2006). Specifically, exercisers in the maintenance stage of PA reported significantly higher intrinsic motivation, identified regulation and introjected regulation, and significantly lower external regulation and amotivation than participants in the preparation state. Other studies that conducted mediation analysis between behavioural regulations and PA behaviour found that autonomous regulations had greater effects on PA behaviour and behavioural intentions than controlled regulation (Sebire et al., 2011, Hagger et al., 2006, Wilson and Rodgers, 2004).

There were no significant differences between the groups in any other self-assessed PA domain or any of the accelerometry outcomes. It is surprising that the group differences in leisure-time PA were not reflected by the objective PA measure. This might be due to limitations of the accelerometer to inaccurately measure certain activities, such as bicycling, swimming, strength exercises, and upper body exercises (Hendelman et al., 2000, Swartz et al., 2000a). Examination of PA diaries showed that at follow-up ALP participants engaged more frequently in such activities (gym visits, bicycling, aerobics, Pilates, and strengthening exercises at home) than the control condition. PA in the control condition was dominated by walking, household, and gardening activities. This could explain the lack of findings in accelerometer outcomes. Another explanation might be that the set cut-points for moderate intensity PA are too high to record the low vibrations produced during PA in the elderly. Despite using lower cut-points, which commonly would be interpreted as mild activity intensity in an adult population, we did not find any changes in the Matthews bouts recordings. The LIFE study (Rejeski et al., 2013) used accelerometry during supervised walking sessions and found a large variability in accelerometer counts between the participants. Where some participants had median activity counts well above the cut-off point for moderate intensity PA (>1952 for Freedson's, >760 for Matthews'), other participants had median activity

counts well below the moderate intensity cut-off-point. Participants in that study were 70- 80 years old. Thus, it is likely that despite being physically active at a perceived moderate intensity, participants in our study may have not met the minimum cut-off point for moderate intensity PA to produce a reading on the accelerometer. However, there are some other interesting patterns in the accelerometer data which indicates a trend for improvements in PA time in the ALP compared to SC. First, at every repeated measurement, participants in the intervention condition engaged in more minutes of moderate 10-min bouts per week (41 min more on average). Second, ALP did slightly less steps per day at baseline but still exceeds the step count of SC at all follow-up measurements. Third, the records for minutes per week in Matthew bouts (760 – 5724 cpm vs 1952 – 5724 cpm with Freedson bouts) are higher in the SC than in the ALP indicating that SC is engaging in less strenuous PA than ALP. However, these results have to be interpreted with caution because the group differences were not significant. This is likely due to the small sample size, a large standard deviation, and the large amount of missing data at primary end-point and at follow-up. Notably, participants in the intervention condition improved their cardiopulmonary fitness post-intervention and maintained this fitness level at follow-up and participants in the control condition decreased their fitness at both repeated measurements. This further supports findings of increased PA levels, despite a lack of statistical significance between group means.

No changes were found in QoL post-intervention and at follow-up. This is likely due to participants reporting high QoL at baseline assessment. QoL was not assessed in other prevention interventions in this population allowing no comparison. But previous studies have reported that study participants entering lifestyle interventions are likely to be healthier than non-participators (van Heuvelen et al., 2005, Harris et al., 2008).

Although, there were no substantial group difference in SEE, mean changes show an increase in the intervention condition in comparison to a decrease or no change in the control condition. Intention was measured because it was previously shown that intention to exercise mediated the effects of autonomous regulation on

behaviour (Hagger et al., 2006). Moreover, SEE has been theorized to be a mediator between motivational regulation and intention (Luszczynska et al., 2011). Whether these psycho-social variables are mediators between motivational regulation and behaviour in patients diagnosed with colonic polyps could not be determined in this study because mediator analysis is not possible with such a small sample size.

Limitations and strengths

The results of this study should be interpreted in the context of several limitations. First, the sample size was very small and we were unable to follow-up all participants which introduced bias to the data set due to large amount of missing data. Drop-outs further contributed to missing data. This resulted in a lack of statistical power to detect changes in the study outcomes. Furthermore, ascertainment bias was introduced to the study because the researcher who carried out all research activities (delivering the intervention, data collection, data analysis) was not blinded to the group allocation of participants. Based on the nature of the study, it was unavoidable to blind the researcher to the group allocation. Thus, the assessments were not blinded, but it was not expected to influence the subjective measures (e.g. body composition). Cardiopulmonary fitness tests were carried out by a blinded assessor because the outcome of the test could be influenced by motivation if the exercise instructor was present. The strengths of the study are the randomised controlled design, the use of subjective PA measures, a long-term follow-up, the measurement of peak VO_2, and a theory-based intervention with a high rate of intervention delivery. Lastly, results indicated the potential of contamination of the control condition with increased physical function in both groups, but no other changes in QoL outcomes. Contamination of the control condition is not uncommon, and it is likely that simply participation in a study increases people's awareness of health behaviours (Wagner and Ingersoll, 2012). Participants consenting to a lifestyle behaviour change study are likely to have an interest in changing their lifestyle behaviour, and thus, the participation might be a motivator.

5.7. Conclusion

The findings in this study suggest that an autonomy-supportive lifestyle intervention with supervised exercise sessions and counselling workshops is feasible and has the potential to evoke changes in PA levels and in behavioural regulations from a more external regulation to a more internal regulation in elderly people diagnosed with colonic polyps. Furthermore, the findings indicate that an intervention based on SDT could be successful in maintaining behaviour changes beyond the intervention. A larger RCT is needed to confirm these preliminary findings, and follow-up time should be extended beyond 12 months.

Chapter 6

A feasibility study of an autonomous supportive intervention in people recovering from with CRC: a randomised controlled trial

6.1. Abstract

Background: Self-Determination Theory (SDT) has been used successfully as a model for health behaviour change in weight loss programs. However, the effectiveness of SDT for promoting PA (PA) behaviour change in CRC survivors is unknown. The aims of this study were to investigate the feasibility of implementing a SDT approach in this population and to obtain preliminary data on the effects of such intervention on motivational regulation for being physically activity. *Design:* The study was a feasibility trial with non-blinded randomized controlled design. *Methods*: Patients (n=28, mean age 65y [SD=8.3], BMI=27.7 [SD=4.6]) recovering from CRC were randomised to a standard care (SC) (n=14) or an active lifestyle programme (ALP) (n=14). The intervention lasted 3month with a 3months follow-up period post-intervention. The ALP received supervised exercise sessions and PA workshops based on motivational interviewing, and SC was encouraged to continue with their usual lifestyle behaviours for the duration of the study. The primary outcomes were feasibility outcomes (recruitment, attrition, attendance). The secondary outcomes were motivational regulation, PA behaviour, physical fitness and strength, quality of life, self-efficacy, intention to exercise, and psychological need satisfaction. *Results*: Missing data was imputed and thus, 28 data sets were available for analysis. Overall recruitment rate was 58.3% of eligible participants. The main barriers were participation for time commitment and the travel distance to the research site. Attrition at 3months was 14% and 29% at 6months follow-up. Attendance at supervised exercise sessions was 79% and at physical activity counselling workshops 71%. Post-intervention, ALP was engaging in 98min more walking time physical activity ($P< 0.05$). Group differences were also observed for body composition with a reduction in body weight (-1.6kg), BMI (-0.04 kg/m^2) and body fat (-1.4%) in ALP compared to an increase in these parameters in SC (+1.1kg, +0.5 kg/m^2, +0.3%) ($P< 0.05$). At follow-up group differences were maintained for BMI (difference in mean change of 2.9 kg/m^2) ($P< 0.05$). At follow-up ALP engaged in more moderate intensity physical activity than SC (difference in mean change=331min, [$P< 0.05$). No differences were observed for behavioural regulation, self-efficacy, intention to exercise, and quality of life at any time-point. Exercise was deemed safe and there were no adverse events throughout the

intervention. *Conclusion*: Recruitment rates were comparable to other studies with this population, but attrition was high. The findings suggest that a 3-month autonomy supportive intervention is effective at changing PA behaviour, but is not likely to evoke changes in behavioural regulation and of quality of life. Other successful studies were longer in duration. A larger RCT should investigate whether intervention duration effects behavioural regulation over time.

6.2. Introduction

It is estimated that 57% of adult bowel cancer patients diagnosed in the UK today will survive ten or more years (CancerResearchUK). The five-year survival rate has increased from 25% in 1971 to 59% in 2011. This means that more people with CRC are alive today, and a significant proportion of patients will be a long-term survivor with the potential to develop second CRCs, comorbid conditions, and long-term effects of treatment (Denlinger and Engstrom, 2011, Yabroff et al., 2004). CRC survivors are at increased risk of a second primary CRC of which 43% occur after 2 years survival, but patients may also have an increased risk of non-colorectal secondary cancers (Greene and Lepper, 1974, Birgisson et al., 2005). Up to 80% of CRC survivors report at least one comorbidity and these may affect long-term physical health and QoL with more than 32% of CRC survivors reporting limitations due to comorbid conditions (Jansen et al., 2010, Denlinger and Engstrom, 2011). Although, CRC survivors generally are reporting well to excellent QoL with comparable QoL to an age-matched non-cancer population, they may suffer from lower physical QoL (Jansen et al., 2010). PA during and after adjuvant treatment for cancer has been reviewed by national bodies and was cited to be feasible, safe, to enhance physical functioning, to benefit primary prevention for comorbidities, and to reduce the risk of death and recurrence (PANEL, 2010, World Cancer Research Fund and American Institute for Cancer Research, 2007). In terms of recurrence and survival, regular weekly PA of at least 18 MET-hours per week (approximately 6 hours of brisk walking) has been positively associated with nearly 50% higher chance of survival and reduced risk of cancer recurrence (Meyerhardt et al., 2006b, Meyerhardt et al., 2009, Meyerhardt et al., 2006a). Please refer to chapter 2 for a more detailed examination of the link between PA and the benefits for survival and reduced risk of recurrence. The American College of Sports and Medicine recommended the same PA guidelines for cancer survivors as for the general population, which is at least 150min of moderate intensity or 75 min of vigorous intensity PA per week. Two to three sessions of strength exercises weekly are also recommended in addition to these guidelines. Despite the evidence of the benefits of PA and the endorsement of PA for safety and feasibility for CRC survivors, the minimum of the PA guidelines are often not met by the majority of CRC survivors.

An Australian survey found that PA declines post-diagnosis from just over 50% meeting the current PA recommendations pre-diagnosis, to 32% at 6 months and 25% at 12 month post-diagnosis meeting these recommendations (Hawkes et al., 2008). Moreover, at 12 months post-diagnosis 61% of CRC survivors were overweight/ obese. A survey with a Korean sample found that CRC survivors engaged in 107.5 min of MVPA per week, which is below the recommended PA guidelines (Chung et al., 2013). There is clearly a need for lifestyle interventions to improve PA behaviour in CRC survivors. Most previous lifestyle interventions in this population were home-based and currently, there is limited evidence to support the efficacy of these interventions for improving QoL, and PA behaviour change (Courneya et al., 2003b, Houborg et al., 2006, Hawkes et al., 2009). Furthermore, studies that did demonstrate a change in PA or QoL were either lacking a control group (Anderson et al., 2010, Houborg et al., 2006) or lacked support for long-term maintenance of PA behaviour change (Pinto et al., 2013, Hawkes et al., 2013). Only one lifestyle intervention has demonstrated significant group differences immediately in the long-term 6 months post-intervention (Hawkes et al., 2013). In Pinto et al's (2013) participants were CRC survivors within 5 years of treatment completion and were randomised to a control group or an intervention group. The intervention group was provided with home PA logs, a pedometer, and encouraged to exercise 10 min at least 2 days per week at the start of the intervention and to gradually increase PA to 30min per day on at least 5 days of the week towards the end of the 12 week intervention. Participants received weekly phone calls to monitor PA participation, identify problems, and solve any barriers. The intervention was underpinned by the transtheoretical model and social cognitive theory. The authors reported significantly more exercise in the intervention group at 3 months, but not at 6 and 12 months. However, the control condition also increased PA at all time-points. It is encouraging that 64.7% of intervention participants were meeting the current PA guidelines at 3 months, but this dropped to 38.9% and 31.6% at 6 and 12 months, respectively. The other RCT demonstrating positive effects on PA behaviour post-intervention offered 11 phone calls to 250 intervention participants which were spread over a 6 month period addressing the cancer experience, CRC-related symptoms, and strategies to enhance improvement

in health behaviours (Hawkes et al., 2013). In addition, the intervention group received a pedometer to monitor PA behaviour, regular motivational postcard prompts, a participant handbook, and a quarterly study newsletter. The intervention was underpinned by Acceptance and Commitment Therapy. The difference between the groups in MVPA per week was not significant immediately post-intervention at 6 months, but at 12 month follow-up there was a mean difference of 23.7 min between the groups. However, the intervention group only increased by 21.6 min of MVPA per week to 85.2 min. Despite the efficacy of the intervention in improving PA behaviour the minutes of PA is below the minimum PA recommendations of at least 150min of moderate intensity PA per week. The intervention focused on multiple health behaviours and it has been suggested that single-behaviour interventions may have a greater impact on the target behaviour then multiple health behaviour interventions (Prochaska and Prochaska, 2011). Multiple behaviour change interventions combining nutrition and PA were more likely to produce positive changes in diet than in PA. Furthermore, a review of behaviour change interventions reported that interventions with an underlying theoretical model are more likely to produce positive intervention outcomes than interventions without an underlying theoretical model (Greaves et al., 2011). Notably, the only two lifestyle interventions with CRC survivors successful at producing a significant effect on PA behaviour post-intervention used an underlying theoretical model to support the intervention.

The lack of evidence of successful interventions with CRC survivors in maintaining PA levels in the long-term raises questions of what could facilitate motivation to be more physically active. Different qualities of motivation (extrinsic or intrinsic) have been associated with exercise participation (Thogersen-Ntoumani and Ntoumanis, 2006). Whether someone feels extrinsically or intrinsically motivated is largely depended on social and environmental factors that facilitate versus undermined intrinsic motivation (Ryan and Deci, 2000). In the light of previous findings in regards to a lack of long-term PA behaviour change of lifestyle interventions with CRC survivors this study will be underpinned by a theoretical behaviour change model that has been shown to be effective at maintaining intervention effects (Williams and Rodin, 1998, Williams et al., 1996). SDT proposes different types of

extrinsic motivation which vary in level of self-determination. These are amotivation, extrinsic regulation, introjection, identification, and intrinsic motivation. The different qualities of these motivational regulations and the processes that facilitate motivational development have been described elsewhere, and the reader may refer to chapter 3. SDT has been shown to be successful at maintaining behaviour change in the contexts of weight loss (Williams et al., 1996), long-term medication adherence (Williams and Rodin, 1998), and maintenance of PA behaviour change (Silva et al., 2011). Thus, SDT is a promising theoretical model for long-term PA behaviour change for a population of CRC survivors. However, no previous study has tested an intervention specifically designed to facilitate autonomous self-regulation and intrinsic motivation for PA in this population.

Aims

This study aimed to investigate the feasibility of a 3-month active lifestyle programme in people diagnosed with CRC. A secondary aim was to obtain preliminary data on the effects of the intervention on motivational regulation for being physically active, actual PA behaviour, psychosocial factors and QoL. We were also interested whether changes post-intervention would be maintained after a 3 month follow-up.

6.3. Methods

The trial was registered with ClinicalTrials.gov and given the identifier: NCT02751892

Study design

This study was a randomized controlled feasibility trial consisting of a 3-months active lifestyle intervention and a 3-months follow-up period. Participants were allocated to an active lifestyle programme (ALP) or the standard (SC) care group. ALP was offered 12 supervised exercise sessions over 3 months at the University of East Anglia and six supportive behaviour change workshops. SC was encouraged to continue with their usual lifestyle. Study outcomes were repeated at 3, and 6-months.The study was approved by the NRES Committee East of England, and the

NHS Norfolk and Norwich Research and Development Department. All documents can be found in the appendices.

Participants

Participants were patients from the NNUH who i) a histologically confirmed diagnosis of colorectal cancer with Dukes stages A-C ii) completed cancer treatment within the last 24 months, iii) be able to understand spoken and written English, iv) score of 80 or more on the Karnofsky Performance Status Scale. The exclusion criteria were: i) already meeting general PA guidelines of 150 min of moderate PA or 75 min of vigorous intensity PA per week, ii) recent myocardial infarction iii) uncontrolled hypertension iv) a pacemaker v) or unstable angina.

Note: An amendment was later added to change the inclusion criteria to include patients who completed treatment in the last 3 years instead of the last 22 months. This was changed because the patient pool of potentially eligible patients was exhausted before recruitment target was met.

We only included patients who completed treatment within the last 24 months. This decision was made because patients could differ in their motivation to make changes to their lifestyle post-intervention based on the proximity to their diagnosis. Closer to their diagnosis, patients might be more motivated (McBride et al, 2003). Patients already doing sufficient amount of weekly PA were not included because they may already have internally regulated behavioural regulation and therefore, would have not responded to the intervention. The reason for exclusion of patients with heart conditions were for safety reasons.

Recruitment

Recruitment took place from August 2013 to January 2014. The CRC Lead and chair of the Colorectal Multi-Disciplinary Team together with a Colorectal Specialist Nurse from the Colorectal Surgical Department at the NNUH identified potential patients from the hospital register. The clinical team sent an invitation letter and a participant information sheet to potential participants. The clinical staff was aware of the inclusion criteria and only sent letters to potentially eligible patients. This decision was made based on the patients' medical record that the health

professionals had access to. A reminder letter was sent to non-responders after 2 weeks. Interested participants contacted the clinical team or the researcher to express an interest in the study and schedule an initial information appointment with the researcher. This appointment took place at the University of East Anglia and served to fully explain the study, answer questions the participant may have, and collect full study consent. Consented participants then received a questionnaire booklet and an accelerometer and a second appointment was scheduled to complete baseline measurements. This second appointment also served as a screening assessment. Participants PA levels from the IPAQ were analysed immediately after data collection. It was up to the researcher's judgement whether the participant was rated as not sufficiently active or too physically active to take part in the study. For example, if a participant met the minimum of 150min of PA per week, but mainly reported household chores such as hoovering, and no activities that require large muscle groups, such as walking, the participant was deemed eligible. If a participant reported regular gym visits which amounted to the minimum weekly PA requirements, the participant was deemed ineligible. After completion of the baseline measurements the participant was randomized to ALP or SC.

Other considerations of the intervention

In the event of a serious adverse event, the researcher would take appropriate measures ensure the safety of the participants. Serious adverse events were recorded by the researcher within 24h of becoming aware of an adverse event.

Trial Steering Committee

A trial steering committee, which consisted of the researcher (LL), the principle investigator (JS), secondary supervisor (JH) (JH is also the clinical collaborator), and third supervisor (NB), and a specialist nurse (UM), met at least every 3 months. At this meeting, the primary focus was recruitment. Researchers reported on the progress of recruitment, and collaboratively, the members of the steering committee came to conclusions about potential amendments to the current

recruitment strategies. The nurse communicated the conclusions from the meeting to other nurses at the hospital, who were involved in recruitment.

Training

Nurses who recruited into the study met with the researchers prior to commencement of the study. Researchers provided the nurses with information about the study. They were informed about the inclusion criteria and provided with a folder that contained patient information sheets, and envelopes to prepare letters to potentially eligible patients.

Randomization

Participants were randomised using nQuery (Statistical Solutions, Cork, UK). A person independent of the research team kept the generated randomisation sequence. After all baseline assessments were completed, the researcher telephoned the independent person to obtain details of group allocation. The researcher (LL) who carried out the assessments, the supervised exercise sessions, and counselling workshops was not blinded to the randomisation of the participants because of logistic reasons. No other researcher worked on this study, thus LL was the only person available to complete all these tasks, and thus could not be blinded to the group allocation of participants.

Intervention

Standard care group

SC was encouraged to continue with their usual lifestyle habits. No health and PA advice was given to SC. Participants were only contacted for follow-up appointments after 3, and 6-months. Supervised exercise sessions were offered to SC after their last appointment.

Active Lifestyle Programme

General format

ALP were offered supervised exercise sessions twice per week for the first four weeks. This was tapered off to once per week for the second four weeks. During

the last month of the intervention participants continued with the exercise at home and were encouraged to achieve 150min of moderate to vigorous PA per week. The times and days of the intervention components were flexible and scheduled to suit participants' availability. Participants could agree on one or two days of the week where most people were available for supervised exercise sessions. However, some participants received one-to-one exercise because full-time employment prevented them from joining the group. Behaviour change workshops to aid the uptake and maintenance of PA were delivered once per week for the first month, then every fortnight during the second month. In the final month of the intervention participants received two supportive phone calls. The exercises and the workshops were led by the same person. This person is a trained REPs level 2 exercise specialist and a trained motivational interviewer. The facilitator kept records of attendance at the end of each supervised exercise session and counselling session. Further details of the content of the supervised exercise sessions and the topics and theoretical rationale for the workshops is described in chapter 4.

Outcome measures

Feasibility outcomes

Feasibility outcomes such as response to letters, number of eligible people, reasons for exclusion, were assessed and are reported in more detail in chapter 7. Other feasibility outcomes such as compliance (attendance at supervised exercise sessions and workshops) and attrition (reasons for drop-out) will be reported here.

Other outcomes assessed the motivational regulation to exercise, PA behaviour, cardiopulmonary fitness, self-efficacy for exercise, quality of life, and body composition. All questionnaires were collected in a questionnaire booklet which the participant could complete at home. Participants were instructed to complete the whole booklet at once and not to fill in parts of the questionnaires on different days.

Body composition

Body weight was measured using the *SECA 711* scale (Seca Medical Measuring Systems, Birmingham, UK) to the nearest 0.1kg. Height was measured with a

stadiometer to the nearest 0.1cm. Weight (kg) and height (m) were used to calculate the Body Mass Index (BMI) (kg / m^2). Body fat was analysed using an *AKERN BIA 101* (Akern Srl, Pontassieve, Italy). Waist and hip circumference were also measured using a *Seca* tape measure.

Physical activity

Accelerometery

The *accelerometer ActiGraph® GT3X* (Actigraphcorp, Pensacola, FL, US) was used to measure participant's free-living PA over a period of seven days with the use of an accelerometer. This is a small unobtrusive device that detects the acceleration produced by the movement of the body. It also allows assessment of frequency, intensity and duration of PA (Ridgers and Fairclough 2011). The ActiGraph® GT3X collects acceleration data from three planes of movement and thus provides a more accurate assessment of PA than uniaxial devices. Accelerometry has been found to be superior over subjective measures when compared against doubly labelled water (Colbert et al. 2011). However, the ActiGraph® GT3X has its limitations. It only gives step and activity counts which cannot be measured during some activities (e.g. bicycling, predominantly upper-body activities). Furthermore, it is not waterproof and therefore, aqua activities cannot be measured. Therefore, participants were given an activity diary over the 7-day wearing period. This is also very useful in providing information on the types of activities participants were engaging in. Participants were instructed on the correct wear position of the accelerometers by the researchers (around the waist and above the right ilia crest).

Accelerometer data is reported as accumulated moderate to vigorous PA (MVPA), i.e. the sum of all movements above 1952 counts per minute (cpm) (Freedson et al., 1998). Because the PA guidelines for health recommend that PA should be carried out in bouts of at least 10 min to contribute towards the PA goals, we also reported PA in terms of 10-min of moderate intensity PA (1952-5724 cpm), and 10-min bouts of vigorous intensity PA (>5724 cpm). However, no vigorous intensity PA was recorded at any time-point (apart from one person). Thus, results are only reported as accumulated MVPA and moderate bouts. There has been criticism of the conventionally used cut-points for moderate and vigorous intensity PA developed

by Freedson et al (1998) (moderate intensity: 1952-5724 cpm, vigorous intensity >5724 cpm) at lower cpms may be more appropriate for the elderly. Thus, we included an additional measure of 10-min bouts with the criteria of 760-5724 cpm for moderate intensity PA was included in the analysis (Matthews et al., 2005) and refer to as 'Matthews bouts' in the remainder of the chapter.

Self-assessed PA

The *International PA Questionnaire* (IPAQ) (appendix 7) is a self-administered questionnaire designed to measure four domains of PA: 1) job-related, 2) transportation-related, 3) house work-related, and 4) recreation-related (http://www.ipaq.ki.se). A benefit of the IPAQ is its tested validity across different languages and therefore, offers a comparable estimate of PA within and between countries. The validity of the IPAQ has been rated as acceptable for total PA (ρ= 0.55) and the different activity domains (Hagstromer et al., 2006).

The questionnaire was delivered in an interview-form with each participant. The questionnaire has been criticised for over-reporting PA and elderly populations may experience difficulties in interpreting the meaning of certain questions (Heesch et al., 2010). We found acceptable validity for the interview-delivered IPAQ (ρ=0.43) in this population (please refer to chapter 8). Before delivering the questionnaire, the researcher explained the different domains of PA to the participant, clarified what moderate and vigorous activities meant, that only activities of a duration of 10 min or longer would be recorded, and emphasized that only the last seven days were to be considered in the answers to the questions. Then the researcher read each question out loud to the participant and helped clarify types of activities if the participant had difficulties answering the question.

Physical activity diaries

Participants were provided with a PA diary which they were asked to complete for 7 consecutive days. These were the same 7 days that they were asked to wear the accelerometer. The diary provided space to record the type of activity, the intensity of the PA as rate of perceived exhaustion (RPE), and duration of the activity. Participants were given instructions by a researcher on how to complete the diary, and were provided with written information on how to rate the PA intensity based

on the RPE scale. The diaries were not analysed because a substantial amount of data was missing, which made diary data not representative. Furthermore, participants did not provide sufficient details in the diaries to make meaningful conclusions about the durations and types of activities performed.

Functional capacity

A test of *cardiorespiratory fitness* was performed on a treadmill using the modified Bruce protocol (appendix 10). The test is a 10-stage walking test, with speed and incline increasing every 3min. The test was terminated when heart rate measured 85% of the predicted maximum (predicted with the Tanaka equation 208-0.7 x age (Tanaka et al., 2001), and perceived intensity was rated as 'hard' by the participant which was determined with the 15-point BORG-scale (scale of perceived exertion, Appendix 1). Results are reported in minutes of treadmill walking until termination of the test.

Intervention-based questionnaires – measures of Self-determination

The Behaviour *Regulation for Exercise Questionnaire* version 2 (BREQ-2) (Appendix 3) was used to assess participant's motivation regulation for exercise (Markland and Tobin, 2004). The original BREQ (Mullan et al., 1997) measured four intrinsic and extrinsic forms of regulation, namely *external, introjected, identified* and *intrinsic*. The BREQ-2 was developed to include *amotivation*. A relative autonomy index (RAI) can also be calculated and a higher score indicates more self-determination. Responses to the 19-item questionnaire were scored on a 5-point Likert scale ranging from 0= "Not true for me" to 4= "very true for me". Research supports the 5-factor model of the BREQ-2 and The Behaviour Regulation for Exercise Questionnaire version 2 (BREQ-2) was used to assess participant's motivation regulation for exercise (Markland and Tobin, 2004). Research supports the 5-factor model of the BREQ-2 and internal consistency was found to be acceptable (Cronbach's alpha ranged from 0.79 to 0.86). Internal consistency was found to be acceptable (Cronbach's alpha ranged from 0.79 to 0.86).

The *Psychological Need Satisfaction In Exercise Scale* (PNSE) measures the satisfaction of the psychological needs autonomy, relatedness, and competence, proposed to enhance self-determination. The 18-items are rated on a 6-point Likert

scale (1= 'True', 6= 'False'). Previous validation research of the questionnaire found high internal consistency (Cronbach alpha > 0.90) (Wilson et al., 2006b). (Appendix 9)

Quality of Life

The *Functional Assessment of Cancer Therapy-General* (FACT-G) is a cancer specific QoL questionnaire. Domains assessed with the questionnaire are physical well-being, social/family well-being, emotional well-being, and functional well-being). Each domain comprises 6-7 items which are rated on a 4-point Likert scale (0= 'Not at all, 4= 'Very much'). Higher scores represent high QoL. Results are reported as a domain score and an overall QoL score.

Fatigue and colorectal specific side-effects were assessed with the FACT subscale F*atigue* (FACT-F) and FACT subscale *Colorectal* (FACT-C). The FACT-F is a 13-item scale and higher scores represent higher fatigue and FACT-C an 11-item scale where higher scores represent better QoL and thus, less CRC treatment side-effects (appendix 8).

The *Intention to exercise* (Appendix 4) is a short instrument consisting of two questions: "I intend to exercise regularly over the next month" and "I intend to exercise regularly over the next 6 months". The questionnaire is based on Ajzen's model of 'Theory of Planned Behviour' (Ajzen, 1991) and has been used in PA behaviour change interventions. Intention is rated on a 7-point Likert Scale ranging from 1= "Completely Agree", to 7= "Completely disagree".

The *Self-Efficacy for Exercise* (SEE) (Appendix 5) is a 9-item questionnaire which assesses self-efficacy to continue exercising under a variety of situations, such as bad weather, pain, lack of enjoyment. A higher score represents higher self-efficacy. A test of validity revealed a high internal consistency (alpha=0.92) (Resnick and Spellbring, 2000).

Tests of physical function

The *Chair sit-to-stand* test measures the muscle function of the lower body. It uses a chair and a stop watch. The aim of the test is to do as many 'sit-and-stands' as

possible in 30 sec. The participant begins in a seated position on a chair and is instructed to rise to a full standing position and return to a fully seated position immediately. The number of times this motion could be repeated over a 30 sec-period was recorded. Only a complete repetition counted towards the final score.

The *Arm-curl test* is a measure of upper body muscle strength and endurance using dumbbells. Upper body strength is an indicator of ability to perform usual daily tasks such as household tasks and getting dressed. The participant is seated on a chair with the back in an upright position. A dumbbell of suitable weight for women and men is chosen for biceps curls over a period of 30 sec. The number of curls performed in 30 sec was recorded.

Grip strength is a measure of maximum hand grip strength and represents upper-limb strength. A dynamometer, a device that measures force, is gripped between the flexed fingers and the base of the thumb. A mean of four measurements comprising two measurements with the left and two with the right hand was recorded.

Analysis

Data preparation

Excel spreadsheets were created for every outcome measure and data was entered into the spreadsheet. All data was examined visually for completeness and errors before being copied to the Statistical Package for the Social Sciences (SPSS) version 22 for analysis. Graphs were created with the GraphPad Prism 6 software.

Post-intervention 15% of participants were lost to follow-up and at 6 months 29% of participants dropped out. Additionally, there was some data missing from questionnaires where participants did not complete some questions for one reason or another. Missing value analysis was carried out with SPSS, and it was observed that data was missing at random. Missing data was then imputed with linear interpolation technique using SPSS. We included all 28 participants in the analysis.

The initial analysis plan

We planned to include all data in the analysis, including non-completers using an intention-to-treat model. In the event of missing data, this was to be imputed with a suitable imputation strategy after examination of the data. Primary and secondary outcome measures were to be examined with repeated measures ANOVA General Linear Model to assess change in dependent variables and to test for between-group differences. This was chosen because there are three time-points at which data is collected, BL, 3, and 6 months. Post-hoc tests were to be selected for the repeated measures variables to examine between group differences at each time-point.

Change of plan of analysis

The data was examined for sphericity which is an assumption for the repeated measures ANOVA. The majority of domains of the IPAQ-L did not meet the assumption for sphericity. Therefore, overall sphericity did not hold for the data set which could result in a loss of power (Fields, 2005).

For normality testing in SPSS, the data were split into groups, and examined with normality plots and normality test (*Kolmogorov-Smirnov)* test of Normality). If significance values were greater than 0.05, the data were deemed normally distributed. If data was not normally distributed, attempts were made to normalise the data by applying log-transformations. Due to the nature of the data (many zero values for PA behaviour, or zero values for amotivation), log-transformation did not normalise the data. Replacing the zero values with very small numbers, (e.g. 0.001) did also not normalise the data.

The ANOVA is considered a robust test against the normality assumption. However, if the sample size is very small, which is the case in our study, there is a greater risk of Type I error (https://statistics.laerd.com). In this case it is recommended to attempt normalising the data. As described above, attempts to do so did not result in normally distributed data for PA behaviour and behavioural regulation.

Besides feasibility outcomes, the primary research interest of the intervention was whether PA and behavioural regulation will be different between the groups post-intervention (at 3 months). The group differences at follow-up (6 months) were

secondary outcomes. Therefore, it was decided to treat the two time-points as separate outcomes as part of the analysis. But because the research question had been formulate to treat 3 months as the primary outcome, this was not a concern. This approach was also endorsed by a statistician.

Therefore, independent t-tests were performed for normally distributed data, and the Mann-Whitney-U test was performed with non-normally distributed data.

Prior to analysis, missing data were imputed with linear interpolation using SPSS. From the imputed data set, change values (3months minus BL, 6 months minus BL) were calculated with the 'compute variable' option in SPSS. The change values were used for the between-group data analysis. Statistical significance was set at $P< 0.05$. Means, standard deviation, and 95% confidence intervals were also computed using SPSS.

Effect sizes were calculated using an online calculator provided by the University of Colorado (www.uccs.edu/~lbecker/). Means and standard deviations for the outcome variables of each group were entered into the calculator and effect size was displayed. Effect size ranges applied were as follows: small= 0.3-0.5, and medium= 0.6-0.8, and large= ≥0.9 (Cohen, 1988).

The outcome of number of participants meeting the weekly PA guidelines was examined with the chi square test. For this, a dummy variable was created to distinguish participants into two categories; meeting the guidelines, and not meeting the guidelines. Chi square analysis was performed with these variables to compare whether the number of participants meeting the guidelines differed between the SC and ALP groups.

The PA diaries were not included in the analysis because most participants did not report their PA in a manner that it could be analysed. Participants did not record the duration of the activity in enough detail so that the researcher could calculate a MET value. Some participants only recorded certain types of PA, such as periods during which they were engaging in exercise, but failed to record other activities such as household activities. Because the data did not seem representative of their 'true' PA the diaries were not included in the analysis.

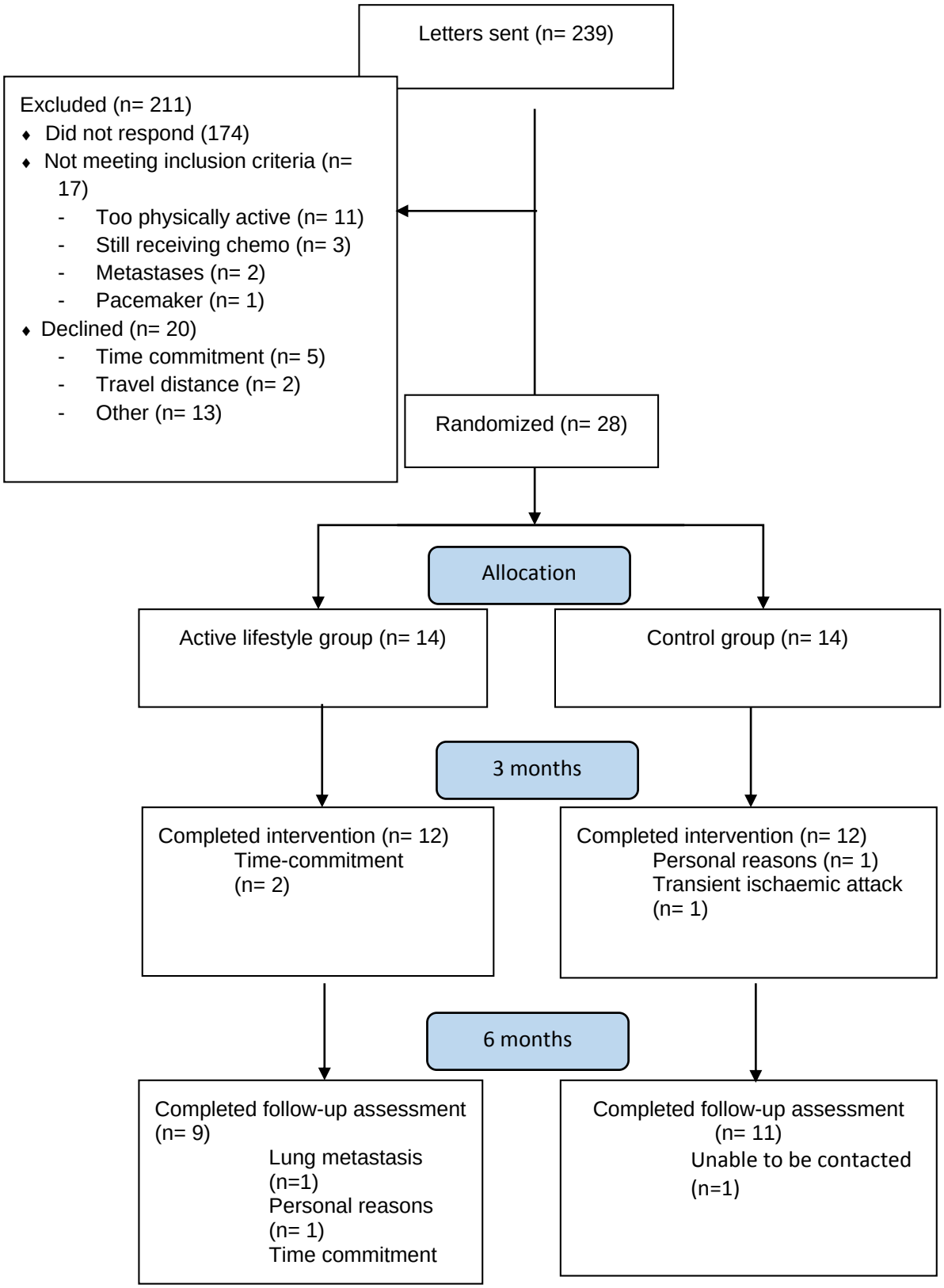


Figure 7 CONSORT diagram of patient recruitment and retention throughout the study

6.4. Results

Primary outcomes

Feasibility outcomes

A detailed description of all recruitment related feasibility outcomes can be found in chapter 7. Briefly, 239 invitation letters were sent and 65 (27%) responses were received. Of these, 31% declined participation, with 26% not meeting the inclusion criteria. The main reasons for exclusion were already meeting the current PA guidelines, or still receiving chemotherapy. Reasons for declining participation were time-commitment and travel distance to the research site. However, the majority of people did not provide a reasons.

After completion of baseline assessments, 28 participants (12% of potential participants, 58% of eligible participants) were randomised to either the Standard Care (SC) group (n=14) or the Active Lifestyle Programme (ALP, n=14).

At completion of the intervention 24 participants were still available for follow-up. In each group two people dropped out. Reasons for drop-out were personal reasons (n=1), health reasons (n=1), and time-commitment (n=2). At the 6 month follow-up appointment a further four participants dropped out, three in ALP and one in SC. Reasons were time-commitment (n=1), personal reasons (n=1), lung metastasis (n= 1) and unable to be contacted (n= 1). This yields a retention rate of 86% at post-intervention, and 71% at follow-up.

Attendance at the exercise sessions was good with 133 out of 168 (79%) supervised exercise sessions attended. Two participants dropped-out immediately after randomisation and attended none of the supervised exercise sessions. Ten participants (71%) attended more than 83% of all offered supervised exercise sessions. The compliance for workshop attendance was 70% (59 out of 84 workshops) and ten participants attended more than 83% of the workshops. Reasons for non-attendance were holidays or sickness.

Secondary outcomes

A summary of the baseline characteristics of both groups can be found in Table 6. Independent t-tests revealed no significant group differences at baseline.

Results for all outcome measures at baseline and post-intervention are presented in Table 7 for normally distributed data and in Table 8 for non-normally distributed data. Data for follow-up measures are presented in Table 9 (normally distributed data) and Table 10 (non-normally distributed data).

Table 6 Baseline characteristics. Values are means ± SD, unless indicated otherwise

Characteristics	SC (n=14)	ALP (n=14)
Sex (M/F)	7/7	8/6
Time since diagnosis in months	13	12
Treatment		
Chemotherapy n (%)	2 (14)	10 (71)
Surgery n (%)	14 (100)	14 (100)
Colostomy	1 (7)	1 (7)
Age ± SD	64.0 ± 14.8	65.5 ± 9.2
Body mass (kg)	78.3 ± 14.8	81.9 ± 18.2
BMI	26.9 ± 3.9	28.4 ± 5.3
Body fat (%)	32.2 ± 4.2	32.6 ± 7.6
Waist-hip-ratio	0.90 ± 0.10	0.91 ± 0.10

Self-regulation and needs satisfaction

There were no significant group differences in mean change of behavioural regulation post-intervention. However, we found a large effect size (*d*) of the intervention for the RAI (*d*= 0.67, *p*= 0.10). ALP was 4.74 points higher in RAI post-

intervention. No changes were observed in amotivation, extrinsic regulation and introjection.

Although, a medium effect size was found for relatedness (*d*= 0.65, *p*= 0.13) there were no significant group differences in mean changes for need satisfaction. ALP increased in the need satisfaction for relatedness (+1.00, SD= 1.7) whereas SC decreased (- 0.07, SD= 1.6) (*P*> 0.05). Both groups increased the need satisfaction for autonomy and competence.

There were no substantial group differences at follow-up for self-regulation. Improvements in autonomous regulation in the intervention condition were not maintained at follow-up. Changes in need satisfaction were not significantly different between the groups at follow-up. However, ALP increased satisfaction of competence and relatedness compared to a decrease in SC and there was a medium effect size for these variables (*d*= .0.75, *p*=0.07 and 0.64, *p*= 0.12).

Self-efficacy to exercise and intention to exercise

There was no significant difference between the groups in mean change for Self-efficacy. The intervention condition increased in intention to exercise post-intervention compared to the control condition (+0.89 vs. -0.53, *p*< 0.05). There were no group differences in changes in self-efficacy and intention to exercise at follow-up.

Quality of life

There were no significant group differences in mean change for any of the Qol domains of the FACT, nor for the fatigue or the colon subscale post-intervention and at follow-up. However, there medium effect sizes at follow-up were observed for fatigue (-0.56) and FACT-C (0.63) with lower levels of fatigue and higher levels of disease-specific QoL in the ALP compared to SC.

PA behaviour

Self-assessed PA

A difference between the groups in mean change was found for the walking domain of the IPAQ at post-intervention. ALP engaged in 98 min more walking PA than SC ($p< 0.05$). There were no differences in any other PA domain of the IPAQ. Changes in walking time from baseline remained significantly different between the groups ($p< 0.05$) at follow-up. Although, ALP did not increase walking time at follow-up but stayed the same as at baseline, SC decreased their weekly walking time by -164 min. Furthermore, there was a difference between the groups in mean change of total MVPA with ALP being 331 min more active than SC ($p< 0.01$). Occupational and household PA and vigorous intensity PA was also higher in ALP than in SC but this was not significant.

Accelerometry

No significant group differences were observed for objectively measured PA at post-intervention. Although, there was an increase in 10-min moderated bouts in the intervention condition versus a decrease in the control condition, the difference in mean change was not significant (+35 min vs -3 min, $d= 0.59$, $p> 0.05$). There were no substantial group differences at follow-up, although ALP spent more time at 10-min bouts, less time in sedentary behaviour, and SC spent more time in Matthews bouts.

Meeting the current PA recommendations

As discussed in the introduction to this chapter, the evidence that PA is inversely associated with a decreased risk of developing CC is consistent with recreational PA but inconsistent with occupational and household PA. In the light of this, only leisure-time and walking PA are considered here, as well as the 10-min bout criteria of acccelerometry.

For self-assessed leisure-time PA, 22.7% of ALP versus 13.6% of SC were meeting the current PA guidelines of at least 150min per week at 3 months ($P=0.44$). At

follow-up 35.0% in the intervention condition versus 15.0% in the control condition were engaging in at least 150min of leisure-time PA per week (P=0.07).

For accelerometry, there were also no differences between the groups at meeting minimum PA guidelines. At 3 months, findings show 9.6% in ALP versus 4.8% (P=0.55) in SC meeting at least 150min of 10-min bouts of PA per week post-intervention. At 6 months, this was unchanged (10% vs 5%, P=0.44).

Body composition and physiological outcome measures

Post-intervention the intervention condition decreased body mass ($p< 0.05$), body fat ($p< 0.05$), and BMI compared to the control condition, although BMI was only marginally significant ($p= 0.05$). ALP lost 1.6 kg body mass (vs +1.1 kg increase in SC, $P= 0.02$), reduced body fat by 1.4% (vs 0.3% increase in SC, $P= 0.02$), and reduced BMI by 0.04 kg/m^2 (vs 0.5 kg/m^2 increase in SC, $P= 0.05$). No changes were seen in waist-to-hip ratio. There were no group differences in change for lower body strength, upper body strength and functional capacity.

At follow-up the change in body mass, BMI, and body fat were still different in ALP compared to SC in favour of ALP, but this was only significant for BMI. BMI reduced by -1.2 in ALP compared to an increase of 1.7 in SC ($p< 0.05$, $d= -0.68$). ALP lost 1.4 kg of body mass compared to a weight loss of -0.2 in SC ($p= 0.53$, $d= -0.30$), and body fat increased more in SC than in ALP ($p= 0.76$, $d= -0.38$). There were no differences in waist-to-hip ratio between the study groups. Furthermore, there were no differences in mean change between ALP and SC in grip strength, chair-sit-to-stand repetitions, arm-curl repetitions, and submaximal aerobic capacity.

Table 7 Changes of normally distributed outcome measures post-intervention with P-values and effect sizes (Cohen's d), Values are means and standard deviations

Normally Distributed Data

Variable	Standard Care				Active Lifestyle Programme					
	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	*P*	*d*
Grip strength (kg)	31.0 (11.8)	31.0 (9.8)	0.2 (2.9)	-1.8 to 2.9	32.0 (7.5)	33.9 (8.3)	1.2 (5.8)	-2.7 to 2.9	.59	.21
Biceps-curl (n)	12.9 (4.7)	15.4 (4.1)	2.6 (3.9)	-.3 to3.6	11.8 (2.5)	14.2 (2.7)	2.5 (2.7)	.2 to 3.4	.96	-.03
Chair-sit-stand (n)	10.6 (2.7)	13.8 (3.6)	2.1 (1.8)	1.1 to 3.4	10.3 (2.7)	14 (4.1)	3.6 (1.9)	2.3 to 4.7	.19	.81
Fitness (min)	10.0 (2.8)	10.4 (2.2)	-0.7 (1.5)	-1.9 to 0.1	10.4 (3.0)	11.1 (2.9)	0.5 (0.8)	-.0 to 1.0	.19	1.00
Self-regulation										
Introjection	0.81 (0.75)	0.72 (0.7)	-0.09 (4.9)	-.3 to .2	0.79 (8.45)	1.05 (0.8)	0.26 (1.1)	-.4 to 1.1	.31	.10
Identification	2.11 (0.93)	2.32 (0.7)	0.21 (0.7)	-.3 to .8	2.35 (1.04)	3.08 (5.4)	0.73 (1.1)	.2 to 1.2	.18	.56
RAI	7.41 (5.16)	8.41 (6.0)	1.00 (4.1)	-1.5 to 3.8	8.48 (5.47)	13.14 (4.0)	4.66 (6.6)	1.4 to 7.2	.10	.67
Needs satisfaction										

Variable	Standard Care				Active Lifestyle Programme					
	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	*P*	*d*
Competence	3.66 (1.3)	3.89 (0.8)	0.24 (1.1)	-.2 to .8	4.00 (1.09)	4.63 (0.5)	0.63 (1.2)	0.2 to 1.3	.39	.34
Autonomy	4.34 (1.51)	4.82 (0.8)	0.47 (1.3)	-.4 to 1.0	4.81 (1.05)	4.83 (0.6)	0.04 (0.8)	-.5 to 7.1	.33	-.40
Relatedness	3.32 (1.80)	3.25 (1.5)	-0.07 (1.6)	-1.1 to 1.2	4.18 (1.49)	5.06 (0.8)	1.00 (1.7)	.1 to 2.1	.13	.65
Self-efficacy	3.74 (2.2)	4.97 (2.1)	1.23 (3.2)	-1.0 to 3.6	5.24 (2.8)	7.88 (1.1)	2.53 (3.2)	.8 to 5.2	.32	.41
QoL										
SW	23.2 (3.8)	22.6 (5.1)	-0.8 (4.1)	-.4 to 3.4	25.4 (2.5)	26.0 (2.2)	-0.01 (2.5)	-2.2 to 1.1	.57	.23
EM	20.6 (2.1)	19.8 (2.9)	-0.7 (1.9)	-1.5 to .1	22.6 (2.4)	21.2 (2.7)	-1.3 (2.8)	-3.6 to .3	.55	-.25
Fatigue	45.7 (6.0)	44.0 (6.7)	-1.7 (4.4)	-3.0 to .8	45.1 (5.8)	46.2 (5.8)	0.2 (4.8)	-8.4 to 2.6	.31	.41
FACT-G	92.1 (11.1)	91.9 (12.3)	0.9 (6.1)	.6to 6.1	99.4 (6.6)	98.8 (7.3)	-2.20 (5.5)	-6.1 (1.3)	.24	-.53
IPAQ										
OCC (min · wk^{-1})	199 (204)	145 (166)	-54 (276)	-312 to 84	244 (239)	125 (192)	-81 (220)	-247 to79	.79	-.11

Variable	Standard Care				Active Lifestyle Programme					
	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	*P*	*d*
Walking (min · wk^{-1})	224 (209)	105 (64)	-120 (222)	-266 to 54	158 (160)	203 (247)	41 (161)	-54 to 162	.05	.83
Leisure time (min · wk^{-1})	119 (179)	130 (92)	11 (222)	-212 to 96	140 (116)	200 (255)	43 (221)	-99 to 192	.72	.32
Total MVPA (min·wk^{-1})	447 (295)	303 (190)	-144 (360)	-474 to 56	448 (257)	413 (334)	-10 (248)	-200 to 161	.28	.43
Accelerometry										
10 min mod bouts (min · wk^{-1})	61 (65)	61 (57)	-3 (72)	-48 to 49	53 (119)	90 (112)	35 (57)	-10 to 42	.15	.59
Matthew bouts (min · wk^{-1})	195 (199)	193 (166)	6 (180)	-131 to 52	127 (180)	177 (153)	33 (140)	-80 to 52	.67	.17
Total MVPA (min·wk^{-1})	129 (101)	157 (104)	27 (92)	-66 to 59	102 (125)	133 (112)	27 (91)	-53 to 36	.99	0
Vector magnitude (cpm)	551 (221)	560 (176)	11 (148)	-129 to 24	457 (190)	482 (151)	23 (102)	-73 to 28	.82	.09
Sedentary time (min · wk^{-1})	2880 (886)	2898 (766)	-310 (1118)	-1164 to 59	2198 (1201)	2749 (620)	-866 (1866)	-2065 to 189	.37	-.36

Table 8 Changes of non-normally distributed outcome measures post-intervention with P-values, Values are in means with standard deviation.

Non- normally Distributed Data

Variable	Standard Care				Active Lifestyle Programme				
	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	*P*
Body mass (kg)	78.3 (14.8)	79.8 (13.6)	1.1 (2.7)	-.9 to 2.6	81.9 (18.2)	80.9 (9.4)	-1.6 (2.1)	-3.0 to -.5	.02
BMI	26.9 (3.9)	28.2 (3.0)	0.5 (1.1)	-.3 to 1.2	28.4 (5.3)	27.5 (3.5)	-.4 (0.8)	-1.0 to 0.1	.05
Body fat (%)	32.2 (4.2)	33.3 (4.9)	0.3 (3.5)	-2.1 to 2.5	32.6 (7.6)	28.6 (6.3)	-1.4 (2.3)	-2.9 to -.1	.03
Waist-hip-ratio	0.90 (0.10)	0.89 (0.1)	0.00 (0.02)	-.07 to 0.02	0.91 (0.10)	0.95 (0.1)	0.01 (0.04)	-.01 to .05	.43
Self-regulation									
Amotivation	0.30 (0.60)	0.19 (0.7)	-0.06 (0.7)	-.5 to .3	0.10 (0.19)	0.06 (0.2)	-0.06 (0.2)	-.2 to 0.0	.82
Extrinsic	0.36 (0.55)	0.46 (0.6)	0.0 (0.3)	-.2 to .2	0.69 (1.13)	0.65 (0.6)	0.03 (0.9)	-.5 to .5	.94
Intrinsic	1.80 (1.14)	2.02 (1.1)	0.18 (0.8)	-.2 to .7	2.17 (1.06)	3.17 (0.9)	0.91 (1.2)	.3 to 1.8	.14
Intention	5.19 (1.6)	5.04 (1.1)	-0.53 (0.7)	-.9 to 0	5.15 (1.6)	6.08 (0.7)	0.89 (1.1)	.3 to 1.6	.04

Variable	Standard Care				Active Lifestyle Programme				
	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	BL Mean (SD)	3 months Mean (SD)	Δ (3 – BL) Mean (SD)	95% CI Δ	*P*
QoL									
PW	25.8 (2.4)	26.2 (2.0)	0.8 (1.5)	0 to 1.9	26.0 (1.8)	26.0 (2.2)	0.3 (1.0)	-.2 to 1.0	.43
FW	22.6 (4.3)	22.6 (4.0)	1.4 (2.8)	-.4 to 3.3	25.4 (2.3)	25.8 (2.0)	0.0 (1.6)	-.8 to .7	.86
FACT-C	21.9 (4.5)	22.5 (4.3)	0.6 (4.3)	-2.1 to 3.5	23.2 (3.7)	24.7 (2.4)	1.7 (3.9)	-.8 to 12.5	.94
IPAQ									
Sit (min · wk^{-1})	2874 (1110)	2785 (755)	112 (191)	-6 to 234	3717 (1717)	3207 (1031)	-329 (890)	-872 to 182	.53
Moderate (min · wk^{-1})	196 (186)	191 (174)	-66 (306)	-285 to 114	283 (222)	168 (209)	-86 (285)	-296 to 93	.78
Vigorous (min · wk^{-1})	26 (74)	6 (19)	-35 (95)	-126 to 138	7.5 (22)	42 (79)	24 (81)	-6 to 80	.34

Table 9 Changes of normally distributed outcome variables at 6 month follow-up

Normally Distributed Data

Variable	Standard Care				Active Lifestyle Programme				
	6months Mean (SD)	Δ (6 – BL) Mean (SD)	95% CI Δ	6 months Mean (SD)	Δ (6 – BL) Mean (SD)	95% CI Δ		*P*	*d*
Biceps-curl (n)	15.4 (4.7)	2.5 (5.6)	-2.3 to 2.2	14.6 (1.6)	3.0 (1.9)	1.9 to 3.7		.77	.12
Introjection	0.81 (0.7)	0.0 (0.9)	-.6 to .4	1.29 (0.8)	0.50 (1.1)	-.1 to 1.1		.21	.50
Identification	2.30 (0.6)	0.20 (1.0)	-.5 to 1.1	2.79 (0.5)	0.43 (1.1)	-.2 to .9		.58	.22
RAI	8.31 (0.6)	0.90 (5.9)	-4.7 to 4.1	11.34 (4.1)	2.76 (6.6)	-1.0 to 4.6		.46	.30
Needs satisfaction									
Competence	3.50 (1.3)	-0.16 (1.4)	-1.3 to .6	4.79 (0.6)	0.79 (1.1)	.1 to 1.3		.07	.75
Autonomy	4.41 (1.2)	0.06 (1.2)	-1.0 to .4	5.30 (0.5)	0.50 (1.3)	-.2 to 1.6		.37	.35
Relatedness	3.26 (1.5)	-0.05 (1.6)	-1.1 to 1.1	5.10 (0.5)	1.00 (1.7)	-.1 to 1.9		.12	.64
Self-efficacy	3.82 (1.2)	0.82 (2.5)	-2.2 to 1.3	6.60 (1.3)	1.22 (3.0)	-.6 to 3.5		.29	.14
Intention	5.33 (1.2)	0.14 (0.4)	-1.1 to -.1	5.56 (0.7)	0.40 (1.8)	-.6 to 1.4		.74	.20
QoL									
EM	20.5 (3.2)	0.1 (2.9)	-2.9 to 1.0	22.5 (1.5)	0.1 (1.4)	-.7 to 1.1		.99	0
Variable	Standard Care				Active Lifestyle Programme				

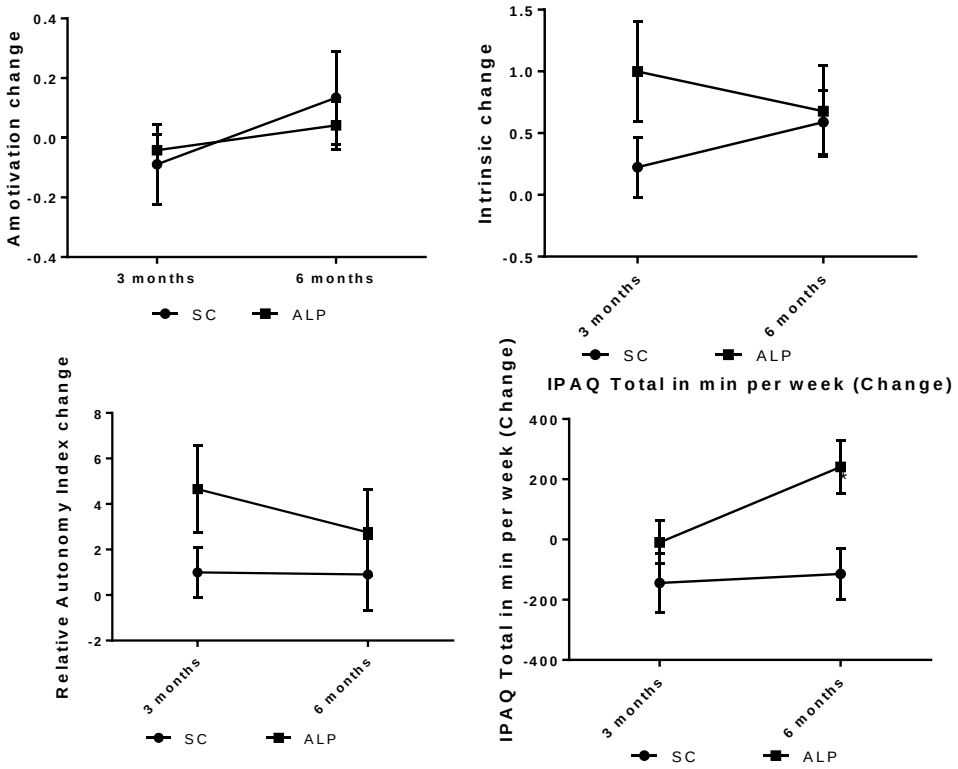
	6months Mean (SD)	Δ (6 – BL) Mean (SD)	95% CI Δ	6 months Mean (SD)	Δ (6 – BL) Mean (SD)	95% CI Δ	*P*	*D*
FACT-G	94.5 (0.7)	0.3 (5.5)	-2.0 to 4.3	100.0 (3.8)	-0.3 (2.7)	-1.9 to 1.4	.77	-.14
IPAQ								
OCC (min · wk^{-1})	210 (246)	11 (195)	-312 to 84	410 (298)	204 (291)	-49 to 322	.05	.78
Walking (min · wk^{-1})	60 (56)	-164 (205)	-326 to 32	163 (151)	0.0 (151)	-102 to 92	.03	0.91
Leisure time (min · wk^{-1})	115 (128)	-4 (241)	-267 to 27	284 (193)	128 (243)	-57 to 246	.18	1.03
Moderate (min · wk^{-1})	257 (262)	60 (202)	-126 to 138	480 (301)	230 (346)	-73 to 334	.13	.60
Total MVPA (min · wk^{-1})	332 (253)	-115 (324)	-435 to 12	663 (261	241 (310)	-19 to 359	.01	1.12
Accelerometry								
10 min-mod bouts (min · wk^{-1})	35 (65)	-28 (57)	-48 to 49	90 (112)	8 (75)	-58 to 43	.17	.54
Matthew bouts (min·wk^{-1})	271 (233)	81 (186)	-131 to 52	161 (148)	17 (79)	-57 to 44	.28	-.45
Total MVPA (min·wk^{-1})	152 (145)	17 (120)	-90 to 2	121 (99)	14 (61)	-37 to 44	.95	-.03
Vector magnitude (cpm)	605 (203)	32 (163)	-97 to 9	494 (144)	35 (107)	-50 to 68	.96	.03
Sedentary time (min·wk^{-1})	2898 (766)	89 (787)	-503 to 608	2749 (620)	-666 (1424)	-1693 to 240	.11	-.66

Table 10 Changes in non-normally distributed outcome measures at 6 months follow-up

Non- normally Distributed Data

Variable	Standard Care			Active Lifestyle Programme			
	6	Δ	95% CI Δ	6	Δ	95% CI Δ	*P*
	Mean (SD)	(6 – BL) Mean (SD)	(6 – BL)	Mean (SD)	(6 – BL) Mean (SD)	(6 – BL)	
Body mass (kg)	80.5 (12.4)	-.2 (6.1)	-4.6 to 3.2	79.4 (9.3)	-1.4 (2.5)	-3.0 to .1	.05
BMI	28.4 (2.8)	1.7 (3.5)	-.6 to 1.3	27.2 (3.7)	-1.2 (4.9)	-1.0 to .0	.04
Body fat (%)	34.5 (4.4)	1.3 (3.0)	-.7 to 3.4	30.6 (6.4)	.3 (2.2)	-2.9 to -.1	.07
Waist-hip-ratio	0.88 (0.1)	0.00 (0.0)	-.1 to .0	0.94 (0.1)	0.00 (0.0)	-.0 to .0	.32
Grip strength (kg)	30.7) (10.1)	-.0 (3.4)	-1.8 to 2.9	32.6 (7.6)	-1.2 (3.7)	-3.3 to 1.2	.29
Chair-sit-stand (n)	14.1 (3.5)	2.6 (1.4)	1.8 to 3.5	14.0 (4.1)	3.4 (3.6)	.8 to 5.2	.40
Fitness (min)	11.2 (1.2)	1.1 (1.8)	.2 to 2.3	12.2 (1.2)	2.0 (3.1)	.7 to 4.2	.40
Self-regulation							
Amotivation	0.42 (0.7)	0.19 (0.7)	-.2 to .7	0.15 (0.3)	0.03 (0.3)	-.1 to .2	.86

Variable	Standard Care			Active Lifestyle Programme			
	6	Δ	95% CI Δ	6	Δ	95% CI Δ	*P*
	Mean (SD)	(6 – BL) Mean (SD)	(6 – BL)	Mean (SD)	(6 – BL) Mean (SD)	(6 – BL)	
Extrinsic	0.41 (0.6)	0.06 (0.6)	-.2 to .2	0.49 (0.6)	-0.14 (0.8)	-.7 to .3	.86
Intrinsic	2.39 (1.2)	0.41 (0.8)	-.1 to 1.0	2.84 (0.6)	0.33 (1.1)	-.3 to 1.1	.86
QoL							
PW	26.6 (2.0)	0.4 (0.9)	-.2 to 1.0	26.8 (1.4)	0.3 (1.0)	-.2 to 1.0	1.00
SW	22.6 (5.1)	0.3 (2.3)	-1.3 to 1.6	24.8 (2.0)	-0.8 (2.4)	-3.6 to .3	.19
FW	22.6 (4.0)	1.6 (2.8)	-.4 to 3.3	25.5 (1.7)	0.0 (1.1)	-.8 to .7	.27
Fatigue	44.0 (6.8)	1.0 (7.4)	-2.3 to 4.8	42.3 (9.3)	-3.7 (9.2)	-8.8 to 2.4	.40
FACT-C	22.5 (4.3)	0.5 (3.2)	-2.1 to 3.5	29.4 (8.6)	5.3 (10.3)	.8 to 12.5	.21
IPAQ							
Sit (min · wk^{-1})	2411 (1146)	138 (766)	-298 to 663	4365 (4187)	1488 (5359)	-750 to 5092	.78
Vigorous (min · wk^{-1})	15 (28)	-26 (101)	-101 to 22	29 (60)	24 (71)	-6 to 73	.71



ALP= Active Lifestyle Intervention, SC=
Standard Care Group, IPAQ= International Physical Activity Questionnaire

Figure 8 Overview of key outcomes for motivational regulation and changes in physical activity behaviour from self-report. Error bars are the standard error of the means.

6.5. Discussion

The primary aim of this study was to investigate the feasibility of an active lifestyle intervention in people recovering from CRC. Secondary aims were to obtain preliminary data on the ability to transform people's feelings of self-determination towards exercising from a more external to a more internal regulation, and to investigate the impact of the intervention on other health outcomes. Moreover, maintenance of changes 3 months post-intervention were also investigated.

The recruitment rate of 58% (of eligible participants) was good in comparison to other studies with this population reporting rates between 34.6% and 70% of eligible participants (Courneya et al., 2003b, Hawkes et al., 2013, Pinto and Ciccolo, 2011). Moreover, the attrition (loss of participants) at 6 months in the present study was high (29%) compared to one other lifestyle intervention with supervised exercise which reported an attrition of 6% only (Bourke et al., 2011). The demand of the supervised exercise sessions in that study was similar to our study (twice per week, and once per week). Yet more people in our study dropped out because of the time-commitment and personal reasons (n= 4) whereas in Bourke et al's (2011) the only one drop-out was due to a medical condition. It is likely that participants in our trial were more likely to drop-out because they were younger (average 65 years) compared to Bourke et al's study participants (average 70 years) and thus, more likely to still be in employment. The two people who dropped-out for time-commitment reasons were both in full-time employment. Other studies reporting low attrition were home-based interventions (Courneya et al., 2003b, Anderson et al., 2010).

A more detailed discussion of recruitment and the different strategies used can be found in chapter 7. To improve recruitment rates in the future, trials should be multi-centred. Reimbursement of travel costs should also be considered as an incentive to participate. Adherence to supervised exercise sessions and PA counselling workshops was high and comparable to other interventions (Hawkes et al., 2013, Bourke et al., 2011).

Besides feasibility outcomes, an important aim of the intervention was to seek preliminary evidence of the effects of an autonomy supportive intervention based

on SDT on motivational regulation and the three psychological needs, autonomy, competence and relatedness, in the context of PA. Post-intervention there was a difference in RAI of 3.66 points between the groups (p= 0.098) in favour of the intervention condition, but there were no other notable differences. Despite a high effect size for intrinsic regulation at 3 months (*d*= 0.72) there was no difference between the groups. Improvements were not maintained at 6 months. Furthermore, at 6 months the need satisfaction for competence was increased in ALP and decreased approaching significance (p= 0.70), and despite no differences for autonomy and relatedness at any time-point, large effect sizes for relatedness were found post-intervention and at follow-up. A possible explanation could be that 3 month intervention is not long enough to produce a meaningful and sustainable change in self-regulation and need satisfaction. It is also likely that one-to-one exercise sessions which some participants received due to work commitments (n=2) they did not receive sufficient support for the need of relatedness. Although, the exercise facilitator is expected to satisfy the need for relatedness, as the person who introduces them to exercise, this might not be sufficient. Peer support to satisfy the need for relatedness might be more important than the support of the facilitator.

The only other autonomy supportive intervention published that found an increase in identification and intrinsic regulation post-intervention, was a study with obese women (Silva et al., 2010b). However, the intervention lasted 12 months, and these positive changes were maintained after a 1-year follow-up (Silva et al., 2011). The previously reported PARC trial of this thesis (chapter 5) also did not find significant differences for identification, and intrinsic regulation at 3 months but did at 6 months. This further supports the notion that a 3 months intervention might be too short to produce a positive effect on feelings of self-determination. Another explanation could be that participants with a diagnosis of CRC are highly motivated to make lifestyle changes and thus, the intervention had little further benefit. The control condition also improved intrinsic regulation, identification, RAI at all time-points. It has been suggested that a cancer diagnosis can be a trigger for behaviour change (Demark-Wahnefried et al., 2005, McBride et al., 2008) and a 31.3% increased amount of PA has been reported in cancer survivors after diagnosis

(Humpel et al., 2007). Moreover, an Australian study found that CRC survivors were more likely to be sufficiently active (at least 150min of MVPA per week) compared to a non-cancer population (Hawkes et al., 2008).

Another critical outcome of the study was PA behaviour. Only walking-time PA and total MVPA from self-assessment were significantly different between groups at 6 months follow-up. Although, there are only few lifestyle interventions with CRC survivors, only one other study has shown a significant intervention effect at a follow-up time-point (Hawkes et al., 2013). In this 6-month telephone intervention PA was assessed with the Godin Leisure Time Exercise Questionnaire, and participants in the intervention condition were doing 28.5 min more moderate intensity PA at 12 months follow-up than the control condition. In the present study a group difference of 169 min of leisure-time moderate intensity PA in favour of the intervention condition was observed. We did not find any improvements in accelerometry, but it should be noted that there was a medium effect size for 10-min bouts at post-intervention and at follow-up (*d*= 0.59 and 0.54) with an increase in weekly 10-min bouts in the intervention group and a decrease in the control group. An explanation for a lack of observed accelerometry changes might be that the set cut-points for moderate intensity PA are too high to record the low vibrations produced during PA in the elderly. Despite using lower cut-points, which commonly would be interpreted as mild activity intensity in an adult population, we did not find any changes in the Matthews bouts recordings. The LIFE study (Rejeski et al., 2013) used accelerometry during supervised walking sessions and found a large variability in accelerometer counts between the subjects. Where some participants had median activity counts well above the cutoff point for moderate intensity PA (>1952 for Freedson's, >760 for Matthews'), other participants had median activity counts well below the moderate intensity cutoff point. Participants in that study were 70- 80 years old. Thus, it is likely that despite being physically active at a perceived moderate intensity, participants in our study may have not met the minimum cutoff point for moderate intensity PA to produce a reading on the accelerometer.

In regards to meeting the weekly PA recommendations of at least 150min of moderate intensity PA more participants in the intervention condition than in the control condition met this criteria. We only considered self-reported leisure-time PA based on the findings that higher intensity PA and longer duration is more beneficial for survival and recurrence. More than half (64.3%) of the participants in ALP met these guidelines at follow-up versus 28.6% in the control condition. This is more than what has been reported for CRC survivors post-diagnosis. A recent survey in Australia found that only 32.4 % of CRC survivors are sufficiently active (≤ 150min moderate intensity PA per week) at 6 months post-diagnosis (Hawkes et al., 2011). These findings suggest that the intervention had a meaningful impact on exercise behaviour. Despite the improvements in weekly self-assessed PA, the participants in the intervention condition did not improve in exercise tolerance and physical functioning, although there was a large effect size (*d*= 1.0) for functional capacity, and for the chair-sit-to-stand test (*d*= 0.81) post-intervention. A recent lifestyle intervention with CRC survivors also found an effect size of 1.0 for exercise tolerance, but this was significantly different between the intervention and control groups after a 3 month intervention (Bourke et al., 2011). The absence of a significant group difference in our study could be because the control condition also improved physical function post-intervention and at follow-up. It is also likely that participants did not engage in sufficient PA at home outside the supervised exercise sessions. Although, participants were encouraged to aim for a minimum of three additional home-based exercise sessions, this was not an exercise prescription and the participant was free to choose to do this or not. This was communicated in this context to keep consistent with an autonomy supportive environment where the participant takes ownership of their decisions.

There were no differences in QoL between the groups at any time-point. Other lifestyle interventions also did not find improvements in QoL (Pinto et al., 2013, Hawkes et al., 2009, Houborg et al., 2006, Courneya et al., 2003b). However, two recent lifestyle interventions with CRC survivors did find significant group difference (Bourke et al., 2011, Anderson et al., 2010). It is likely that QoL scores were already

high at baseline, and thus, creating a ceiling effect making a further improvement unlikely. Baseline results in our study were higher for FACT-C and FACT-F than in Bourke et al's (2011) study, making this a likely possibility. Participants were on average 10 months post-diagnosis when entering the study. This may be sufficient time to recover from treatment side-effects and using a general QoL questionnaire (such as the SF-36) might be more suitable for this population.

Limitations

Strengths of the study include the randomised controlled design, the use of subjective PA measures, a follow-up period without participant contact, and the use of an underlying theory to support the intervention.

The results of the study should be interpreted in the context of several limitations. First, the sample size was very small which likely decreased the statistical power. Furthermore, ascertainment bias was introduced to the study because the researcher who carried out all the research activities (recruitment, delivering the intervention, data collection, data analysis) was not blinded to the allocation of participants. Another limitation is the use of the submaximal fitness test. The modified Bruce may not be suitable for this population. Some participants were uncomfortable with treadmill walking and withdrew from the test after a short period. It was also noted that the transition from stage 3 to 4 is not tolerated very well (incline is 12% and speed increased by 0.8 miles per hour). Most participants terminated the test at this stage despite not having reached their termination heart rate of 85% of the maximum heart rate. They felt uncomfortable with the drastic increase in speed together with the incline of the treadmill and feared falling. A ramp-test might be more suitable where the participant can choose a comfortable speed for the whole duration of the test, and the incline increases every 2 min. A bicycle test might also be considered, because the fear of falling would be eliminated. Furthermore, it should be considered that some participants did receive one-to-one supervised exercise sessions because they were working full-time and thus, not able to join the group sessions. This may have negatively affected the need for relatedness, and may explain the small change in relatedness in the ALP group. Finally, no changes in QoL may be attributable to the fact that inclusion of

participants was within 3 years of completed treatment. It is likely that participants have recovered from treatment side-effects at that point, which would have reduced any potential effects of the intervention on QoL. However, this inclusion criterion was set, because there was a limited patient pool available to be approached and extending the post-treatment inclusion criteria increased the number of potential participants. It would have been of higher valued to approach participants immediately post-treatment, but this was not possible with the limited time available to complete the study.

6.6. Conclusion

The findings of the study suggest that a 3 month autonomy supportive lifestyle intervention with supervised exercise and PA counselling is feasible. However, 3 months intervention time might not be sufficient in length to evoke changes in behavioural regulation but was effective at changing PA levels after the intervention and at 3 month follow-up. A larger-scale RCT with a longer intervention period and longer follow-up is needed to investigate whether a longer intervention will be more effective at evoking changes in behavioural regulation.

Chapter 7

The effectiveness of different recruitment strategies in people at elevated risk of and recovering from CRC

7.1. Abstract

Background: The purpose of this study was to determine the effectiveness of different recruitment strategies used to recruit patients into the PARC and MOVE active trials. Lifestyle behaviours and reasons for non-participation were also evaluated.

Methods: Potentially eligible patients to PARC were recruited via nurses, and clinical invitation letters. The latter was the only recruitment strategy used to recruit CRC survivors into MOVE. Surveys to investigate quality of life (QoL), barriers to exercise, reasons for non-participation, and PA (PA) behaviour were sent to patients who did not respond to the clinical invitation letters.

Results: For PARC, 736 potentially eligible patients were identified. Letters and approach via nurses were most successful with 8.5% (N= 11/141) and 8% (N= 8/100) randomization yield, respectively. Recruitment during clinic visits yielded only 2.4% (N= 12/495). The randomization yield for MOVE was 12% (N= 28/235). For both study populations, main reasons for non-participation were time commitment and travel burden. Non-participants perceived themselves as moderately active, and more than 50% were meeting the current PA guidelines. The majority of non-participants did not report health problems.

Conclusion: The number of patients randomized to both studies was lower than anticipated. Consideration of accessibility to research sites and study commitment should be made when planning studies with these populations.

7.2. Introduction

Successful recruitment is indispensable to a high quality RCT. Not meeting recruitment targets can jeopardise a trial by being underpowered and the chance of seeing statistically significant results is reduced despite true group differences. In the worst case, poor recruitment can lead to the termination of a trial (Treweek et al., 2013a). Not being able to complete a trial, because of poor recruitment, is unethical towards patient volunteers who committed their time to participation (Altman, 1981). Finally, poor recruitment often leads to an extension of trials which results in additional costs and time burden to the researchers and clinical staff involved in the recruitment processes (Treweek et al., 2013a).

Previous studies have examined recruitment rates of RCTs. A review from the Medical Research Council (MRC) found that only 55% of UK funded trials are meeting their recruitment targets and 53% of trials did not apply for an extension (Sully et al., 2013). Most literature on recruitment issues focus on patient-centred reasons for non-participation and reasons include the patient's inability to make a decision, not willing to be randomised to a control group, time commitment, traveling to the research sites, lack of interest, and others (Gul and Ali, 2010, Ross et al., 1999). However, research governance, ethical approval, and clinical staff have also been identified as a source of exacerbation of the recruitment process (Treweek et al., 2013b).

Recruitment reviews mainly include medical trials (e.g. drug treatments) and there is little knowledge about recruitment into lifestyle interventions. With a growing recognition of the benefits of PA for prevention and survival of cancer (World Cancer Research Fund and American Institute for Cancer Research, 2007) reports of recruitment into PA interventions in this population are needed. Often, publications of RCTs are lacking a detailed account of recruitment targets and sample size making it difficult to identify the successful components of recruitment to inform future trials. An evaluation of PA interventions with breast cancer survivors found that only half of the studies reported sample size and participation rate (White et al., 2009). PA interventions with cancer survivors have reported varying recruitment rates from only 7-70% (Pinto et al., 2004, Courneya et al.,

2003b, Daley et al., 2007, Bourke et al., 2011). To address these low recruitment rates and improve upon them, knowledge of the reasons people refuse participation and the characteristics of non-participators is needed. Only a few studies investigated these. Findings of characteristics of non-participants are contradictory with some studies reporting that trial participants are more active and have better health than non-participants (van Heuvelen et al., 2005, Harris et al., 2008) and with other studies reporting participants to have poorer health (Ives et al., 1994). Moreover, some studies found that participators were more active than non-participators (van Heuvelen et al., 2005, Harris et al., 2008). This may contribute to selection bias during recruitment to RCTs and volunteers in trials may not be representing the overall study population. More reports on recruitment strategies and their outcomes are needed to improve recruitment success. Furthermore, research is needed to identify the medical profile of participators and non-participators, and the barriers to participation.

Participants in lifestyle RCTs with people undergoing bowel cancer screening and people diagnosed with CRC are likely to be older. Elderly people may have specific requirements to make participation in RCTs more attractive. This study set out to give a detailed description of the recruitment strategies employed, and identify the reasons for non-participation in an active lifestyle intervention with people diagnosed with colonic polyps and CRC.

Aims

The study will provide:

1. A review of the recruitment methods employed and present the challenges of each of the recruitment strategy.
2. An investigation of differences in deprivation as determined by the Index of Multiple Deprivation (IMD) from postal codes and travel burdens of participants and non-responders.
3. An explanation of reasons for non-participation, health status and PA levels in non-responders to a study invitation by ways of a brief survey.

7.3. Design

This study will report the recruitment strategies of two trials, the PARC and MOVE trial. Details of the PARC and MOVE trials have previously been reported in chapters 5 and 6. Briefly, both trials were feasibility studies with a randomized controlled design allocating participants to an active lifestyle intervention or a control group. Participants were patients identified as being at increased risk for developing CRC (PARC) or people recovering from CRC (MOVE). Participants' characteristics were described in chapters 5 and 6. Participants in the intervention received supervised exercise sessions and PA counselling sessions for 6 months (PARC) or 3 months (MOVE). Participants were followed-up 6 months (PARC) or 3 months (MOVE) post-intervention.

7.4. Methods

Methods for postcode analysis and surveys

Postcodes from study participants and non-responders to clinical invitations were used for this study. Furthermore, letters were sent to non-responders to investigate non-participators characteristics and explore the reasons for refusal to take part in the study. These letters were only sent to people who were recruited via clinician invitation letter. The letters contained a brief one-page survey and a stamped self-addressed return envelope.

Ethical approval was sought to use postcode data from non-responders to initial study invitations, and send a brief survey to them. Return of the survey acted as consent to the study. This was approved by the NRES Committee East of England, Norfolk, the Research & Development Office of the Norfolk and Norwich University Hospital (NNUH), and the Research and Enterprise Service at the University of East Anglia.

Measures

Reasons for not taking part were presented as a multiple-choice question stating: "Do any of the following factors play a role in your decision making not to take part in the study?" 'Yes' or 'No' responses were given to the following statements:

'Distance to the research site', 'health', or 'time commitment'. Space for 'other reasons' was also provided.

Quality of life (QoL) was assessed with the European Quality of Life 5 Domains (EQ-5D) questionnaire. The validated questionnaire is a brief and simple questionnaire ideally suited for use in postal surveys. It assesses five health domains: mobility, self-care, usual activities, pain/ discomfort/, and anxiety/ depression. Answering the questionnaire is cognitively simple and only takes a few minutes. Each domain has five levels or responses ranging from 1 'no problems' to 5 'unable' or 'extreme' problems. Data from the EQ-5D was reported as the frequency of people having problems (levels 2-5 of the EQ-5D) or having no problems (level 1-2) with each individual QoL domain as recommended in the scoring guidelines (www.euroqual.org).

Barriers to engage in PA were investigated with a 9-item non-validated questionnaire. The items of the questionnaires were chosen based on previously reported findings of barriers, such as 'time' and 'costs' (Rogers et al., 2014b) but also included other items that were deemed to be worth exploring with this population. These additional items were included based on qualitative findings of a fellow-researcher who interviewed research participants of both trials (personal conversation with Kelly Semper, 'PhD', University of East Anglia, February 2013). Some sample items of the questionnaire included, "I don't know what exercises to do", "I don't know how much exercise to do", and were rated on a 10-point Likert Scale ranging from 1 -10 (Strongly agree - strongly disagree). Higher scores reflect less barriers to the items, and lower scores higher barriers. Because no cut-off score is associated with 'low barriers' or 'high barriers', the median score was used as the cut-off. This was adopted from Schwarzer (Schwarzer, 2009) who recommends using this strategy for the analysis of self-efficacy.

Personal rating of PA status was assessed with a single question: "Would you describe yourself as: 1- inactive, 2-somewhat active, 3-moderately active, or 4- very active?" PA behaviour was assessed with the Godin Leisure Time questionnaire (GLTQ). The questionnaire assesses the frequency of strenuous, moderate, and mild activities per week during a typical week. A modification was made to record time

in minutes of PA per typical week in addition to frequency. Examples of PA for each intensity category were added to reflect usual activities of the elderly, and domestic PA examples, e.g. heavy gardening in the strenuous PA category, and washing window in the moderate PA category, were added to the questionnaire. Results were also categorised for either meeting the current PA guidelines of 150min of moderate PA or 60min of vigorous PA per week, or not meeting these guidelines.

Analysis

Postcodes were analysed with the Geographical Information System (GIS) package ArcGIS v10.1. A digital representation of the road network was constructed using the Ordnance Survey Meridian data (Ordnance Survey, 2014) and network routing algorithms were used in the GIS to identify the most direct route along the road network from each patient's home to the UEA, and to calculate the total distance and travel time for that route. All calculations assumed car travel. As a measure of neighbourhood material deprivation, the Index of Multiple Deprivation (IMD) score (McLennan et al., 2011) was calculated for each individual based on the Census Lower Super Output Area zone that their postcode was allocated to.

Statistical analysis was carried out with the Statistical Package for the Social Sciences (SPPS), version 22. Differences between participants and non-participants were calculated if data was available for both study populations using the Mann-Whitney U test. Means and standard deviations were calculated for nominal survey data and frequencies for categorical data.

7.5. Part A: PARC

While this thesis investigated the effects of an active lifestyle intervention based on Self-Determination Theory on people's motivation to become more physically active, another researcher investigated the effects of PA on biomarkers in the bowel tissue (unpublished thesis, Barnabas Shaw, 'PhD', University of East Anglia). This required taking samples of the bowel tissue during the colonoscopy. Hence, people were only eligible to take part in the study if they agreed to have research biopsies taken during their screening colonoscopy. Taking extra research biopsies does not

increase the discomfort of the screening colonoscopy and is not painful for the patient. This was explained to the patient.

Participants

Participants were patients with a positive diagnosis of bowel polyps and were identified either via the *National Bowel Cancer Screening Programme* or colonoscopy attendance register at the NNUH. Inclusion criteria were i) a diagnosis of 'low' (<5 polyps of <1cm in size), 'intermediate' (>5 polyps of <1cm in size or one polyp >1cm) or 'high' (>1 polyp of >1cm in size) risk polyp as a result of the screening colonoscopy; ii) aged 60 years and above and iii) physically able to partake in regular exercise. Exclusion criteria were i) physical activity levels that meet the most recent American Cancer Society (ACS) guidelines of 150min of moderate intensity PA or 75min of vigorous intensity PA per week, ii) presence or history of other co-morbid conditions which might preclude patients from safely undertaking regular exercise, including cardiovascular or pulmonary disease or stroke; iii) presence of other colorectal conditions (e.g. inflammatory bowel disease) or known familial colorectal cancer syndrome; iv) chronic use of any treatments or alternative therapies that may affect the results of any study of colorectal tissue e.g. high corticosteroid, anticoagulant or laxative use, regular enemas, high dose vitamin or antioxidant supplements, etc.; v) previous diagnosis of cancer; vi) inability to adequately understand written and spoken English, vii) presence of drug controlled type II diabetes mellitus and viii) current involvement in other ongoing research.

Note: In the original protocol the inclusion criteria were restricted to having a diagnosis of an 'intermediate' (more than 5 polyps smaller than 1cm or one large polyp of at least 1 cm) or 'high' risk (more than 1polyp of more than 1cm in size). This was changed at a later stage because patients were excluded from the study if they had less than 5 small polyps of less than 1cm in size. This change was made to broaden the inclusion criteria. In the original protocol patients were also included if they were taking NSAIDS on a daily basis. This was also changed at a later stage to increase recruitment. This will be further discussed in the proceeding paragraphs.

Recruitment strategies

Approach via National Bowel Cancer Screening Nurse

Primary recruitment took place via the *National Bowel Cancer Screening* (NBCS) programme where patients are invited to the hospital for a screening colonoscopy. Patients were seen by a NBCS nurse for a pre-assessment appointment at least 7 days prior to their colonoscopy. During this visit a NBCS nurse briefly explained the study to the patient and provided them with an information sheet. The nurse also sought consent from the patient to be contacted by a researcher to discuss study participation. If the patient gave consent to be contacted, a member of the research team phoned the patient at least 24 h after the appointment with the nurse. During this phone call the researcher asked the patient a few health questions to establish the patient's eligibility for the study and allowed questions about the study to be asked. If the patient was interested in taking part a member of the research team arranged to meet the patient at the hospital on the day of their colonoscopy appointment. During this meeting the potential participant gave consent for five research biopsies to be taken during the procedure in the event that the surgeon diagnosed polyps in the bowel. Full study consent was not given at this meeting because a diagnosis of bowel polyps was an inclusion criterion. If no bowel polyps were diagnosed the participant was thanked for their interest in the study and informed that no further contact would be made.

If bowel polyps were identified the researcher phoned the patient at least 48 h after their colonoscopy to make an appointment to meet a researcher at the research site where full study consent was sought and further eligibility screening carried out.

Twelve months of recruitment were anticipated and the aim was to recruit a total of 120 patients this way. Each week the nurses scheduled approximately 24 pre-assessment appointments with patients on the NBCS programme. During screening colonoscopies, approximately 40% of patients are diagnosed with polyps (Hewitson, 2008) and 10% with CRC. Therefore, it was estimated that each week there would be approximately 12 eligible patients. Based on a Cochrane review of

PA interventions, a recruitment rate of 25% was estimated (Foster et al., 2008) anticipating three participants per week, 12 per month, and 144 over 1 year of recruitment.

Invitation letters

Due to poor recruitment via the primary recruitment strategy letters were sent to patients with a previous diagnosis of bowel polyps. Letters were sent by the Colorectal Surgeon who identified potentially eligible patients. Letters were sent in two batches of approximately 30-70 for logistical reasons. The letters contained a personalised invitation letter and a participant information sheet. If the patient was interested in the study they could contact the researchers or the Colorectal Surgeon with the contact details provided in the letter. The letters were not limited to patients on the NBCS programme but also sent to other patients with a diagnosis of bowel polyps regardless of the route of diagnosis.

After first contact was made with the researcher, a meeting was scheduled at the research site with the potential participant. During this meeting the study was fully explained to the potential participant, full study consent was taken, and further eligibility screening undertaken.

Invitation via clinics

Patients who attended the hospital for a screening colonoscopy were given a patient information sheet by a clinical member of staff upon their arrival for their appointment. As part of this appointment a nurse had a private consultation meeting with the patient before their procedure. At the end of this meeting the nurse asked the patient whether they would be interested in speaking to a researcher about an ongoing study and referred to the information sheet that the patient received upon arrival. If they were interested the researcher explained the study in detail. This took place in a quiet place at the hospital before their scheduled appointment for colonoscopy. If the participant was interested after the detailed description of the study, the participant signed a consent form to have research biopsies taken during the colonoscopy if polyps were identified, and to be contacted by the researcher after the procedure. The researcher would then call

potentially eligible participants after at least 48 h to make an appointment for a meeting at the research site where full study consent was sought and further eligibility screening was carried out.

7.5.1. Results

Overall recruitment

A flow diagram of the overall recruitment is shown in Figure 9. Participants were recruited over a period of 14 months. All recruitment strategies taken together, a total of 736 patients were approached, either by letter, by a researcher at a clinic, or by a NBCS nurse. The randomisation yield was 4.2% (N= 31/736) for all invited potential participants and 12.1% (N= 31/256) of all participants assessed for eligibility. Nearly half of potential participants (49%, N= 363/736) who were approached by the research team were ineligible. Main reasons were not meeting the age criteria of the study (38%, N= 124/323), not having polyps (17%, N= 55/323), a diagnosis of cancer (10%, N= 33/323), having other health problems (12%, N= 43/323), or already meeting the PA guidelines (7%, N= 24/323). A further 40 patients were excluded because they were inpatients or prisoners.

Forty-six percent (N= 342/736) of people that were approached in person by either a nurse or the researcher declined to take part. The distance to the research site was given as the main reason for not wanting to take part (24%, N= 81/342), followed by not having enough time (16%, (N= 56/342). Other reasons for non-participation were not being interested in the study (4%, N= 13/342), unwilling to be randomised (4%, N= 16/342), and not wanting to speak to a researcher (2%, N= 8/342).

Consent for biopsies

In total 99 patients (n= 54 approached by NBCS nurses, and n= 45 approached by researchers during clinics) gave consent to have research biopsies taken. Forty-four percent of these (n= 12 from NBCS route, n= 32 from clinics) were eligible for the study based on the outcome of the colonoscopy. Three were excluded (n= 1 from NBCS route, n= 2 from clinics) during further screening due to being too physically

active, and 21 withdrew after research biopsies were taken (n= 1 from NBCS route, n= 20 clinic).

Extension of the trial

The trial was set out to be a 6-months intervention with a 6-month follow-up, thus, demanding a 12-month commitment from the participants. Based on potential participants attending the NBCS a 12 months recruitment period was deemed to be sufficient to meet the recruitment target of 120 people. Despite the efforts of implementing new recruitment strategies, the recruitment goal was not met after the proposed recruitment period. Hence, the recruitment period was extended for a further 6 months. However, this compromised the ability to follow-up participants because the project time was not extended. Of the 31 patients randomised, seven were not able to be follow for 6 months after the intervention.

An account of the different recruitment strategies and difficulties experienced

Recruitment was closely monitored on a regular basis. Researchers liaised with consultants and the lead specialist nurse on the recruitment process. This included receiving updates on recruitment, exchange of contact details of potential participants, and gentle reminders to hand out invitation letters to potential participants. If set targets were not met (e.g. it was anticipated to receive 12 contacts from specialist nurses each week), the steering committee, (which consisted of the researchers, academic supervisors, hospital consultants, and the lead specialist nurse) discussed opportunities to increase recruitment. The following recruitment strategies were implemented, and amendments put in place where necessary. See Table 11 for an overview of the recruitment yields of each strategy.

The *approach via NBCS nurses* was proposed as the primary recruitment strategy. However, in the first two months of recruitment only two patients were recruited this way as opposed to the proposed 24 patients to be recruited in this time frame. The exact number of patients approached by the nurses is not known because no record was kept by the nurses.

In summary, 100 patient contacts were passed on to the researcher of which eight people were randomised to the study, yielding a recruitment rate of 8% (N= 8/100) for this strategy. Of the 92 patients not randomised, over half declined (54%, N= 54/92) to participate and nearly half (45%, N= 42/92) did not meet the inclusion criteria. Thus, if only eligible patients are taken into the equation for recruitment rate, this strategy yielded a 16% (N= 8/50) recruitment rate. Reasons for being excluded were: no diagnosis of colonic polyps (48%, N= 24/42) or a 'low risk' diagnosis (5%, n= 2/42) (low risk diagnosis refers to a diagnosis of less than 5 polyps), a diagnosis of cancer (19%, N= 8/42), chronic use of treatment that effects the study of colorectal tissue (14%, N= 6/42), a recent myocardial infarction (7%, N= 3/42), having drug-controlled diabetes (5%, N= 2/42), and being physically unable to take part in exercise (5%, N= 2/42). The main reasons for not taking part were: time commitment (20%, N= 10/50), travel distance to the research site (22%, N= 11/50), not being interested in the study (6%, N= 3/50), not wanting to give research biopsies during the colonoscopy (4%, N= 2/50), or being too nervous before the colonoscopy to be making a decision on study participation (4%, N= 2/50). A further 18% (N= 9/50) of patients were not able to be contacted after they agreed to be contacted by a researcher.

Some patients (3%, N= 3/100) declined participation after speaking to a researcher and declined participation after attending the research unit for an informational meeting before providing study consent.

Although, most of the reasons for exclusion were beyond the researcher's control 24% (N= 10/42) of ineligible patients were excluded because of the strict inclusion criteria. Hence, an amendment to the protocol was made to include people with a 'low risk' diagnosis (less than five small polyps, and no adenoma), and people taking medication that effects the study of colorectal tissue. It was acknowledged that this decision may have a negative effect on the ability to analyse bowel tissue, but it would not have a negative effect on the outcomes of the behaviour change part of the study. In addition to changes to the inclusion criteria, another recruitment strategy was also implemented.

Study invitation letters were sent to patients on the NBCS programme and who had previously been diagnosed with bowel polyps. One-hundred-forty-one letters were sent to potential participants and responses were received from 24 patients (17%, N= 24/141). After contacting interested patients 46% (N= 11/24) were randomised and more than half were excluded or declined participation. Reasons for exclusion were already meeting the current PA guidelines (8%, N= 2/24), and medical reasons (16%, N= 4/24). A third of respondents declined because of the time commitment (28%, N= 2/7), and travel distance (28%, N= 2/7). The recruitment yield (number of patients randomised divided by number of letters sent) was 8.5% (N= 11/141). Based on the number of patients randomized divided by eligible patients who responded to clinician letters, a recruitment rate of 61% was achieved.

Only two batches of letters were sent over a 10 months period, with approximately 70 letters each batch. The strategy appeared to be too time consuming for the clinician. This led to a final amendment of the protocol to implement another recruitment strategy.

The inclusion criteria were expanded to include patients not part of the NBCS programme, but were referred via their GP to the NNUH for a screening colonoscopy. A third recruitment strategy, to recruit patients at the clinic, was also implemented.

For *recruitment at the clinic* a researcher was present at the Gastroenterology Unit to speak to potentially eligible patients after they were asked for permission by one of the clinical nurses. There were a minimum of two and a maximum of five parallel colonoscopy clinics twice a day five days per week with approximately 7 patients on each clinic list. Because of time-commitment the researchers were only available to attend 1-3 clinics per week resulting in a minimum of 7 and a maximum of 21 patients being approached each week.

Over a period of 6 months the researchers approached 495 patients. Overall, a recruitment yield of 2.4% was achieved. More than half (63%, N= 315/495) of patients approached were excluded for not meeting the inclusion criteria. Reasons for exclusion were age (45%, N= 124/275), being physically unable to take part in

PA (12%, N= 34/275), a diagnosis of cancer (9%, N= 25/275), no diagnosis of colonic polyps (9%, N= 24/275), already meeting PA recommendations (7%, N= 20/275), health problems (12%, N=32/275), and not willing to be randomised (5%, N= 15/275). A further 8% of potential participants were excluded because they were inpatients or prisoners, thus, not making them eligible to take part in the study. Over a third (34%, N= 168/495) of approached patients declined to take part in the research. Reasons provided were distance to travel to the research site (40%, N= 68/168), the time commitment of the intervention group (26%, N= 44/168), not being interested (5%, N= 9/168), refusal to speak to a researcher (5%, 8/168), not willing to be randomised (5%, N= 9/168), and not wanting research biopsies to be taken (3%, N= 5/168).

There was concern that participants may be approached more than once because of the implementation of additional recruitment strategies at later stages. However, if patients were identified with a polyp they would not be seen by a consultant for a follow-up screening for at least another year. This reduced the likelihood that a patient would be approached twice, first by the specialist nurse, and then again at the clinic. Furthermore, letters were sent to patients on the NBCS programme and to people who were diagnosed with polyps outside the NBCS programme. There was a likelihood that patients previously approached by a specialist nurse have received an invitation letter. But patients who were approached by a specialist nurse were likely to be patients who had their very first screening, and thus, no previous polyps. And patients who received invitation letters were likely to have had a diagnosis of a polyp in the past 5 years. This reduced the likelihood that patients were invited to the study more than once.

Responders and non-responders

Table 12 shows the IMD, distance to the research site, and travel time for participants and non-responders. Significant differences were seen for all variables between participants and non-responders. There was a mean difference of 7.4 for IMD (P<.001), 17.7 km for distance (P<.001), and 19.8 min for travel time between the populations with higher IMD and shorter travel distances and time for study participants.

Survey responses

Reasons for not taking part

In total 72 surveys were sent to non-responders of which 44 people returned the survey yielding an overall 61% response rate. Main reasons that were provided for not taking part in the main trial were travel distance to the research site reported by 59% of survey respondents and time commitment reported by 47%. Both, time and travel distance were often reported together (34%). Other reasons for non-participation were caring for family, being in full-time employment, or being worried about the safety of exercising.

Quality of life

Table 13 shows all survey responses. Most people reported problems with pain (34.1%) and least problems were reported for the self-care domain (6.8%). About one third of responders reported problems with mobility and usual activities (31.8% and 25.3%, respectively), and 13.6% reported problems with anxiety and depression. The majority of people who reported health problems rated their problems as moderate. Severe or extreme/unable problems were only reported by a small amount of people, for mobility (4.5%), usual activities (2.3%), pain (2.3%), and anxiety (2.3%).

Barriers to exercise

Overall, survey participants' barriers to being physically active were low with a mean score of 7.2 (SD= 2.7). After assigning people to 'having low barriers' or 'having high barriers' with the individual items, based on the median score, more than 50% of the sample fell in 'low barrier' category (Table 14). However, the most often reported barriers were for lack of motivation, the costs of exercising, not knowing what exercise to do, and not having a friend to exercise with. The least often reported barriers were: not knowing where to exercise, not feeling safe to exercise in the neighbourhood, not having time, health problems, and not knowing how much exercise to do.

PA behaviour

The Godin leisure time PA questionnaire showed that the main intensity of PA was moderate (202 min per week, SD= 253 min) and mild (138 min per week, SD= 234). Participants also engaged in 90 min (SD= 163) per week of vigorous intensity PA. Over half of the sample (59%) met the current PA guidelines of either 150min of moderate intensity or 75 min vigorous intensity PA per week.

When asked how active they perceive themselves to be the main response was 'moderately active' (57%) and the least response 'inactive' (7%). Fourteen percent of all survey participants rated themselves as 'somewhat active', and 20% as 'very active'.

Recruitment yield	Overall from all strategies	Specialist nurses	Invitation letter	Clinic approach
Randomized/total approached (%)	31/736 (4.2)	8/100 (8)	11/141 (8.9)	12/495 (2.4)
Randomized/eligible (%)	31/256 (12.1)	8/50 (16)	11/18 (61)*	12/180 (6.6)
Randomised/respondents to letters (%)	N/A	N/A	11/24 (46)	N/A

Table 11 Overview of recruitment strategies

*For letters, only people who responded could be assessed for eligibility. Because only 24 responded, and 6 were ineligible, only 18 were eligible.

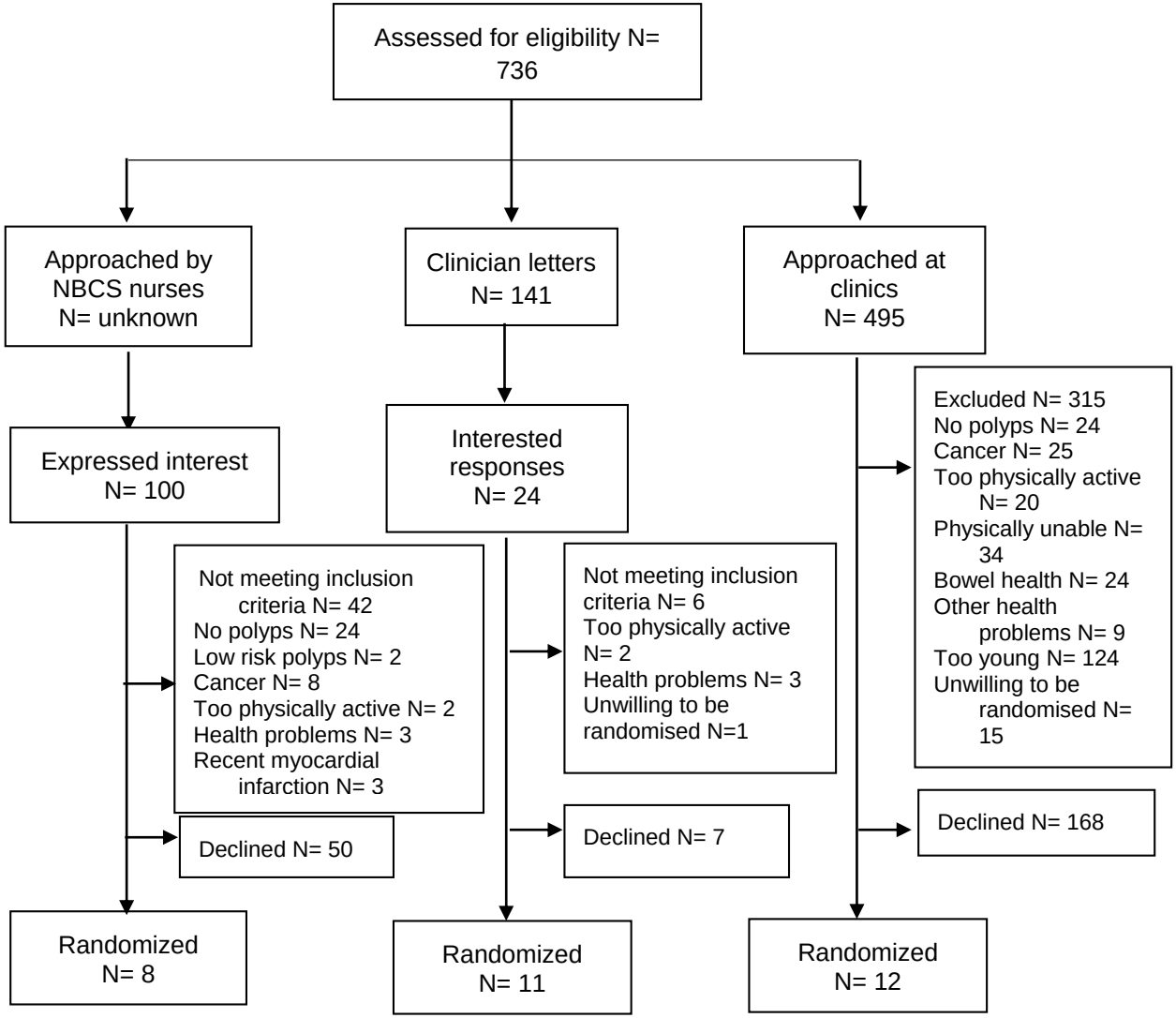


Figure 9 Flow diagram of patient recruitment. NBCS=National Bowel Cancer Screening Nurse

Table 12. Differences between participants and non-participants for IMD distance to the research site and travel time to research site.

	PARC participants N= 31 Mean (95% CI)	PARC non-responders N= 44 Mean (95% CI)	P value
IMD	11.7 (10.3, 13.1)	19.1 (16.8, 22.0)	< 0.001
Distance to research site in km	20.0 (15.1, 25.0)	37.7 (33.9, 41.6)	< 0.001
Travel time to research site in min	31.1 (25.1, 37.1)	50.9 (46.1, 55.7)	< 0.001

Table 13. Survey responses for QoL, PA, PA behaviour

Variable	PARC-non-responders n= 44 (%)
Problems with:	
Mobility	11 (31.8)
Self-care	3 (6.8)
Usual activity	11 (25.3)
Pain	15 (34.1)
Anxiety/ Depression	6 (13.6)
PA level	
Inactive	3 (7)
Somewhat	6 (14)
Moderately	25 (57)
Very active	9 (20)
PA behaviour (min per week)	Mean (SD)
Mild	138 (±234)
Moderate	202 (±253)
Vigorous	90 (±163)

Table 14 Barriers to exercise in non-responders to study invitations, score range is 1-10, ranges for low or high barrier presented for each item

Item	**PARC-non-responders N (%)**
I don't know what exercise to do	
Low barrier (8-10)	18 (46.1)
High barrier (1-7)	22 (54.0)
I don't know how much exercise to do	
Low barrier (8-10)	23 (52.3)
High barrier (1-7)	16 (36.4)
I don't have time to exercise	
Low barrier (10)	23 (52.3)
High barrier (1-9)	14 (31.8)
My health prevents me from exercising	
Low barrier (10)	25 (56.8)
High barrier (1-9)	14 (31.8)
I cannot afford the costs of exercising	
Low barrier (10)	19 (43.2)
High barrier (1-9)	18 (40.9)
I cannot get myself motivated to exercise	
Low barrier (9-10)	20 (45.5)
High barrier (1-8)	18 (40.9)
I don't have anyone to exercise with	
Low barrier (8-10)	20 (45.5)
High barrier (1-7)	18 (40.9)
There is nowhere to exercise in the area where I live	
Low barrier (10)	21 (47.7)
High barrier (1-9)	16 (36.4)
I don't feel safe exercising in my neighbourhood	
Low barrier (10)	27 (61.4)
High barrier (1-9)	9 (20.5)

7.6. Part B: MOVE

Participants

Participants were patients from the Norfolk and Norwich University Hospital (NNUH), Norwich, United Kingdom who were diagnosed with CRC as identified by the CRC Lead. Patients were included if they were meeting the following inclusion and exclusion criteria: i) histologically confirmed diagnosis of colorectal cancer with Dukes stages A-C ii) completed cancer treatment within the last 24 months, iii) be able to understand spoken and written English, iv) score of 80 or more on the Karnofsky Performance Status Scale

Exclusion: i) already meeting general PA guidelines, ii) recent myocardial infarction iii) uncontrolled hypertension iv) a pacemaker v) or unstable angina.

Recruitment

The primary recruitment strategy for this trial was by postal invitation letter from a Colorectal Surgeon. Patients with a diagnosis of CRC within the last 2 years were identified by two Cancer Specialist Nurses (CSN) at the NNUH who prepared the invitation letters which contained a personalised letter and a participant information sheet. No other eligibility criteria were assessed at this stage. The letter contained the nurses' and the researcher contact details. Follow-up letters were sent after 4 weeks to patients who did not respond to the first invitation letter. If the patient called the nurses to express an interest in the study the nurses advised the patient to call the researcher. During the phone call with the researcher preliminary inclusion criteria were assessed and an appointment was scheduled at the research site or the hospital, depending on the patient's preference. During this visit the study was explained in full detail and a full study consent form signed. Further eligibility screening was undertaken at this appointment and a second appointment 7 days later.

7.6.1. Results

Response rate and randomization yield

Figure 9 shows the flow of recruitment. Two batches of clinician invitation letters were sent over a period of 3 months with 239 letters being sent in total. Sixty-five responses were received of which 31% (N= 20/65) declined to participate, 26% (N=

17/64) did not meet the inclusion criteria, and 43% (N= 28/65) were randomised. A quarter (N= 5/20) of people declined because of the time commitment asked of participants and 10% (N= 2/20) were unable to travel to the research site. More than half (65%, N= 13/20) were not able to be contacted after they first expressed an interest or gave no reason for not wanting to participate. The majority of people excluded from participation were already meeting the recommended PA guidelines (65%, N= 11/17). Other reasons for exclusion were still receiving chemotherapy treatment (18%, N= 3/17), being diagnosed with metastasis (12%, N= 2/17), or having a pacemaker (6%, N= 1/17). The recruitment yield (number of patients randomised divided by number of letters sent) was 12% (N= 28/239). Based on the number of patients randomized divided by eligible patients who responded to clinician letters, a recruitment rate of 58% (N= 28/48) was achieved.

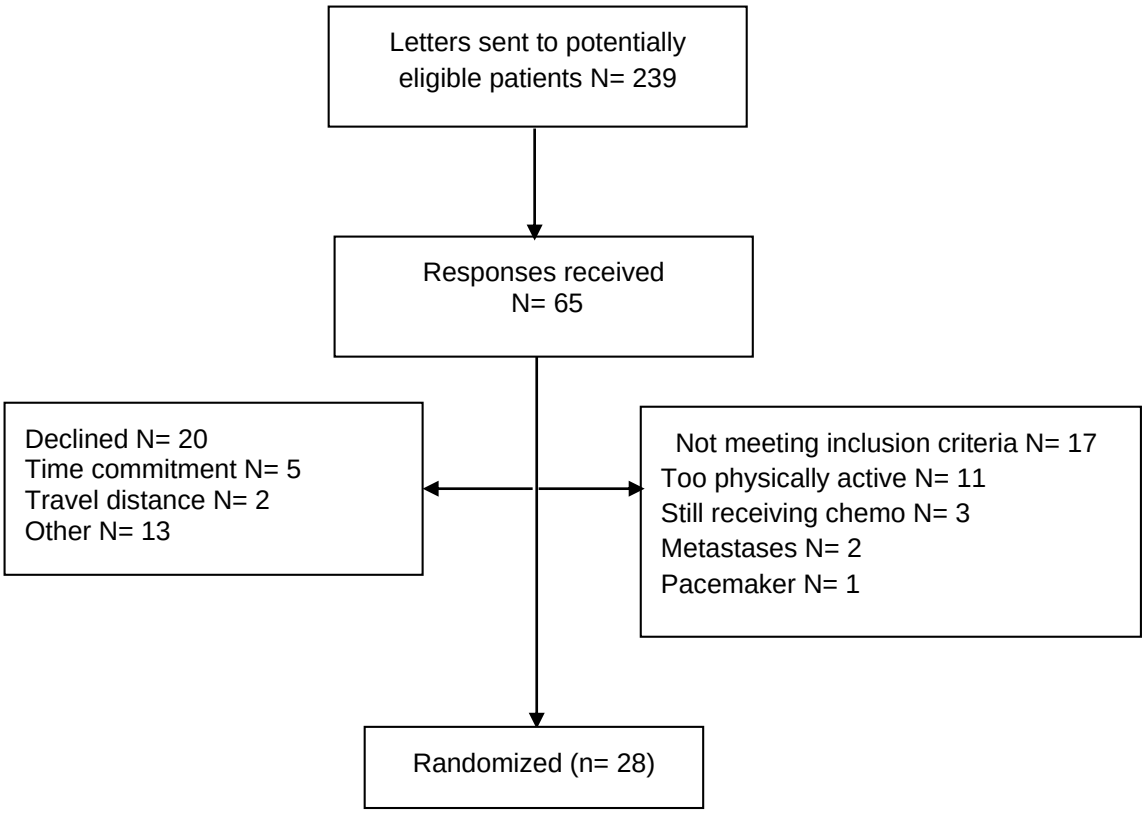
Responders and non-responders

MOVE participants were significantly more affluent than non-responders (P<.05) (Table 15). Although, MOVE non-responders lived on average 3.3 km further and would have spent 4.7 min more time traveling to the research site, this difference was not significant.

Survey responses

Reasons for not taking part

In total, 170 surveys were sent to non-responders of which 100 people returned the survey yielding and overall 59% response rate. Main reasons for not taking part in the study were travel distance to the research site and time commitment. Both, time and travel distance were often reported together. Other reasons for non-participation were caring for family, being in full-time employment, being too old for participation, being worried about safety of exercising, forgetting to respond, and not having received an invitation letter to the study. One person said that they 'never volunteer for anything'.



`Figure 10 MOVE recruitment

Table 15. Differences in IMD (index of multiple deprivation), distance and travel time to research site between non-responders and study MOVE participants.

	MOVE participants N = 28 Mean (95% CI)	**MOVE non-responders N= 100 Mean (95% CI)**	**Test for t-trend P value**
IMD	11.0 (8.8, 13.5)	16.2 (14.9- 17.7)	< 0.001
Distance to research site in km	16.0 (11.9, 21.0)	19.3 (17.3- 21.1)	.21
Travel time to research site in min	25.6 (21.1, 31.3)	30.3 (28.0- 32.71	.20

Table 16. Survey responses to QoL, perceived PA level, and PA behaviour.

Variable	MOVE-non-responders n= 100 (%)
Problems with:	
Mobility	27 (28.7
Self-care	11 (11.7)
Usual activity	27 (28.7)
Pain	41 (43.6)
Anxiety/ Depression	24 (25)
PA level	
Inactive	5 (5)
Somewhat	18 (18)
Moderately	56 (56)
Very active	19 (19)
PA behaviour (min per week)	Mean (SD)
Mild	133 (±199)
Moderate	184 (±253)
vigorous	49 (±133)

Quality of life

Table 16 shows all survey outcomes. Most people reported problems with pain (43.6%) and least problems were reported for the self-care domain (11.7%). About one third of people reported problems with mobility and self-care (31.8% and 25.3% respectively), and 13.6% reported problems with anxiety and depression. The majority of people who reported health problems rated their problems as moderate. Severe or extreme/unable problems were only reported by a small amount of people, for mobility (5.0%), usual activities (3.2%), pain (3.2%), and anxiety (2.3%).

Barriers to exercise

Overall, survey participants' barriers to being physically active were low with a mean score of 7.7 (SD= 2.3). After assigning people to 'having low barriers' or 'having high barriers' with the individual items, based on the median score, more than 50% of the sample did only report low barriers to exercising (Table 17). However, the most often reported barriers were a lack of motivation, no time to exercise, not knowing how much exercise to do, and not having a friend to exercise. The least often reported barriers were the costs of exercise, not knowing where to exercise, not knowing what exercise to do, health problems, and safety.

PA behaviour

When asked how active they perceive themselves to be the main response was 'moderately active' (56%) and the least response 'inactive' (5%). Eight-teen percent of all survey participants rated themselves as 'somewhat active', and 19% as 'very active'. The Godin leisure time PA questionnaire showed that the main intensity of PA was moderate (184 min per week, SD= 253 min) and mild (133 min per week, SD= 199). Participants also engaged in 49 min (SD= 133) per week of vigorous intensity PA. Over half of the sample (53.5%) met the current PA guidelines of at least 150min of moderate intensity or 75 min vigorous intensity PA, or a combination of both.

Table 17. Items of barriers to exercise. Range score was 1-10. Ranges are given for having 'low barriers' and 'high barriers'.

Item	MOVE-non-responders N (%)
I don't know what exercise to do	
Low barrier (8-10)	52 (52.5)
High barrier (1-7)	31 (31.3)
I don't know how much exercise to do	
Low barrier (9-10)	43 (43.3)
High barrier (1-8)	39 (39.4)
I don't have time to exercise	
Low barrier (10)	41 (41.4)
High barrier (1-9)	38 (38.4)
My health prevents me from exercising	
Low barrier (10)	46 (46.8)
High barrier (1-9)	35 (35.4)
I cannot afford the costs of exercising	
Low barrier (10)	54 (54.5)
High barrier (1-9)	27 (27.3)
I cannot get myself motivated to exercise	
Low barrier (9-10)	42 (42.4)
High barrier (1-8)	40 (40.4)
I don't have anyone to exercise with	
Low barrier (10)	42 (42.4)
High barrier (1-9)	39 (39.4)
There is nowhere to exercise in the area where I live	
Low barrier (10)	47 (47.5)
High barrier (1-9)	33 (33.33)
I don't feel safe exercising in my neighbourhood	
Low barrier (10)	56 (56.6)
High barrier (1-9)	24 (24.2)

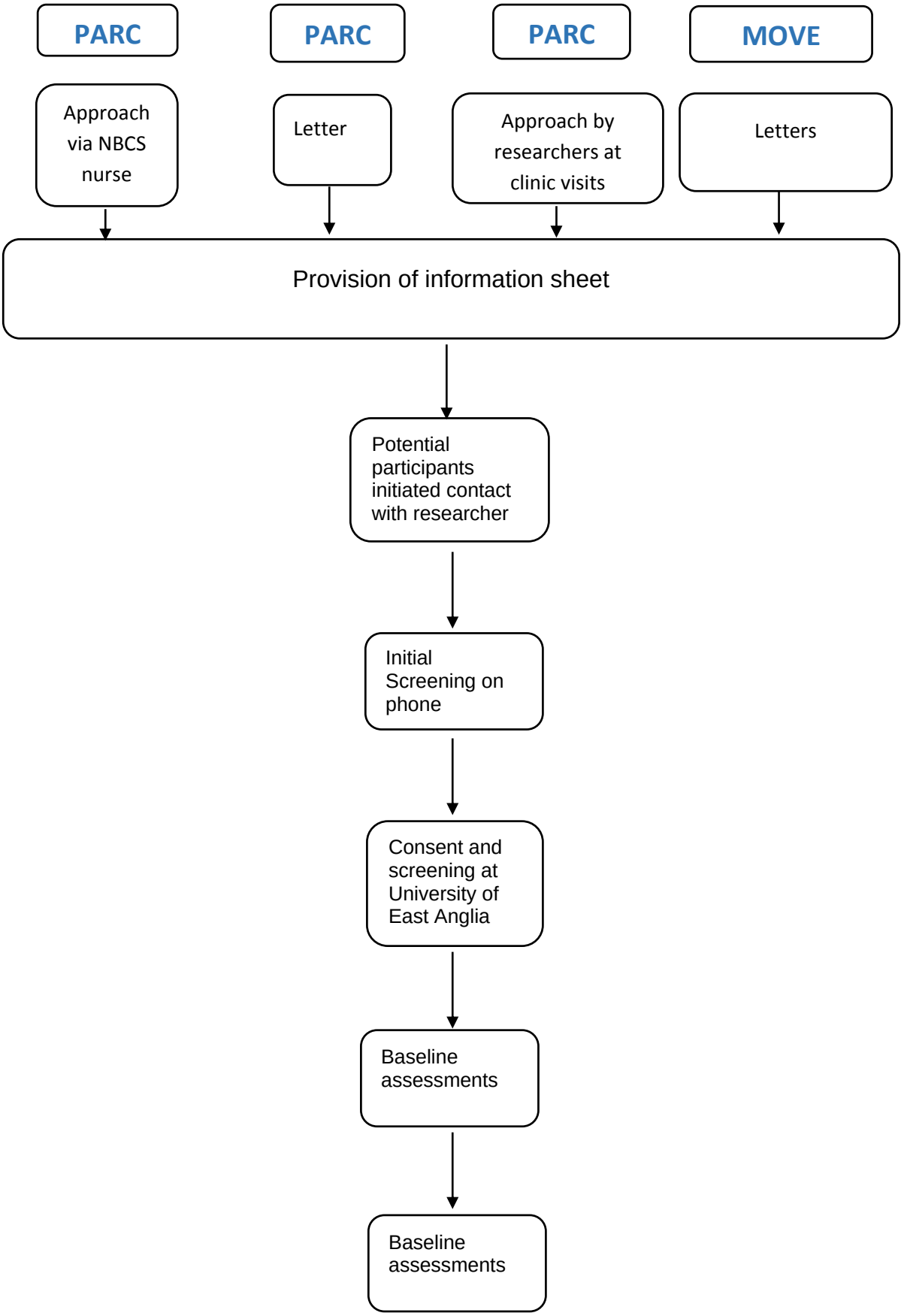


Figure 11. Overview of recruitment processes of both studies. NBCS = National Bowel Cancer Screening Nurse

7.7. Discussion

Recruitment strategies were different for PARC and MOVE and thus, will be discussed independently in the following paragraphs of this discussion. A detailed discussion of the survey outcomes, and postcode analysis will follow where results for PARC and MOVE will be discussed together. A combined discussion was chosen to avoid repetition.

Recruitment and eligibility of PARC participants

Overall we were able to recruit and randomize 8% of eligible subjects and 4% of those who were identified as potential participants. Compared to other lifestyle interventions in the CRC prevention setting recruitment rates from 32% (Treweek et al., 2013b) to 61 % (Emmons et al., 2005) were achieved. However, these trials required little face-to-face contact with the researchers. Although, the interventions were more than 3 months long, the participants did not have to attend intervention treatments because the intervention was home-based. On the contrary, the present study was rather time-consuming. Participants in the intervention group were encouraged to attend two weekly supervised exercise sessions for 3 months and one weekly supervised exercise session for another 3 months. The sessions lasted about one hour and taking together the time of the session itself and travel time to the research site, this could have taken two hours of the participant's time per visit. In addition, the total length including follow-up time (12 months) of this trial could have been a barrier to participation. More about barriers and time commitment will be discussed together with the survey outcomes in section 5.3 of this chapter.

It was found that recruitment via clinical invitation letter and via NBCS nurse was most successful, and that recruitment via clinics was the least successful. One explanation is that letters were only sent to patients that had a previous diagnosis of polyps, increasing the chance that they were eligible. The letter was signed by the Consultant Gastroenterologist, which may have also influenced people's decision making. Moreover, patients recruited by specialist nurses were patients that had a previous positive result from the faecal occult blood test, further increasing the likelihood to be diagnosed with a polyp. In contrast, patients that were seen in clinic may have been referred to a colonoscopy due to symptoms such as change of bowl habit. Likely diagnosis were inflammatory bowel disease or other

bowel conditions, but not polyps. This could have contributed to the low eligibility of patients from the clinic recruitment route, and thus, a low recruitment rate. Another explanation could be that patients feel more receptive to research information from a health professional vs a researcher.

Another major barrier to achieving the recruitment target was the large number of people not meeting the inclusion criteria, a problem commonly reported in other trials (Korde et al., 2009, Donovan et al., 2014, Ott et al., 2006). Only half of the identified potentially eligible subjects met the inclusion criteria to take part in this trial. Similar rates were reported in other prevention interventions. A PA intervention with women at increased risk of breast cancer (Korde et al., 2009) and a RCT for osteoporosis prevention in breast cancer survivors (Ott et al., 2006) both excluded half of identified subjects due to not meeting the inclusion criteria. It is to be expected that the more stringent the inclusion criteria are, the larger the number of people excluded from participation. In this present trial the inclusion criteria were particularly strict, because the trial was informing two different research outcomes: behaviour change after an exercise intervention, and an analysis to investigate the effects of exercise on epigenetic changes in colorectal tissue. This may have exacerbated recruitment. Compared to other screening trials with people at increased risk of CRC and a rather low number of inclusion criteria (Treweek et al., 2013b, Emmons et al., 2005), inclusion criteria in this trial were restricted to not meeting the current PA guidelines, not having a diagnosis of drug-controlled diabetes mellitus, the absence of medication that could have an effect on the investigation of bowel tissue (e.g. chronic use of aspirin), and not having other morbidities of the bowel such as inflammatory bowel syndrome. Whereas, in other trials the only restrictions were age, BMI, being physically able to undertake exercise, and have a diagnosis of colonic polyps (Emmons et al., 2005, Treweek et al., 2013b). In this age group restrictions especially for taking NSAIDS pose a large barrier to recruitment since most NSAIDS are routinely prescribed to older people at higher risk for gastrointestinal or cardiovascular morbidities (http://www.nice.org.uk/advice/ktt13). In this trial 14% of interested patients were excluded for taking NSAIDS which led to an amendment of the protocol to include this patient group. Lastly, having to consent to have research biopsies taken may have acted as a barrier for participants to take part in the study. It was explained to the patients that taking extra biopsies does not pose an additional risk and is part

of the standard procedure if a polyp was identified. However, patients may have been nervous about the procedure and thus, decided not to give consent for research biopsies to be taken.

While the previously discussed obstacles to successful recruitment were research design related or patient-related, it is important to also consider recruiter related issues. These obstacles are often not reported in recruitment studies. Recruitment can be very time consuming, and be burdensome to clinical staff. Although, support of the research might be in their best interest, they are often overloaded with clinical responsibilities and do not have the time to dedicate to recruitment (Pinto et al., 2004). It was felt that in this trial NBCS nurses, despite their efforts, did not have the time to approach all the potentially eligible participants who attended a pre-screening clinic. It was anticipated to receive around 12 patient contacts from the NBCS nurses each week, but often the researchers were only passed as little as one patient contact per week or even none. Qualitative research with research nurses revealed some important issues that might hinder research nurses from recruiting patients in to research studies (Donovan et al., 2014). Donovan and colleagues (2014) found that nurses perceived a conflict between caring for patients and recruiting them to RCTs and that they felt they could use their clinical judgement to decide who to approach about the research. Another theme that occurred in this qualitative study was that nurses not only made their own judgement of whom to approach about research, but also it appeared that nurses were uncomfortable to approach some patients based on their character. These issues highlight the need for support and training for recruiters (Donovan et al., 2014).

Recruitment of MOVE participants

The recruitment of CRC survivors to the active lifestyle intervention yielded a 12% randomisation rate (number of people randomized divided by letters sent). This is comparable to other PA interventions with CRC survivors (Bourke et al., 2011, Pinto et al., 2013). However, one exercise intervention with this population was able to recruit 27% of identified potential participants (Courneya et al., 2003a). It is possible that recruitment in the latter trial was higher because participants were not restricted by their current PA levels. Whereas, in this trial the main reason for exclusion was already meeting the PA activity guidelines. This has also been a

prominent exclusion criterion in a home-based PA intervention with breast cancer survivors. Another reason could be the design of the intervention. Where this intervention required taking part in supervised exercise, Courneya et al's (2003a) trial was home-based. Other home-based PA trials with cancer survivors have also demonstrated better recruitment rates, contributing to the assumption that recruitment in this trial was low because of the requirement to attend supervised exercise Another study with CRC patients recruited 71% of patients that were assessed for eligibility (Cheville et al., 2013). However, cancer patients in this study had a diagnosis of advanced stage IV. This population difference might be an important factor for recruitment success.

Survey findings

The main findings of the surveys and post code analysis identified travel distance to the research site and time commitment as the main barriers for non-participation. Other findings demonstrate that non-responders have good health, with most survey participants reporting none or only slight problems with the five QoL domains. People also perceived themselves as being moderately physically active and reported more than 150min of moderate intensity PA per week. Findings of this study are in agreement with previous findings (Rogers et al., 2014a, Gul and Ali, 2010).

Barriers to participate

The barriers of travel and time commitment can be dependent on the research design (Gul and Ali, 2010). This is further confirmed by the findings that study participants in both trials lived closer to the research site and spent less time traveling than non-participants. Cited reasons for not having the time to take part were often related to family commitments and work commitments. This highlights the need to create interventions that allow flexibility to meet participants' needs. Although, the design of this study tried to accommodate for this, and offer a flexible intervention schedule, it may have not been clearly outlined in the patient information sheet.

One person responded that they never volunteer for anything. This was only one response, but may have been the thoughts of others who did not respond to the survey for that exact reason. Perhaps, even if all aspects of the trial have been

attempted to accommodate every need of the participants, there might just be some people that cannot be reached, because they have a lack of interest to participate in trials. In some ways 'volunteerism' is a bizarre phenomenon and "[it] simply should not occur" (Snyder and Omoto, 2009). It is time consuming, but yet people engage in it. It has been argued that people only volunteer to achieve personal gains (Snyder and Omoto, 2009). Then it can be argued that people who volunteer for clinical trials associate this with some sort of personal benefit. And then perhaps, people who are lacking an interest may also lack the knowledge of the potential benefits that might be associated with participation. For example, in the REFLUX trial patients were weighing up the potential benefits for themselves against the disadvantages, in this case this meant receiving surgical treatment sooner (McCann et al., 2010). This assumes the knowledge of the potential benefit of a trial. In the context of cancer and cancer prevention, (Stead et al., 2012) found that patients did not know the causes of adenomas and were lacking an understanding of the importance of lifestyle changes for cancer prevention. Thus, an invitation to a lifestyle behaviour change intervention might not have led to an interest in participation because no personal benefits could be identified (Stead et al., 2012). This could also be the case for CRC survivors. Although, recruitment strategies focus on the mode of recruitment, e.g. via clinics, mailings, advertisements, perhaps more attention should be given to the understanding of the benefits of an intervention.

Characteristics of non-responders

In terms of PA, non-responders perceived themselves as being moderately active and also reported more than 150min of moderate intensity PA per week. This could be a reasons for not being interested in participation because they perceived themselves as being sufficiently active (Rogers et al., 2014a). This is also in agreement with other studies that reported that non-participants are more active than trial participants (van Heuvelen et al., 2005, Harris et al., 2008). Qualitative research with non-participators to a PA intervention with older people found that the predominant explanation for non-participation was the perception that they were already doing enough PA (Rogers et al., 2014a, Crombie et al., 2004). Crombie et al (2004) raises the concern that older people perceive themselves as active but the majority of their activities are of light intensity. This poses a challenge on

recruiting this population to programmes aimed at increasing leisure time PA. Some of the survey responders indicated the mode of PA engaged in, and easy walking, household, and gardening activities were among the most often cited activities. Responses were similar for PARC and MOVE non-responders. Fitness activities such as swimming, and cycling were cited the least. This is in agreement with Crombie et al's (2004) findings. Findings from the short barrier questionnaire in this survey also confirm this. 'Not knowing how much exercise to do', and 'not knowing what exercise to do' were identified as barriers for both PARC and MOVE non-responders.

The majority of survey participants reported none to slight health problems and this was similar for high risk patients and CRC survivors. A slightly bigger proportion of cancer survivors reported problems with pain and anxiety compared to high risk patients. However, QoL from non-responders in this study is similar to non-responders in a PA intervention with people aged >60 years (Rogers et al., 2014b).

Limitations and weaknesses

The results of the study should be interpreted in the light of its limitations. Socio-demographic characteristics of people who declined to take part in the study were not logged and it would have been useful to have this information to compare to responders and participants. This also limited the postcode analysis to the recruitment route via letters, because this information was not available from people approached via nurses and researchers. Another limitation is that the NBCS nurses did not keep a record of the number of people they approached about the study. Information on reasons for not approaching patients, or reasons for declining to be contacted by a researcher would have been informative for future recruitment strategies. Moreover, socio-demographic data was not collected from people who responded to the surveys apart from the postcode to calculate the IMD.

Another weakness is that survey responses could not be compared with study participants. The survey was initially intended to include the same questionnaires as were used in the study. However, in consideration of the poor recruitment rates and response rates to previous study invitations, it was decided to keep the survey limited to one page. Having to complete several pages of questionnaires could have been a barrier to completing the survey. Response rates to surveys in older people

has been reported to be less than 50% (Crombie et al., 2004). Compared to these findings, response rates to surveys in this study were 64% for PARC non-responders, and 59% for MOVE non-responders.

A strength of this study is that the randomisation yields of each individual recruitment strategy were discussed individually, which other studies have failed to do. Furthermore, recruitment obstacles were also considered in the light of recruiter-related issues, and not solely of participant-related issues. We have also attempted to compare demographic characteristics between participants and non-responders, although this was limited to postcode data. The brief barrier questionnaire provided unique evidence of the lack of knowledge about mode and intensity of PA which has not been previously reported in these populations.

Recommendations

In consideration of the barriers to research participation, especially in regard to time commitment and travel distance, research should be offered in multiple centres to reduce burdens of traveling. This has been previously recommended and proven to be successful (Treweek et al., 2013b, Treweek et al., 2013a). However, this also requires more resources which raises the costs of the trial. Other successful recruitment strategies have previously been identified and should be carefully considered before planning recruitment (Treweek et al., 2013a).

7.8. Conclusion

Clinician invitation letters and approach via NBCS nurses were most successful in the recruitment compared to an approach during clinics by a researcher. Overall, recruitment of high risk patients was poor and recruitment of CRC survivors acceptable compared to other trials. Unique differences in circumstances of people at increased risk of cancer and people diagnosed with cancer may be important elements of recruitment success with these populations.

Chapter 8

Validation of the International PA Questionnaire against different accelerometer cut-points in an elderly population at elevated risk of CRC

8.1. Abstract

Introduction: The International PA Questionnaire (IPAQ) was developed to assess self- reported PA (PA) and to allow comparison across countries. The self-administered questionnaire has been validated for younger populations but it is also used in studies with older people. The present study investigated the validity of an interview-administered IPAQ long version (IPAQ-L) in a sample of participants aged >60 years at elevated risk of, or recovering from CRC. *Methods:* Baseline data from male (n=32) and female (n=20) participants (mean age and standard deviation: 67.9 ±6.6 years) recruited for PA intervention studies were included in the analysis. Participants had been diagnosed with bowel polyps or were recovering from curative bowel cancer treatment. Different accelerometer criteria were applied (Freedson cut-points: 1952-5724 cpm, and Matthews cut-points: 760-5724 cpm). Spearman rank order correlation coefficient was used to investigate associations between subjective PA from the interview-administered IPAQ-L and objectively measured movement counts (accelerometry). *Results:* Moderate significant correlations were observed for IPAQ measures of total weekly PA and walking PA with both accelerometer criteria (Freedson: ρ=0.43, ρ =0.38, and Matthews ρ=0.44, ρ =0.44 for total IPAQ and walking PA respectively). A large significant correlation was observed between walking PA and Freedson cut-points (ρ =0.57), and a moderate correlation with Matthews cut-points (ρ=0.41). Sedentary time was moderately and significantly correlated (ρ =0.33). Correlations with self-reported moderate intensity PA household PA were not significant. *Conclusion:* Our results show that an interview-administered IPAQ-L shows acceptable validity for total PA, walking PA and sedentary behaviour, but not for household PA and non-walking moderate intensity PA.

8.2. Introduction

There is strong evidence of the benefits of PA (PA) for the maintenance and improvement of health. Studies have shown that leading an active lifestyle reduces the risk of developing a variety of diseases including certain types of cancer, stroke, cardiovascular diseases, diabetes, and loss of bone density (DoH, 2011). Worldwide a lack of PA is estimated to cause 9% of all premature deaths (Scholes and Mindell, 2013). In relation to bowel health, risk reductions for developing CC of 22% (Friedenreich et al., 2006) to 52% (Nilsen et al., 2008) have been reported. In addition, a 30% risk reduction for the development of bowel polyps is also evident from cohort studies (Wolin et al., 2011). Evidence also suggests that people at elevated risk of CC can experience survival benefits from engaging in a physically active lifestyle with studies showing a 49% reduced risk of death from colon cancer associated with physical activity (Meyerhardt et al., 2006). However, accurate ways of monitoring PA levels in this population are needed to test this hypothesis. It is important to be able to measure the intensity, duration, and frequency of PA to accurately determine the amount of PA that is beneficial for the prevention of the development of CRC and the reduction of the risk of recurrence of the disease. Furthermore, the accurate measurement of PA is also important to evaluate the efficacy of PA interventions within cancer survivor-based studies.

The latest PA guidelines for the maintenance and improvement of health published by the Department of Health (2012) recommend at least 150min of moderate intensity PA (aerobic exercise), or 75 min of vigorous intensity PA (or a combination of both) per week. This should be spread out over the week in bouts lasting at least 10 min. Muscle strengthening exercises at least twice a week is also recommended. Records from the Health survey for England 2012 show that only 58% of men and 52% of women aged 65-74 years are meeting the general PA guidelines mentioned above (Scholes and Mindell, 2013). It should be noted that according to these guidelines each activity bout has to last 10 min to count towards the goal of 150min, but it is not required to accumulate a minimum of 30min in one day, which was a requirement of the 2004 recommendations (Craig et al., 2009). In contrast, for the prevention of CC, the World Cancer Research Fund recommends moderate PA of at least 30min every day of the week and this should be increased to 60min or more of moderate intensity exercise or 30min vigorous intensity exercise every day once

fitness levels improve (World Cancer Research Fund and American Institute for Cancer Research, 2007). In light of these recommendations (30min of moderated intensity PA per day) only 26% of men and 22% of women aged 65-74 years were sufficiently active in 2012 (Scholes and Mindell, 2013). In 2008, PA was also assessed with accelerometry producing a much lower number of PA participators (6% of men and 4% of women meeting the recommendations) (Craig et al., 2009). This demonstrates the limitations of self-reported PA but also raises questions whether accelerometers are reliable measures of PA as some activities cannot easily be measured using this technology.

Objective measures such as accelerometers are often considered to be the most accurate method of measuring PA because they reduce recall and social desirability biases. However, the high cost of accelerometry, and burden on the patient due to wear time make it a less desirable tool for use with large populations. Additionally, potentially vigorous activities such as cycling, swimming, and gardening are very difficult to measure with accelerometry (Matthews, 2005). Self-administered questionnaires are favoured for large-scale assessments because of their low costs and ease of administration. The International PA Questionnaire (IPAQ) is a PA measurement tool developed to measure PA across ages and countries to enable international comparison of PA. There are two versions of the IPAQ, a short version (IPAQ-S), and a long version (IPAQ-L). Both measure PA over the last seven days. The IPAQ-L records PA from five PA domains (occupation, household, transport, leisure-time, and sedentary time) and discriminates PA by moderate and vigorous intensity. The IPAQ-S includes four general questions about PA including time spent at moderate and vigorous intensity PA, walking activities, and sitting. Validity of the IPAQ-L has been tested previously among people aged 18-65 years and acceptable results were reported for construct validity (Hagstromer et al., 2006, Macfarlane et al., 2011, Craig et al., 2003). Reported correlation coefficients (ρ) between total PA recorded with the IPAQ-L and accelerometer ranged from 0.33 to 0.55. However, only one validation study with an elderly population could be identified which reported a correlation of ρ=0.25 (Cerin et al., 2012).

A problem that is frequently reported with self-administered PA questionnaires is the risk of over- and under-reporting (Janz, 2006, Prince et al., 2008a). Particularly older people aged 65-89 years were found to have difficulties answering the IPAQ-

L in regards to understanding what questions meant with 'duration', 'frequency', and 'intensity' (Heesch et al., 2010). Participants failed to understand that the questionnaire only asked for activities of the last 7 days and tended to give answers of a *usual* week. Furthermore, participants tended to include activities that lasted less than 10 min despite the questionnaire only requesting activities that were performed for at least 10 min. Other problems occurred in deciding whether an activity was of moderate or vigorous intensity, especially when the activity varied in intensity (e.g. cycling uphill and downhill). Participants were also confused about the walking –domain of the questionnaire. Some participants wanted to include all activities around the house and garden because they were standing and walking. Or they included driving time in answers to the walking question because they drove to the place where walking was performed. Finally, participants often reported the same activity in several domains. These findings highlight the problems of processing and comprehending IPAQ questions and provide a strong rationale for further validation studies with the elderly. Interview administration could help to clarify issues of intensity, duration, and frequency and the answers may be less susceptible to over-reporting. A study by Rzewnicki (2003) delivered the IPAQ in two different ways via a phone interview. Firstly, the IPAQ questions were read to the participants as they appear on the questionnaire (IPAQ-1). Afterwards the interviewer asked additional questions, so as to clarify what activities the participant referred to when listing vigorous activities (IPAQ-probe). If the interviewer rated that activity as less intense than vigorous, it was moved to a different category (moderate) or removed from the questionnaire. The results showed significant larger volumes of vigorous PA for the IPAQ-1 than for the IPAQ-probe (Rzewnicki et al., 2003).

Only one previous study was designed to assess the validity of an interview-delivered IPAQ-L against an objective measure with older adults (Cerin et al., 2012). The Spearman correlation coefficient between total PA measured with the IPAQ and accelerometry was p=0.25, which is weaker than validation studies with younger adults (Hagstromer et al., 2006, Craig et al., 2003). Weaker correlations with the elderly could be attributable to a misinterpretation of the questions from the IPAQ-L as described above (Heesch et al., 2010). However, measurement error related to the objective measurement tool should also be considered. Although, accelerometers are believed to record PA with high accuracy, cut-points for

sedentary, moderate and vigorous intensity PA have generally been calibrated with younger people aged <60 years old and may not reflect actual intensity of PA in older adults (Freedson et al., 1998, Swartz et al., 2000a, Leenders et al., 2006, Berntsen et al., 2010, Hendelman et al., 2000). Older people tend to move more slowly, either because of physical limitations, or lower levels of fitness than younger adults (Cerin et al., 2012, Ozemek et al., 2013). The most commonly used accelerometer cut-points for PA at different intensities are Freedson's cut-points for which moderate intensity is measured at 1952-5724 counts·min^{-1} (cpm)and vigorous intensity at ≥5725 (cpm) but these were determined on a treadmill by assessing accelerometer counts at different walking or running speeds (Hall et al., 2013, Copeland and Esliger, 2009, Freedson et al., 1998, Kozey et al., 2010). Therefore, there is a lack of evidence for the validity of Freedson's cut-points in relation to free-living physical activities in elderly populations. Some calibration studies in people ≥65years of age have been conducted (Swartz et al., 2000, Miller et al., 2010, Hall et al., 2013, Copeland and Elsinger, 2009) but there is currently no consensus on the optimal cut-points to be used with the elderly populations.

Apart from the lack of studies in older populations, previous IPAQ validation studies have only reported total moderate to vigorous intensity PA (MVPA) rather than MVPA from 10-min bouts (Hagstromer et al., 2006, Tomioka et al., 2011). This is a limitation because the IPAQ was designed to assess PA that lasted at least 10 minutes and it is important to assess outcomes from the IPAQ to a comparable outcome from the accelerometer. Hence, the aim of the present study was to assess criterion validity of the interview- administered IPAQ-L against different measurement criteria of the accelerometer in people aged >65 years at elevated risk of CRC or currently recovering from treatment after CRC. A second aim was to investigate the criterion validity of the interview-delivered IPAQ-L against lower accelerometer cut-points, than the commonly used Freedson cut-points.

8.3. Methods

Participants

The validation study used baseline data from two different PA intervention studies. Participants were aged 60-88 years and diagnosed with either bowel polyps or were recovering from bowel cancer. None of the participants were physically restricted in carrying out moderate-intensity PA.

Data collection

Participants attended the University of East Anglia and were fitted with an accelerometer and instructed to wear it during waking hours until their next appointment which was scheduled at least 7 days later. At this second appointment accelerometer data was downloaded onto a computer and the IPAQ was completed in an interview setting to capture the PA levels of the last seven days (corresponding with accelerometer wear-time).

Data scoring

The IPAQ was scored according to its original guidelines (http://www.ipaq.ki.se). PA was reported in minutes per week for each domain and intensity and was divided into several categories: i) total PA minutes per week which is the sum of all, moderate, and walking PA, (total IPAQ) ii) total moderate PA which included all moderate PA except walking (Mod IPAQ), iii) total leisure time PA (Leisure IPAQ), and the sum of occupational and household activities (OH IPAQ). Vigorous intensity activity was not included in the analysis because only five participants engaged in this type of activity.

IPAQ-L interview

Before reading out the questions to the participants the interviewer counted back 7 days to make sure the participant was clear about the 7 days that were covered by the questionnaire. Then the interviewer introduced the concept of the IPAQ, by explaining the five different domains of PA, and that each domain will be answered separately. At this point participants were instructed not to report activities such as walking in more than one domain. *Duration* and *intensity* that individual questions referred to were also explained to the participants. The interviewer specified that the duration of each activity recorded in the questionnaire had to be at least 10 min and the interviewer gave an example to clarify this concept. Intensity was explained with the 15-item BORG scale (range 6-20) (Borg, 1982) that the researcher showed to the participant at each question. The participant was instructed how to interpret the BORG scale with a rating of 12-13 considered to represent moderate intensity activity and >14 vigorous intensity activity. Once the interviewer was satisfied that the participant understood the concept of the IPAQ the questions were read out. When the participant reported

moderate or vigorous intensity activity the interviewer probed the participant to specify the type of activity that was performed and whether the activity was performed for at least 10 min. If the interviewer felt that the activity reported was not at that claimed intensity the interviewer either changed the intensity or excluded it from the questionnaire. For example, if someone reported vacuuming to be vigorous the interviewer presented the Borg scale to the participant. If the participant rated PA intensity at less than 14 on the Borg scale, the activity was recorded in the moderate intensity category or not recorded if a value of <12 on the Borg scale was reported. If the reported time spent at an activity exceeded several hours, the interviewer tried to clarify with the participant how much time was spent at the activity and how much time was resting time. This process was undertaken for all domains of PA.

Accelerometry

Participants were fitted with a GT3X accelerometer (Actigraph, Pensacola, FL, USA) on the right hip. The device is a tri-axial accelerometer measuring accelerations on a vertical, antero-posterior, and medio-lateral plane. Acceleration data are collected over a set time interval, called epochs, and the total amount of accelerations is recorded as *counts*. The epoch period was set at 1 min as recommended by previous calibration studies (Freedson et al., 1998, Hendelman et al., 2000, Miller et al., 2010). Each participant wore the accelerometer for at least 5 days in the seven-day period. On return of the device, data were downloaded onto a computer and examined for valid wear-time. Accelerometer records were included if wear-time was at least 10 h per day on a minimum of 5 days per week including a weekend day (Choi et al., 2011). Time spent at moderate and vigorous intensity PA was recorded every epoch of recorded time, and as 10 min-bouts of PA at 1952-5724 cpm (moderate) and ≥5725 cpm (vigorous) (Freedson et al., 1998). PA in 10 min-bouts was also presented as Matthews bouts (moderate intensity: 760-5724 cpm) (Matthews, 2005) (Table 18.) Furthermore, step counts per week and average vector magnitude in cpm per week are also recorded and used in correlation analysis. As there was a lack of vigorous intensity PA recorded only moderate intensity PA was reported in the study. Moderate intensity measures that were included in the analysis were total accumulated moderate intensity PA from the accelerometer at ≥ 1952cpm (total ACC) (Freedson et al., 1998), total moderate PA in 10-min Freedson's bouts (Freed PA) (Freedson et al., 1998), and

total moderate PA in 10-min-Matthews bouts at ≥760 cpm (Matt PA) (Matthews, 2005). These abbreviations will be used throughout the following text to describe the different activity domains criteria of each method.

Table 18 Counts per minute (cpm) and corresponding PA intensity (METs) used to compare with measures of self-reported PA from IPAQ

METs	Freedson (1998) cpm	Matthews (2005) cpm
3-6 (moderate intensity)	1952-5724	760-5724
≥6 (vigorous intensity)	≥5725	≥5725

Data analysis

Data was analysed with the Statistical Package for the Social Sciences (SPSS) for Windows, version 22. The Shapiro-Wilk test of normality revealed non-normal distribution for outcomes of PA. Due to the nature of the data which contains 'zero-values' for e.g. non-participation in walking activities, log-transformation was not suitable. Therefore, non-parametric tests were performed. Differences in PA behaviour between males and females were tested with the Mann-Whitney-U test and correlation statistics was performed with the Spearman rank correlation. Judgements of the strengths of the correlation coefficient (ρ) were made according to Hopkins (Hopkins, 2002). Thus, the following criteria for ρ were applied: 0-1 trivial, 0.1-0.3 small, 0.3 to 0.5 moderate, 0.5-0.7 large, 0.7-0.9 very large, and 0.9-1 nearly perfect. To assess the limit of agreement between the two methods, Bland-Altman plots were plotted with the raw data. However, this revealed a high amount of heteroscedasticity. Therefore, the % difference between the two methods was also plotted with the Bland-Altman method. Values closer to zero suggest greater limits of agreement, whereas, the more dispersed the values are, the greater the differences between IPAQ and accelerometer.

8.4. Results

Data were available from 52 participants of which 38% (n=20) and 62% (n=32) were females and males, respectively. Participants were on average 67.9 (range 60-80) years old and had a BMI of 28.7 $kg \cdot m^{-2}$ (SD±4.7) (Table 19). Women were on

average 4 years younger than men (P<0.014). There were no other significant differences between genders (Table 19).

Table 20 shows the correlations between the different accelerometer cut-points and domains of the IPAQ of the overall sample. The correlation with walking PA was the strongest, followed by leisure-time PA, and total PA of self-reported PA. No significant correlations were observed between the IPAQ measures of moderate intensity PA and household/occupational PA and the accelerometer criteria. However, the correlations were larger with Matthews bouts than with Freedson bouts and total ACC. Sedentary time was significantly correlated between the two methods (Table 19). Correlations between vector magnitude and IPAQ measures were moderate and significant for walking and leisure-time PA, but not for total IPAQ, moderate IPAQ time, and occupational/household PA. Gender differences were observed for the correlations between IPAQ domains and the accelerometer measures (Table 21). In men, the correlations between total IPAQ and all accelerometer criteria were small (total ACC, and Matt PA) to moderate (Freed PA) and non- significant. These were significant in women showing large correlations between total IPAQ and accelerometer cut-points of Freed PA, and Matt PA, and a very large correlation with total ACC. Similarly, there were only trivial correlations between IPAQ domains of moderate PA and household PA and accelerometer measures of total ACC and Matt PA in men, but large significant correlations in women. The correlations with Freed PA and these IPAQ domains (mod PA, and OH PA) were non- significant in both, men and women. In men, the walking domain of the IPAQ was moderately significant correlated with two accelerometer measures (Total ACC, and Freed PA). This correlation was very large and significant in women. The correlation of walk IPAQ with Matt PA was small and not significant in men, but large and significant in women. The correlations between leisure IPAQ and the accelerometer measures were also stronger in women than in men, showing moderate significant correlations for men, and large (between leisure IPAQ and Freed PA and Matt PA) to very large correlations (between leisure IPAQ and total ACC) in women.

The agreement between the two methods is shown in Bland-Altman plots in Figure 12. Large heteroscedasticitiy was observed for the difference between the two methods. The plots showing the % difference between methods show largest bias

between the total IPAQ and time spent in Freedson bouts (154%), followed by the % difference between the total IPAQ and recordings (92%). The % difference between the total IPAQ and Matthews bouts produced the lowest bias (78%). However, the IPAQ overestimated PA compared to all three methods of accelerometry, where overestimation was largest compared with the Freedson bouts, followed by total accelerometer recordings and Matthew bouts.

Table 19 Descriptive statistics of study participants.

Variable	All (n=52) Mean ± SD	Men (n=32) Mean ± SD	Women (n=20) Mean ± SD
Age (yr)	67.9±6.6	69.8 ±4.4	64.8±8..4
BMI ($kg \cdot m^{-2}$)	28.7±4.7	29.0±4.3	28.1±5.4
Self-assessment			
IPAQ ($min \cdot wk^{-1}$)			
Total IPAQ	441±301	431±297	456±316
Mod IPAQ	264±212	250±224	288±193
Walk IPAQ	176±199	182±211	168±182
leisure IPAQ	120±152	134±168	96±121
OH IPAQ	239±231	230±240	254±219
Sedentary	3025±1392	3193±1514	2742±1139
Accelerometry			
Mean counts$\cdot min^{-1}$	190±95	191±101	189±89
Total ACC ($min \cdot wk^{-1}$)	120±110	100±99	153±122
Freed PA($min \cdot wk^{-1}$)	53±81	46±85	64±76
Matt PA ($min \cdot wk^{-1}$)	168±169	143±147	209±197
Steps$\cdot wk^{-1}$	39939±12700	43711±5659	3872±14432
Sedentary ($min \cdot wk^{-1}$)	3919±1380	4051±805	3708±757

Table 20 Spearman correlation coefficients (r) between IPAQ (long-version) and accelerometer-based Measures in overall sample. [a]P≤0.05, [b]P≤0.01, [c]P≤0.001, PA= PA, ACC= accelerometer, Total PA includes moderate and walking PA, OH= occupational and household activity

Acc / IPAQ	Total ACC	Freed PA	Matt PA	Steps count	Sedentary time	Counts per minute
	All	All	All	All	All	All
Total IPAQ	.39[b]	.43[b]	.38[b]	.46[a]		.27
Mod IPAQ	.16	.16	.23	.23		.14
Walk IPAQ	.54[c]	.57[c]	.41[b]	.49[a]		.34[a]
leisure IPAQ	.45[b]	.44[b]	.44[b]	.47[a]		.32[a]
OH IPAQ	-.08	.19	.25	.31		.12
Sedentary					.33[a]	

Table 21 Spearman correlation coefficients between IPAQ-L and accelerometer-based measures by gender with 95% Confidence intervals

	Total ACC (min·wk^{-1})		Freed PA (min·wk^{-1})		Matt PA (min·wk^{-1})		Sedentary time		Counts per minute	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
IPAQ										
Total IPAQ	.24	.71[b]	.32	.58[b]	.19	.62[b]	-.20	-.17	.24	.20
95% CI	(-.13 to .55)	(.36 to .88)	(-.06 to .60)	(.17 to .82)	(-.20 to .50)	(.27 to .85)	(-.54 to .16)	(-.66 to .37)	(-.11 to .61)	(-.24 to .70)
Mod IPAQ	.02	.50[a]	.10	.33	.08	.58[a]	-.25	-.15	.19	.30
95% CI	(-.34 to .38)	(.03 to .78)	(-.27 to .44)	(-.16 to .70)	(-.29 to .42)	(.15 to .82)	(-.58 to .16)	(-.58 to .42)	(-.23 to .47)	(-.34 to .62)
Walk IPAQ	.42[a]	.84[c]	.40[a]	.81[b]	.29	.60[b]	.05	-.21	.30	.12
95% CI	(.08 to .68)	(.61 to .94)	(.05 to .66)	(.56 to .93)	(-.08 to .58)	(.19 to .83)	(-.32 to .42)	(-.66 to .33)	(-.07 to .66)	(-.18 to .77)
leisure IPAQ	.41[a]	.73[b]	.37[a]	.57[a]	.36[a]	.65[b]	.16	-.18	.26	.37
95% CI	(.06 to .67)	(.73 to .89)	(.01 to .64)	(.15 to .82)	(.01 to .64)	(.27 to .86)	(-.24 to .51)	(-.61 to .29)	(-.02 to .69)	(-.06 to o.76)
OH IPAQ	.02	.46[a]	.17	.26	.01	.60[b]	-.37[a]	-.14	.16	.09
95% CI	(-.34 to .38)	(-.01 to .76)	(-.20 to .50)	(-.24 to .65)	(-.35 to .37)	(.18 to .83)	(-.66 to .03)	(-.62 to .43)	(-.12 to .46)	(-.39 to .51)
Sedentary							.40[a]	.11		
95% CI							(.03 to .58)	(-.47 to .53)		

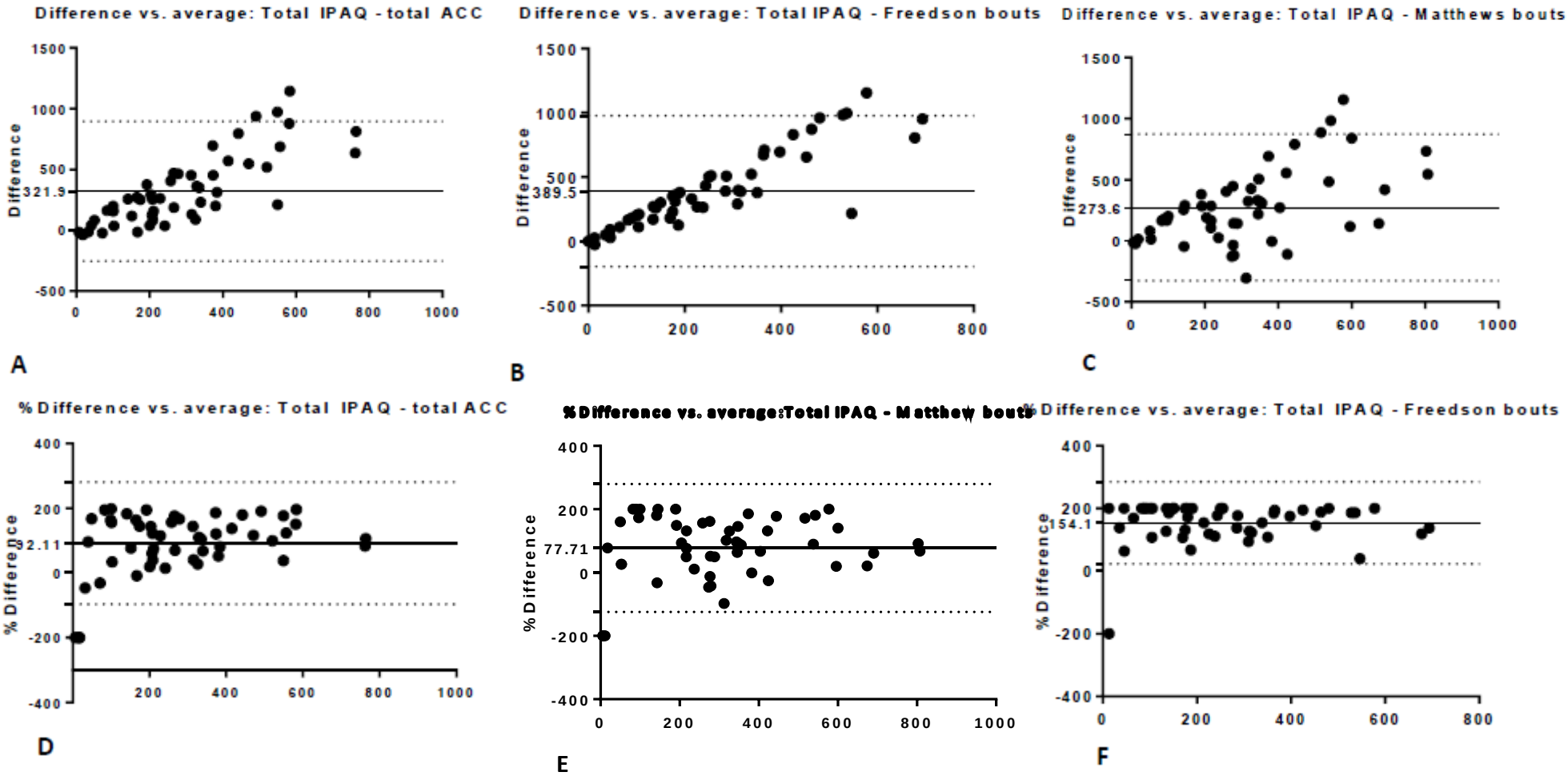


Figure 12 A, B, and C show Bland-Altman plots for the difference between A) total IPAQ and total accelerometer time, B) total IPAQ and time spent in Freedson bouts and C) Total IPAQ and time spent in Matthews bouts. D, E, and F show the Bland-Altman plots for % difference between D) total IPAQ and total accelerometer time, E) total IPAQ and time spent in Freedson bouts and F) Total IPAQ and time spent in Freedson bouts

8.5. Discussion

This is the first European study to validate the IPAQ-L against accelerometry with an elderly population (≥60 years) at elevated risk for CRC and people recovering from CRC. Previous validation studies mostly included younger healthy adults aged 19-64 years (Hagstromer et al., 2006, Craig et al., 2003). Only two studies could be identified that validated the IPAQ-L in an elderly population (Deng et al., 2008, Cerin et al., 2012). However, one of the studies included a considerable amount of people aged less than 60 years old and pedometers were used as the objective measure (Deng et al., 2008). The other study recruited older healthy people aged ≥65 years from Hong Kong (Cerin et al., 2012). Walking was the main activity performed by the participants, whereas common PAs of older Europeans, such as yard and garden work were under-represented. Despite suggestions that Freedson's cut-points (1952-5724 cpm) (Freedson et al., 1998) underestimate moderate intensity PA, especially PA other than walking (Rothney et al., 2008, Hendelman et al., 2000, Berntsen et al., 2010) previous studies did not use lower cut-points for the validation of the IPAQ in the elderly. Validation studies commonly used Freedson cut-points to discriminate between light, moderate, and vigorous PA (Cerin et al., 2012, Kolbe-Alexander et al.2006, Deng et al., 2008, Craig et al., 2003, Tomioka et al., 2011, Hagstromer et al., 2006). In addition, most studies only included total PA from the IPAQ in the analysis and did not consider the different PA domains that the IPAQ measures. A detailed analysis of the relationships between individual PA domains of the IPAQ-L and accelerometer can provide a more comprehensive assessment of the criterion validity of this questionnaire. Another question this study set out to answer was whether an interview-administered IPAQ, with additional verbal explanations of PA intensity, type of activities and emphasis on the criterion to only include 10-min-continuous bouts of PA, shows stronger correlations with objective accelerometer data than self-administration of the IPAQ. Furthermore, the validity of the IPAQ-L against alternative cut-points to those recommended by Freedson were also investigated. Accelerometer data were also considered as 10 min-bouts and it was hypothesised that correlations of 10 min-bout PA time with PA variables from the IPAQ would be better correlated than the total minutes of PA recorded by accelerometry with IPAQ measures.

In comparison to other IPAQ validation studies, the present study demonstrated larger correlation coefficients for walking PA and sedentary time. Results for total

PA and time spent at moderate intensity PA were similar to previous findings. Specifically, correlations between self- reported walking and accelerometer variables in the present study ranged from moderate to large (ρ= 0.41 to 0.57) compared to small to moderate correlation coefficients (ρ=0.11 to 0.36) from previous validation studies (Cerin et al., 2012, Hagstromer et al., 2010). Similarly, correlations for sedentary behaviour in previous validation studies were moderate in the present study (ρ =0.33) and small in previous studies ranging from ρ=0.16 in a Chinese sample (> 65 years) (Cerin et al., 2012) to ρ =0.23 in a Swedish sample (>65 years) (Hurtig-Wennlof et al., 2010). However, the Swedish study used the short version of the IPAQ. The correlations between self-reported total PA and accelerometry in the present study are comparable to original validation studies of the IPAQ (Macfarlane et al., 2011, Craig et al., 2008) but are stronger compared to an elderly Chinese sample (Cerin et al., 2012). Finally, correlations for self-reported moderate intensity PA were small to moderate in previous studies (Hagstromer et al., 2010) (Cerin et al., 2012) which is also similar to the findings of this study.

Reasons for lower correlations with walking PA in the study by Cerin (2012) could be due to age differences. A large proportion of the Chinese study sample was aged ≥75 years, whereas the majority of participants in the current study were aged between 60 and 70 years (Cerin et al., 2012). Walking pace may have been less dynamic in the Chinese sample because of a decline in fitness with age. However, correlations in a Swedish sample of peopled aged ≥65 years that were described as fit and active (Hurtig-Wennlöf et al., 2010), the correlations with walking were also lower compared to the present findings. Considering the similar characteristics of the Swedish study sample with the participants of the present study, similar correlations would be expected with walking time. Interestingly, correlations between walking time and accelerometry in younger adults (Macfarlane et al., 2011) were also lower (ρ=.25) compared to the present study. This difference is unlikely to be due to the younger adults not meeting the cut-point threshold for moderate activity, unless they walked very slowly. In light of these findings it can be suggested that an interview-administered IPAQ is more accurate in reporting walking PA than a self-administered IPAQ. Emphasizing the intensity of walking, and probing the participant for actual walking time to exclude periods of rest may have contributed to a more accurate reporting of walking PA. In turn,

probing participant's responses to the PA questions in the IPAQ may have also contributed to a better understanding of the sedentary questions. No other validation study has previously reported moderate significant correlations between the two measures for sedentary time.

In regards to the different accelerometer criteria, the use of Matthews cut-points and accumulated PA in 10-min bouts did not yield different correlations than the measure of continuous activity counts as previously reported in validation studies. All three accelerometer criteria were significantly correlated with total IPAQ, walking time, leisure time PA and sedentary behaviour, but not with moderate intensity PA and occupational/household PA. This is in agreement with findings that accelerometry is more accurate at measuring walking activities but not at measuring activities that involve upper-body movements, such as gardening, and household activities which are recorded with the moderate PA and occupational/household domain of the IPAQ. (Hendelman et al., 2000). Furthermore, accelerometers are in general unable to distinguish between walking conditions such as uphill walking or carrying heavy loads, and have been shown to underestimate activities such as cycling, and resistance exercises (Hansen et al., 2013, Swartz et al., 2000a). In order to overcome this problem lower cut-points than the commonly used Freedson cut-points have been recommended to capture a greater variety of PA other than walking (Matthews, 2005, Swartz et al., 2000b). In this study, correlations of IPAQ measures with lower cut-points (Matthews bouts) were not overly different from the correlations with Freedson bouts. However, slightly stronger correlations, although not significant, were noted for self-reported moderate intensity PA and occupational/household PA with Matthews bouts. One other validation study with an elderly population included Freedson cut-points (1952-5724 cpm) and a lower set of cut-points (100-1951 cpm) (Cerin et al., 2012). The correlations with PA recorded with the self-administered IPAQ were stronger for the lower cut-points than with Freedson cut-points. This further supports the notion that lower cut-points could be more meaningful to report PA of the elderly. However, the study population was older than the current study sample which could have contributed to these findings.

These stronger correlations of self-reported moderate intensity PA and occupational/household PA with Matthews bouts compared to Freedsons bouts

became more apparent when comparing the genders. Correlations for moderate intensity PA and occupational/household PA was stronger in women than in men. Women reported in general more minutes of these types of activities which could explain the findings. Other gender differences were also observed. Overall, all correlations for each accelerometer criteria were stronger in women than in men, despite the smaller sample size of women in the study. This could indicate that women might be more accurate at reporting PA than men. This finding is contrary to a systematic review of self-reported PA in adults (Prince et al., 2008a). Comparing outcomes of self-reported PA to accelerometer recordings, women were found to over-report PA to a larger degree than men. It is possible that the gender of the interviewer administering the IPAQ-L could have affected the responses to the self-reported PA questionnaire. The IPAQ interviewer was female and may have had a different effect on responses in females compared to males. It has been shown that men are influenced by a female observer when asked to rate their perceived exhaustion (RPE) during cycling exercises (Winchester et al., 2012). Men reported a higher RPE in the presence of a female observer than in the presence of a male observer. Although, this is a different context, the gender of the IPAQ interviewer is likely to have had an effect on their responses. However, the results from the current study need to be interpreted with caution due to a small sample size of males and females and further research is needed to explore the gender differences in measuring self-reported PA with an interview-administered IPAQ.

Bland-Altman plots showed that overall the IPAQ over-estimates PA in relation to accelerometry and that accelerometry under-estimates PA. This is in agreement with previous findings. A systematic review found that self-reported PA estimates are higher than estimates from objective measures (Prince et al., 2008b).

Limitations of accelerometers should also be considered in the interpretation of the data. The devices have been calibrated with younger adults (Freedson et al, 1998), and against treadmill walking, therefore limiting the interpretation of data captured from non-walking activities. Participants in this study were encouraged to do a variety of activities, such as swimming, resistance exercises, bicycling. These may not be captured accurately by the accelerometers (Strath et al, 2012). It is also important to consider individual differences in exercise capacity and the resulting

differences in absolute and relative intensity for selected activities (Strath et al, 2012). Where absolute intensity may have similar mechanical efficiency (for example when walking at 3mph), but as for relative intensity, this could be perceived as light intensity for an individual with high exercise capacity but as moderate or even vigorous intensity for someone with low exercise capacity. Older adults are likely to perceive PA as more moderate to vigorous than younger people (O'Donovan et al., 2010) and therefore, the accelerometers may not capture movement accurately in this population.

This study is novel in several ways and addressed some of the limitations of previous IPAQ validation studies. It is the first validation study with an elderly population at elevated risk of, or recovering from CRC and it administered the questionnaire in an interview form. Over- reporting of the IPAQ has previously been noted to be an issue and interview delivery of the questionnaire was suggested (Rzewnicki et al., 2003, Rütten et al., 2003). Strength of the study is that PA from the IPAQ, which is recorded only if it lasted a minimum of 10 min, was compared to 10 min-bouts of PA recorded with the accelerometers. Different cut-points for moderate intensity PA were also included in the analysis because the commonly used cut-points were developed with younger people and calibrated against treadmill walking activities only. Interviews were carried out by the same interviewer with every participant, eliminating inter-rater bias.

Delivering the IPAQ in an interview-form could be a limitation. Social desirability could have contributed to over-reporting of PA (Janz, 2006). The sample size was small and despite findings of gender differences further validation studies with a larger sample size including both males and females are needed to confirm the findings of this study. Another limitation is that the accelerometers do not accurately measure varying intensities of PA (walking at an incline or carrying heavy loads), and PA other than walking (cycling, swimming, upper-body activities) (Hansen et al., 2013, Welk, 2002, Kozey et al., 2010).

In conclusion, findings of the study show that an interview-administered IPAQ-L has acceptable validity for the assessment of total PA and different domains of PA in elderly people. The results suggest that an interview-administered IPAQ may be more accurately recording walking PA and sedentary time in the elderly at elevated risk for CRC. Although, correlations of IPAQ measures with Matthews

cut-points were not superior to Freedsons cut-points, the findings suggest that lower cut-points may be a more appropriate measure for non-walking activities. The results also indicated some gender differences in the responses to the interview-administered IPAQ- L and suggest that the gender of the interviewer could affect responses of self-reported PA. However, further research with a larger sample size of elderly people at risk of or recovering from CRC is needed.

Chapter 9

Discussion

"There is nothing wrong with change, if it is in the right direction."

-

- Winston Churchill

9.1. Overview

Each finding chapter already includes a comprehensive discussion of the findings and thus, these will not be repeated here. This final discussion chapter serves to bring the studies of this thesis together and discuss the findings in light of the two different study populations and the differing durations of the autonomy-supportive interventions described in this thesis. First, I will provide a summary of the findings of PARC and MOVE, and afterwards offer a brief discussion of the feasibility of a PA intervention with CRC survivors and patients diagnosed with colonic polyps. Both interventions will be discussed alongside each other because the conclusions drawn in regards to feasibility were similar for both studies. Differences between the populations will be highlighted. I will then go on and discuss the outcomes of the interventions in relation to the duration of the interventions and the contribution of this to the design of behaviour change interventions in these populations.

9.2. Summary of the main findings

PARC study

Recruitment to the trial was identified as a main barrier, which resulted in a small sample size and limited statistical explorations. In summary, an overall recruitment rate of 4.2 % was achieved. Recruitment via specialist nurses and letters was more successful than recruitment at clinics (8 % vs 4 % recruitment yield). Time commitment and travel distance were identified as the main barriers to participation. Retention rate was acceptable with 71% which is comparable to other studies. Adherence to the workshops and supervised exercise sessions was also acceptable with 65%. The main reasons for non-attendance were illness, work commitments, family commitments, and holidays. There were no adverse events of the intervention.

Besides feasibility outcomes the question of whether an autonomy supportive intervention would shift more extrinsic regulations to more autonomous regulations was investigated. The intervention condition had higher levels of intrinsic regulation post-intervention compared to SC ($p< 0.01$), but this was not maintained at follow-up ($p=0.08$). Both groups increased in introjected and extrinsic regulation but the control condition increased to a greater extend. Amotivation was different between the groups at post-intervention, with a reduction in amotivation

in the intervention condition and an increase in the control condition. These changes were not different at follow-up.

In regard to PA behaviour, the portion of participants meeting the current PA guidelines of at least 150min of moderate intensity or 75 min vigorous intensity PA per week, was generally higher in the intervention condition than in the control condition. Data from cardiopulmonary fitness support these findings, with the intervention condition having higher levels of fitness at post-intervention. At follow-up there was no difference in fitness between the groups, but the control condition declined below baseline value in fitness over the study period whereas the intervention condition did maintain baseline fitness.

No group differences were observed for body composition and QoL at any time-point.

MOVE study

Of 239 invitation letters sent to potentially eligible participants, 65 (27%) responses were received. Of those, 58% were randomised to the study arms, which yielded an overall recruitment rate of 12%. The main reasons for declining participation were time commitment and travel distance. Postcode analysis did not show that non-participators lived significantly further away from the study site than participators. At follow-up 71% of randomised participants were retained. Participants in the intervention condition attended 79% and 70% of the offered supervised exercise and workshop sessions, respectively.

There were no differences in motivational regulation between the groups at any time-point. However, there was a tendency for higher intrinsic regulation post-intervention in the intervention group compared to the control group, with a difference in change of +0.7 points between the groups (effect size of 0.72). There was no difference in change at follow-up. Although, not significant, at post-intervention the intervention condition increased the RAI by 3.5 points more than the control condition (effect size= 0.67). At follow-up the difference in change was only 1.86, also in favour of the intervention. None of the measures for need satisfaction were different between the groups at any time-point, but there was a tendency for higher relatedness and competence post-intervention and at follow-up in favour of the intervention group.

Intention to exercise was higher in ALP at post-intervention, but not at follow-up. No differences were found for self-efficacy at any time-point. No group differences were observed for QoL at any time-point.

Changes in self-reported PA were larger post-intervention and at follow-up in the intervention condition compared to the control condition. Post-intervention there was a group difference for walking only with a mean change of +203 min vs -120 min (p= 0.05), for ALP and SC respectively. At follow-up changes in walking PA (+0.0 min vs -164 min, p= 0.03) and total MVPA (+241 min vs -115 min, p= 0.01) were different between the groups. Measures of accelerometry were not different, but there was a tendency for ALP to do more PA in 10-min bouts post-intervention and at follow-up (mean group difference 29 min, and 65 min). In regards to the adherence to the current PA guidelines for health (minimum of 150min of moderate or 75 min of vigorous intensity PA per week, in bouts of at least 10 min), there were no differences between the groups at any time point.

There were differences in changes in body composition between the groups at post-intervention, but changes were not at follow-up. In summary, the mean difference in change between the groups post-intervention was 2.7kg for body mass, 1.7% for body fat, and 0.54 kg/m^2 for BMI. At follow-up the differences in change were 1.2kg for body mass, 1.0% for body fat, and 2.9 kg/m^2 for BMI in favour of the intervention condition. No significant changes were observed for lower and upper body strength, and functional capacity.

9.3. Feasibility of recruitment into MOVE and PARC

The reasons why potential participants declined participation or were excluded were already discussed in detail in chapter 7, but I would like to offer some suggestions that would apply to both populations studied in this thesis for future research to address these barriers. Half the participants that were not randomised were ineligible, but also a large proportion of patients (46%) declined for reasons such as time commitment, travel distance to the research site, and not being interested. For obvious reasons we cannot coerce uninterested patients into taking part in research studies, but certain conditions could be altered to make research participation more attractive. In these particular studies of the thesis, research sites closer to participant's homes could have led to greater participation. Multi-centred studies could also help to address this barrier. Time commitment is more difficult

to address. It has been reported that supervised exercise sessions might be more effective for long-term adherence than home-based interventions (Bauman et al., 2002, Antikainen and Ellis, 2011).

Patients with colorectal polyps vs patients diagnosed with colorectal cancer

Compared to other lifestyle intervention studies in the CRC screening setting, the recruitment rate in the PARC study was very poor. We identified recruitment via health professionals (contact with specialist nurses or letters from Consultant Gastroenterologist) as being more successful than recruitment via clinics, where researchers introduced the study to the patients. Participants for the MOVE study were only recruited via letters from health professionals and the overall recruitment rate was better than for the PARC trial (12% vs 4%). Comparing recruitment rates of clinician letters only, MOVE recruitment was still better than for PARC. Not only was the overall yield higher in MOVE (12% vs 8.5%) but also the response rate to letters was higher for the MOVE study (27% to 17%). This could suggest that people recovering from CRC might be more motivated to partake in a lifestyle intervention than people diagnosed with colonic polyps. This phenomenon, that people feel motivated to change health behaviours after a significant health event, including cancer, has been described as the *teachable moment* (McBride et al., 2003). In the health care setting, the term is described as the opportunity to promote health behaviour change after a particular health event. McBride (2003) proposed a model to describe the teachable moment. This is largely based on the Health Belief Model and defines the teachable moment as a 'cue to action'-event. As such, a teachable moment can present itself as a threat of a negative outcome and lead to motivation to alter health behaviour. Thus, the higher recruitment success with people recovering from cancer compared to people with polyps could be attributed to the teachable moment phenomenon. However, a polyp is the precursor of CRC, and thus, should also evoke a teachable moment in patients at increased risk. Two reasons could explain why at-risk patients might be less likely to participate in a health behaviour intervention. First, being diagnosed with a polyp and its subsequent removal during colonoscopy could act as a 'health certificate' (van der Aalst et al., 2010). No action or further treatment is required, giving the patient no reason to worry, and encourages to

continue the current health behaviours. Studies that compared health behaviours after colonoscopy between patients diagnosed with colonic polyps to patients that did not have a polyp diagnosis consistently found a reduction of PA levels after colonoscopy or no change in the patients with polyps. In comparison, patients without polyp diagnosis were more likely to make small improvements (Hubbard et al., 2014). Second, it is likely that patients with polyps are not aware of the risk of polyps in the development of CRC. For a teachable moment to motivate behaviour change, the individual has to perceive the event as a personal threat. A recent qualitative study confirmed that there may be a lack of knowledge about the connection between polyps and cancer risk (Stead et al., 2012). In this study, patients were interviewed after a colonoscopy and questioned about their understanding of the significance of polyps (Stead et al., 2012). Patients generally perceived a polyp as a minor abnormality and several patients did not appear to know that a polyp could be pre-cancerous. Patients further were unaware of the causes of adenomas, and thus, thought that information about lifestyle changes that was provided to them, made little sense. Being reassured by the clinician letter, that polyps were removed and that the risk of cancer was unlikely, made the need for healthy lifestyle behaviour change questionable and encouraged continuation of the current lifestyle behaviours. Whether cancer survivors are more knowledgeable about the benefits of healthy lifestyles for survival after a cancer diagnosis is unknown, but it is likely that the diagnosis presents a threat to the personal health which encourages behaviour change.

Cancer survivors have been shown to be more likely than the general public to eat healthy diets and have quit smoking, but were not more likely to engage in PA (Wang et al., 2014). Another study showed that cancer survivors made changes to dietary, smoking and PA behaviour (Humpel et al., 2007). However, the number of cancer survivors making positive changes to PA behaviour was much smaller than the proportion of people making positive dietary changes (31.3% vs 81.1%). These findings suggest, that cancer survivors are more likely to make health behaviour changes after a cancer diagnosis, than patients after a polyp diagnosis, but the change of PA behaviour is limited. This may have resulted in the low recruitment rate for the PARC study compared to the MOVE study. If a lack of understanding between the causes of polyps and the significance of polyps prevent an interest of an at-risk population to engage in healthier behaviours, then information in study

participant information sheets should highlight the benefits of the lifestyle behaviour change intervention and its significance on their current health condition. This could however lead to a reluctance of participants to wanting to be randomised to the standard care group. But it might make participation more attractive to patients and patients in the standard care group could be offered the intervention after the completion of the study. In both studies described in this thesis, participants of the standard care group were offered to take part in the intervention after they completed their last assessment. However, only one person took up on this offer (from the MOVE study, none in the PARC study). A patient preference design where patients are allocated to the study arm they prefer, has made little to no difference to the number of patients recruited into trials (Treweek et al., 2013a).

9.4. Considerations of the Intervention

Perhaps, supervised exercise sessions could take place less frequent at the beginning of the intervention, and be complemented with home-based exercise at this stage. This could be a more acceptable way of 'easing' participants into supervised exercise sessions and make the intervention more attractive to people who are new to exercise, but would also have cost implications. So far, most supervised exercise interventions start with a higher frequency of supervised exercise at the beginning of the intervention, and taper off the sessions towards the maintenance phase. Nobody (to my knowledge) has started with a low-frequency intervention which increases frequency throughout the intervention period. When choosing tools for behaviour change interventions, goal setting is frequently used and was identified as a successful tool for behaviour change (Buchan et al., 2012). It is well recognized that effective goals for behaviour change are goals that are relevant to the individual, realistic and matching the individual's skills but yet be challenging. Thus, at the start of a behaviour change intervention, one might start with a small but attainable goal of walking for 10 min three times per week. This goal could then be adjusted to 20 min three times per week further into the intervention when the participant is more competent at the task. The progressive design could also be applied to the design of supervised exercise interventions, by starting the intervention with a low intensity, and progressing to a higher amount of commitment. For example, the intervention could start as a home-based intervention to start getting the participant engaged in the behaviour,

and provide knowledge about the behaviour and its importance, and then increase the intensity and include supervised exercise session. However, a drawback of this approach could be a lack of social support (relatedness) during the home-based period of the intervention. Relatedness has been linked to long-term maintenance of PA and thus, is an important intervention ingredient (Springer et al., 2013). Relatedness was also identified as the need (besides autonomy and competence) that was most highly correlated with perceived autonomy support (Edmunds et al., 2006). Despite the controversy of this finding (autonomy would be expected to be highly correlated with perceived autonomy support), it highlights the importance of relatedness as a nutrient in the satisfaction of all three psychological needs, and thus, enhance intrinsic motivation. Thus, if the here suggested design to start with a home-based educational intervention and transition to a supervised intervention, the design has to carefully be considered in order to not jeopardise support for any of the three psychological needs. Virtual peer groups that offer support via mobile apps or website domains could be one tool for such a design.

Duration of the intervention and its potential effects on motivational regulation

Although, there is good evidence that PA interventions are successful at increasing PA at least in the short-term, the evidence of such interventions to produce long-term and sustainable PA behaviour changes is inconsistent (Fjeldsoe et al., 2011). This is partly because of a lack of interventions with a follow-up period to assess maintenance (Fjeldsoe et al., 2011), but also because the components of an intervention that are needed to produce a maintenance effect are not established (Bauman et al., 2002). Besides an evaluation of the behaviour change techniques used (e.g. goal setting, self-monitoring) the design in terms of frequency and duration of intervention components has also been investigated as a predictor of behaviour change outcomes. Longer duration of the intervention, and a higher number of participant contacts have been identified as predictors of short-term and long-term success of behaviour change interventions (Fjeldsoe et al., 2011, Greaves et al., 2011). In particular, interventions producing a maintenance effect (significant group differences at the end of the intervention and at follow-up in at least one outcome measure) had a mean duration of 21 weeks and a mean of 13 intervention contacts, whereas trials that did not achieve maintenance of the target behaviour

were shorter than 21 weeks and had a mean of 7 intervention contacts (Fjeldsoe et al., 2011). However, the authors also compared the ratios of intervention contact (contacts over duration) and showed no difference in the proportion of intervention contacts between trials with higher ratios of intervention contact and those with lower ratios of contacts. This indicates that prolonged duration of the intervention is more important than higher frequency of contact. Despite these findings, more research is needed to evaluate the duration and frequency of interventions. Attention should be drawn to the fact that the standard deviation for mean weeks of intervention duration that produced maintenance effects was 16. This highlights the large variability in interventions. Furthermore, intervention intensity cannot be judged on its own, because the use of behaviour change techniques used in these interventions are also thought to effect its efficacy in long-term behaviour change. It is expected that longer interventions also use more behaviour change techniques. Trials that compare different durations and frequencies of contacts within the same setting, based on the same behaviour change model with the same behaviour change techniques used, are needed to clarify which intervention intensity is more likely to produce maintenance of behaviour. Only one study has investigated the effect of different contact frequencies on PA outcomes (Simons-Morton et al., 2001). The intervention consisted of three study arms: an advice group (physician and health educator advice only), an assistance group (same advice as advice group, additional counselling session, monthly mailings), and a counselling group (all components of advice and assistance group, plus frequent telephone counselling). Contact with the participants was spread over the 24 months study period and varied by group. At the end of the intervention (24 months) the average of intervention contacts was 3 for the advice group, 22 for the assistance group, and 41 for the counselling group. The authors showed that for women the assistance and the counselling interventions were similar in increasing physical fitness at 24 months, and total PA was only significantly different between the counselling and assistance group, but not compared to the advice group. And for men, no intervention arm was superior over the other in producing positive intervention effects. It should be noted that all intervention arms received contact over the whole study period, only the frequency differed. This supports Fjeldsoe et al's (2011) conclusion, that a prolonged intervention is more important than the frequency of contact.

The strength of the studies described in this thesis is that they were conducted by the same person, using the same behaviour change techniques, the same ratio of intervention contact, but differing duration. This allows a comparison of the trends of motivational regulation and PA behaviour outcome measures post-intervention and at follow-up with respect to the different durations of the intervention components. The duration of PARC was twice as long as MOVE, with 6 months active intervention time, and 6 months follow-up time, compared to 3 months for each component in MOVE. Based on the main findings of both studies, significant group differences in motivational regulation were only observed for PARC but not for MOVE. Post-intervention, significant intervention effects were observed for amotivation, identified regulation, and intrinsic regulation in favour of the intervention condition. For MOVE, at post-intervention there were no significant intervention effects in amotivation, but medium effect sizes (not significant) for identified and intrinsic regulation were observed in favour of the intervention group. As for PA outcomes, intervention participants in PARC engaged in more leisure-time PA than the control group, although this was only borderline significant. And in MOVE the intervention condition did significantly more walking than the control group post-intervention. Thus, both interventions were able to achieve a short-term effect on PA and motivational regulations post-intervention disregarding the length of the intervention. The effects on motivation regulation, however, were stronger in PARC, but due to the small sample sizes, this has to be interpreted with caution.

At follow-up (12 months for PARC and 6 months for MOVE), the differences in motivational regulation post-intervention observed in the PARC study were maintained, although, this was not significant anymore for identified regulation because of a slight increase of this regulation in the control condition. In MOVE, there were no intervention effects at follow-up for amotivation, identified and intrinsic regulation. However, introjected regulation showed a medium effect size with higher levels for the intervention group compared to the control group. In both studies, PA behaviour was higher in the intervention conditions compared to the control conditions in both studies (borderline significance for leisure-time in PARC; significant for walking and total PA in MOVE). This demonstrates that a 3 months intervention is able to achieve a maintenance effect of PA behaviour at least 3 months post-intervention, but that motivational regulation is more externally

regulated. In contrast, a 6 months autonomy supportive intervention can produce a maintenance effect of PA behaviour at least 6 months after the end of the intervention, and motivational regulations are more internalized. This would indicate that a 6 months intervention might be producing 'higher quality' motivation which is also maintained at follow-up, increasing the likelihood that the positive changes in PA will be maintained beyond the end of the intervention, and perhaps beyond the end of the 6 months follow-up period. Future studies should extend the follow-up periods to investigate the longitudinal effects on motivational regulation.

The findings from the studies of this thesis could explain why shorter interventions (less than 21 weeks) have not demonstrated long-term maintenance of the intervention effects. However, the differences between the studies could be due to the different populations of the studies, and not be attributable to the duration of the intervention alone. This warrants further investigation.

9.5. Other considerations of feasibility

Attendance at the intervention components was comparable to other studies. Although, every effort was made to offer a flexible schedule for supervised exercise sessions and workshops, participants preferred to stick to certain times of the week. In an intervention that lasts for 6 months (PARC, and 3 months for MOVE), it is not to be expected that every session will be attended, because other life commitments get in the way. The main reasons for missing a supervised exercise session were illness, holidays or family commitments. These cannot be prevented over a 6 month period. Thus, we are of the opinion that 65 % attendance for PARC and 79% for MOVE is very good.

There were no adverse events during the intervention, unless people had existing health conditions. Two people had health problems (Multiple sclerosis, back pain), and despite being considered safe to take part in the intervention (approval of GP and physiotherapist was sought) the participants dropped out because of a worsening of their condition. Whether this was related to the exercise sessions is unknown. In any case, this highlights the importance of an experienced exercise instructor to carry out the supervised exercise sessions. The instructor in this study was a REPs level 2 gym instructor, and another instructor was a physiotherapist. Communication between the two instructors often helped to identify physical

needs of participants to tailor the exercises and ensure the participant's safety. Therefore, it is unlikely that the nature of the exercises contributed to a worsening of the patient's condition.

Lastly, cardiopulmonary fitness testing was safe with both populations and no adverse events were recorded. However, it should be noted that in the MOVE study two participants did opt not to complete the Bruce walking test because they expressed discomfort on the treadmill. None of the PARC participants refused to complete the bicycle test. This suggests that cycling might be more accepted by elderly people.

Based on the findings of attrition, attendance, and 'safety' of the intervention, we conclude that the intervention is feasible but multi-centre approaches should be considered in future studies to reduce the travel burden to the intervention site. Intervention design (self-selection to group allocation, frequency of supervised exercise sessions) needs to be carefully considered to maximise recruitment but to not jeopardise behaviour change.

Usability of the Interview-delivered International PA Questionnaire as outcome measure

The IPAQ was delivered as an interview form because its accuracy, especially in an elderly population, has been questioned (Heesch et al., 2010). We also used this opportunity to investigate criterion validity of the interview-delivered IPAQ-L against acceleromtery. The main findings included higher correlation coefficients for walking time, total PA, and sedentary time compared to findings from other validation studies with an elderly population (Cerin et al., 2012). Furthermore, it was found that lower cut-points might be more accurate for measuring non-walking PA. In terms of practicality of delivering the IPAQ-L in an interview form, this format allowed clarification of the meaning of the questions. It was felt that participants would have been likely to over-report PA, especially walking times. Often participants tended to want to report walking at several occasions, and it was because of the probing of the interviewer that these errors were identified and corrected. Furthermore, it was clear during the assessment that participants would have struggled with the interpretation of the intensity of PA and the durations of PA. A limitation of the interview-delivered IPAQ-L is that it can take considerable

time to complete. Times to complete the questionnaire ranged widely between participants, from as little as 10 min to as long as 40 min. This needs to be taken into account when choosing this mode of assessment.

In neither study of this thesis did we find significant group differences in accelerometry outcomes but in self-reported walking and total PA (MOVE trial), despite moderate correlations between the measures. Based on our findings in Chapter 8, self-reported PA from the IPAQ tends to be over-reported- and acceleromtry data under-reported. Which one of the tools provided a 'true' reflection of PA behaviour is impossible to know from the results of this study. Individual differences in physical health may contribute to the large difference between the subjective and the objective measure. For example, one participant with a spinal cord stimulator and limited lung function due to surgery in the past, increased self-reported PA by 185 min at 6 months, but decreased total PA from accelerometry by 9 min only. At this time-point she had registered with the gym and reported going to a fit class for elderly people twice per week. Another participant without any apparent PA limitations decreased on self-reported PA by 190 min but increased total PA from accelerometry by 74 min at 6 months. This participant engaged in a large amount of occupational PA at BL but in more structured exercise at 6 months. This indicates that accelerometers are limited at measuring certain types of PA modes, but are also limited to accurately capturing PA levels in people with physical limitations. It has been suggested that vector magnitude might be a more accurate measure to capture PA levels, however, this measure did not show significant group differences in our studies. Future studies using accelerometry should consider developing individual cut-points by measuring PA intensity during a period of controlled activity. One previous study was successful in showing changes in PA levels post-intervention only with the use of individual cut-points but not with generic cut-points (Rejeski et al., 2013). Thus, the use of accelerometry in an elderly population, although considered the 'gold standard' for PA assessments, warrants further investigation. In the meantime, the use of an interview-delivered IPAQ could provide an alternative for PA assessment in this population.

9.6. Final comments about the intervention's practicality

In both studies of this thesis, supervised exercise sessions and workshops took place in small groups of 2-6 people. This was largely due to the limited size of the exercise facilities and thus, limited availability of equipment. Small groups allow the participants to engage with each other and friendships between the participants were made quickly. A review that investigated the question whether the effectiveness of large intervention groups versus small intervention differs, could not be identified. But it is likely that smaller groups offer more social support because in such a small group everyone gets to know each other, and conversation is thus encouraged. Whereas in a larger group, a feeling of anonymity might prevent participant interaction. Another perceived benefit of the small group environment is the ease of management in terms of recording participant's exercise intensities, perceived rates of exhaustion, and monitoring progress of the individual. Furthermore, the identification of physical limitations and addressing these by tailoring the activity to the individual's needs can be done with less disruption of the session in a small group session. This also ensures that everyone's needs are met. But this could be addressed by a thorough physical examination at the beginning of the intervention, and an individual exercise introduction before the group sessions.

In terms of modes of PA, all the equipment was used equally by men and women, but men may have preferred dumbbells and women elastic bands. Furthermore, women more often used the recumbent bicycle than men. This is only observational by the exercise instructor, but might be relevant for future design of supervised exercise sessions.

The workshops were well received and encouraged discussions amongst the participants. Although, a set schedule was developed before the intervention, it was noted that a schedule of behaviour change techniques should be a guidance and not a final curriculum. The first workshop was largely the same for all groups, but subsequent workshops were based on participant's interests and current knowledge and interests about PA. For example, some people wanted to know more about the mechanisms that are likely to underlie the relationship between higher levels of PA and reduced CRC risk. Some participants brought this up during

the first session, although, this was not scheduled until the second workshop. Thus, this information was provided during the first workshop if all other group members agreed. The order of topics during the workshops was largely dictated by the participant's interests and 'readiness' to become more active. All topics were covered in all groups, but the order differed in some groups. Keeping the focus on the topic is a challenge in group settings, and Wagner and Ingersoll (2012) recommend to not meander to other topics. But the authors also suggest that group leaders tailor the content broadly and address client's experiences and interests. This approach was also viewed as autonomy-supportive because the participants could address the questions that were most important to them.

Finally, it was noted that some participants who expressed high competence to exercise at least 150min per week (assessed during the workshops) and who had past experiences of being an exerciser, became less interested in the workshops. Whether this was really a lack of interest, or just the perception of the instructor is unknown. An evaluation of the acceptability of the workshops could have been carried out to investigate this, but this was not part of the study. Future studies should collect data about participant's acceptability of the intervention.

9.7. Design of potential RCTs based on the feasibility findings

The following sections will describe two potential RCTs that are informed by the findings of the two feasibility trials of this thesis. The first RCT to be described will be an active lifestyle intervention for patients diagnosed with polyps or adenomas. I will refer to this trial as PARC RCT. The second RCT will be an active lifestyle intervention for patients diagnosed with colorectal cancer, and I will refer to this trial as MOVE RCT.

PARC RCT

The reader may refer to Chapters 2, 3 and 5 for a background of the literature and a rationale for an RCT for PA behaviour in this population. Since the completion of the above feasibility studies, no new literature has emerged to address the gaps in the literature. The proposed RCT will be informed by the findings of the previously described PARC trial.

Aims and objectives

To evaluate the impact of an active lifestyle intervention on changes in PA, and its effects on the maintenance of the PA behaviour in the long-term. Specifically, the RCT will ask the following question: "Will an active lifestyle intervention based on Self-Determination Theory be effective at increasing PA levels post-intervention?" A secondary aim is to evaluate the effectiveness of the intervention to maintain PA behaviour change up to 2 years post-intervention.

Design

The study will be a parallel group RCT with two study arms. One group will receive the active lifestyle intervention (ALP), and the other group will continue with their standard care (SC) and thus, will serve as the control group. Randomisation will be carried out so that there are equal numbers of participants in each group.

Methods

Study setting

The study will be carried out in the UK. Recruitment will take place at multiple sites and the interventions will utilise established exercise facilities and programmes. Research data collection will take place at the participating NHS site, and the exercise facilities.

Participants

Participants will be patients undergoing a bowel screening colonoscopy. The inclusion criteria will be as follows: i) a diagnosis of at least one polyp or adenoma after screening colonoscopy, ii) aged 60 years and over (in line with the age criteria for routine colorectal cancer screening if the trial would take place in England, but can be 50 years and over if the trial would be carried out in Scotland), iii) able to undertake PA, iv) and able to provide informed consent. Exclusion criteria will be insulin dependent diabetes mellitus, and any cancer diagnosis.

Interventions

The ALP group will receive PA behaviour change advice for 6 months. The intervention will consist of three parts, a home-based exercise component, a supervised exercise component, and a PA counselling component. All components of the intervention will be informed by Self-Determination Theory (SDT).

Participants will be randomised to either a standard care group (SC) or an active lifestyle group (ALP). The SC group will continue with the standard care provided for the period of the intervention, but will be offered the intervention at the end of the study.

Prior to the supervised exercise sessions, each participant will attend a one-to-one introduction session with the exercise facilitator. This session will take place at a local community exercise facility to familiarise the participant with the environment which is thought to facilitate competence to visit the site for self-directed PA throughout and post-intervention. At this session the participants will receive an induction to different modes and intensities of exercise to familiarise themselves with the sensation of different intensities. This will support the participants' competence at carrying out PA at an individually suitable intensity, and facilitate feelings of safety. Participants will also learn the sensations that they should expect when carrying out moderate to vigorous intensity PA so that they are able to monitor the exercise intensity when they will be doing the exercises at home. At this session the exercise facilitator will assess the participant for their PA capacities and demonstrate exercises that are suitable for the individual. Potential functional limitations of the participant can be addressed and suitable exercises be identified. This session will also serve as an educational session where the exercise facilitator will explain the basics of PA, such as safety, warning signs when to stop exercising, how to monitor intensity, reasons for exercising at moderate to vigorous intensity, the benefits of such exercise intensity, and the principles of exercise (FITT principle).

At the end of this session the facilitator will design an individualised home-based exercise programme for the participant. This will be designed together with the participant, and include exercises carried out during the induction session. The participant will be given a choice of exercises that can easily be performed at home, and a plan of exercises that can be performed at the exercise facility on autonomous visits. This will facilitate autonomy as it gives the participant an option

of the modes of exercise, and the preferred location. The participant will set a personal goal as to how often and how long they want to do the exercises for the first week. Thereafter, they will be instructed to aim to build up the frequency to most days of the week and increase the duration to 30 min per session.

Participants will also be offered to take part at two supervised exercises classes per week at the community facility. One of the classes will be organised by the researchers, and the other class will be a session that is already on offer at the centre. This will aid transition from the intervention to self-guided exercise post-intervention, as the researcher-led class will be discontinued post-intervention.

Every fortnight, an exercise counselling session, based on motivational interviewing, will be held. These will take place in small groups either prior or after the researcher-led supervised exercise class, based on participants' preferences. The counselling will help the participants to identify personal benefits of PA, barriers, and goals. The sessions will also include some educational content informing the participants about the relationship between colorectal polyps and cancer and the role of PA as a preventative measure.

Outcome measures

Study outcomes will be assessed post-intervention (at 6 months). Follow-ups to assess the maintenance effects of the intervention will be at 1 and 2 years post-intervention.

The primary outcome measure will be self-reported PA behaviour which will be assessed with the IPAQ. PA will be reported as minutes of PA per week. Secondary outcomes will be variables of behavioural regulation which will be assessed with the BREQ-2 questionnaire, cardiopulmonary fitness with a bicycle ergometer, and body composition (body weight in kg, body fat in %, waist and hip circumference in cm).

Recruitment

To aid recruitment, a research nurse will be appointed to oversee participant recruitment. An invitation letter will be signed by the consultant and sent together with the letter informing the patient about the outcome of their colonoscopy. The invitation letter will contain some brief information about the association between

lifestyle behaviours such as PA, and the risk of polyps and the resulting potential risk of colorectal cancer. It will also explain that polyps, once removed, can come back. (This approach has to be discussed with NHSH R&D and NRES to ensure that this is not against ethical regulations. However, this approach is considered more successful, as a previous study has reported that patients after colonoscopy did perceive the removal of a polyp as a 'health certificate'. Thus, change of lifestyle was not considered because it seemed unnecessary (Stead et al, 2012)). This will aid to bridge the knowledge gap that patients may have about their diagnosis and their current lifestyle behaviour and may increase recruitment as it forms a teachable moment (as described above).

The invitation letter will contain information about the study, a return slip to express an interest in the study, and the contact details for the research nurse. If the patient does not respond to the initial invitation letter, the research nurse will phone the patient after 2 weeks to discuss participation. This approach has been shown to improve recruitment success (Treweek et al, 2013a). If participants agree to participate, a face-to-face meeting will be arranged to obtain written consent, and undergo baseline measurements.

PARC RCT-Sample size calculation (power calculation)

The sample size calculation was based on the research question: "Will an activity lifestyle intervention increase PA levels post-intervention?" Therefore, the variable 'leisure-time PA' was used to calculate the sample size. Based on the feasibility results from the PARC feasibility trial an effect size of 0.52 was found for change in PA. This was entered into the online sample size calculator, and it was estimated that 116 participants (n=58 in each arm) will be required for a fully powered RCT (www.sample-size.net/sample-size-means/). This proposed RCT would not collect biopsies to inform another trial, therefore the inclusion criteria will be less strict. In the feasibility trial nearly 50% of participants were not eligible, and the majority of reasons for non-eligibility could be avoided if patients are approached post-biopsy (unlike in the feasibility trial). Therefore, we estimate that 429 participants need to be approached to account for 25% (n=322) ineligibility (based on findings from Anderson et al, 2014), approximately 50% (n=161) rate of people who decline, and an attrition rate of 72% (n=116) (these numbers are based on the findings of the

feasibility study described in this thesis, but are also similar to another study with this population by Anderson et al, 2014).

This is likely to require multiple sites to recruit successfully into the study. The researchers will have to investigate the number of patients that are diagnosed with polyps at the research site per year, to estimate the potential number of participants that can be recruited in the given time that is available for recruitment to determine how many sites should be included. This will be influenced by the funding that is available for the study.

MOVE RCT

The intervention for MOVE RCT will be very similar to PARC RCT. Therefore, in the following sections I will outline the objectives, design, recruitment and participants that are specific to a RCT with people diagnosed with colorectal cancer. Where the intervention will be similar to PARC RCT, I will refer to the previous paragraphs for reference and only emphasise the differences to avoid repetition in this section.

Aims and objectives

To evaluate the impact of an active lifestyle intervention on changes in PA, and its effects on the maintenance of the PA behaviour in the long-term. Specifically, the RCT will ask the following question: "Will an active lifestyle intervention based on Self-Determination Theory be effective at increasing PA levels post-intervention?" A secondary aim is to evaluate the effectiveness of the intervention to maintain PA behaviour change up to 2 years post-intervention.

Design

The study will be a parallel group RCT with two study arms. One group will receive the active lifestyle intervention (ALP), and the other group will continue with their standard care (SC) and thus, will serve as the control group. Randomisation will be carried out so that there are equal numbers of participants in each group.

Methods

Study setting

The study will be carried out in the UK. Recruitment will take place at multiple sites and the interventions will utilise established exercise facilities and programmes.

Research data collection will take place at the participating NHS site, and the exercise facilities.

Participants

Participants will be patients previously diagnosed with colorectal cancer. The inclusion criteria will be as follows: i) a histologically confirmed diagnosis of colorectal cancer with Dukes stages A-C, ii) completed surgery and adjuvant treatment iii) able to safely undertake PA, iv) and able to provide informed consent. Exclusion criteria will be i) Karnofsky rating of less than 80, ii) unstable angina, iii), uncontrolled hypertension, iv) and recent myocardial infarction.

Ethical approval and research governance approval will be obtained from the relevant entities.

Interventions

The intervention will be similar to the PARC RCT intervention. Participants in the ALP group will receive PA counselling, supervised exercise and a home-based exercise programme for 6 months. And the SC will continue with their usual care.

The difference to PARC RCT will be that education material for the PA counselling group sessions will be tailored to patients diagnosed with colorectal cancer. The exercise facilitator will also receive training to be aware of specific risks of PA to patients recovering from colorectal cancer, such as risk of infections when using public pools if the patient is fitted with a colostomy bag. All the other components of the intervention will be the same as for PACT RCT.

Outcome measures

Study outcomes will be assessed post-intervention (at 6 months). Follow-ups to assess the maintenance effects of the intervention will be at 1 and 2 years post-intervention.

The primary outcome measure will be self-reported PA behaviour which will be assessed with the IPAQ. PA will be reported as minutes of PA per week. Secondary outcomes will be variables of behavioural regulation which will be assessed with the BREQ-2 questionnaire, cardiopulmonary fitness with a bicycle ergometer, and body composition (body weight in kg, body fat in %, waist and hip circumference in

cm). Quality of life will also be assessed with the SF-36. The SF-36 is a quality of life questionnaire unspecific to colorectal cancer, but the feasibility study did not show changes in the cancer specific quality of life measures. Other studies have also failed to show changes in quality of life post-intervention (Bourke et al, 2011, Hawkes et al, 2013, Courneya et al, 2003). Perhaps at the time of recruitment patients have already recovered from their treatment side-effects, resulting in an inability of a cancer-specific tool to detect changes. Therefore, the SF-36 will be used as it is suitable for a general elderly population.

Recruitment

To aid recruitment, a research nurse will be appointed to oversee participant recruitment. A research nurse will approach patients at follow-up clinic visits and provide some information about the study. An invitation letter will be given to the patients by the research nurse. The invitation letter will contain information about the study, a return slip to express an interest in the study, and the contact details for the research nurse.

Patients who are not on active follow-up will receive an invitation letter that will be signed by the consultant. The research nurse will take responsibility for preparation and mailing of the invitation letters. The letter will contain the patient information sheet, a return slip to express an interest in the study, and the contact details for the research nurse.

For both routes of recruitment, if the patient does not respond to the initial invitation letter, the research nurse will phone the patient after 2 weeks to discuss participation. This approach has been shown to improve recruitment success (Treweek et al, 2013a). If participants agree to participate, a face-to-face meeting will be arranged to obtain written consent, and undergo baseline measurements.

MOVE RCT-Sample size calculation (power calculation)

The sample size calculation was based on the research question: “Will an activity lifestyle intervention increase PA levels post-intervention?” Therefore, the variable ‘leisure-time PA’ was used to calculate the sample size. Based on the feasibility results from the MOVE feasibility trial an effect size of 0.36 post-intervention (3months) was found for change in PA. This however, does not reflect a potential

effect size at 6 months intervention. No other study with this population has conducted a 6 months supervised exercise programme. The 6 months effects size in the MOVE feasibility study was 1.03. The PARC feasibility study demonstrated a 0.52 effect size for leisure time PA at 6 months post-intervention. Therefore, the sample size calculation for MOVE RCT was based on the findings of the PARC feasibility study as this is more representative of the proposed intervention in terms of the timelines. Also, if our assumptions are correct that a 6 months intervention would be more effective than a 3 months intervention, we would expect a higher effect size than the 0.36 found at 3 months in the MOVE feasibility study.

The data (based on effect size of 0.52) was entered into the online sample size calculator, and it was estimated that 116 participants (n=58 in each arm) will be required for a fully powered RCT (http://www.sample-size.net/sample-size-means/). In the feasibility trial only 27% responded to the invitation letters. In a study with this population, nurse led recruitment at follow-up clinics yielded only 17% interested responses (Bourke et al, 2011). Thus, I estimate 22% (mean of 17% and 27%) responses as "interested". Based on this response rate 1427 potential participants have to be approached to account for an expected 22% (n=314) response rate, with only 74% (n=233) being eligible, a decline rate of 30% (n= 163), and a drop-out rate of 29% (n=116).

This is likely to require multiple sites to recruit successfully into the study. The researchers will have to investigate the number of patients that are diagnosed with polyps at the research site per year, to estimate the potential number of participants that can be recruited in the given time that is available for recruitment to determine how many sites should be included. This will be influenced by the funding that is available for the study.

9.8. General directions

The development and implementation of PA interventions with an elderly population has many challenges. Older people may have different motivators and barriers to PA than younger people (Baert et al., 2011). Therefore, it is important to recognise these and plan PA programmes with these challenges in mind. Some of the barriers that were identified in this study, and mirror those of others, were lack of motivation, not knowing what exercised to do, costs of exercise, and not having

the social support to exercise. The lack of knowledge of exercises can be addressed with educational material as part of an intervention, but lack of motivation, and social support, especially for home-based exercises, is more difficult to address. This poses a challenge as to what form the exercise programme should take on. Should it be home-based? Should it be supervised? If supervised exercise addresses the issues of knowledge and social support, how can we provide social support post-intervention? In the feasibility interventions of this thesis, I attempted to bridge the gap between supervised-exercises and home-based exercises, by providing information about local supervised community exercise programmes and encourage participants to attend. This provided an opportunity for the participants to make new social connections with other people interested in exercising, outside the intervention environment. As concluded from the above studies, we still need to identify the components of interventions (e.g. duration of intervention, frequency of support), to develop a 'recipe' for successful behaviour change interventions (Fjeldsoe et al., 2011).

Besides the setting of the intervention, other factors also have to be considered. There is no consensus on what is the best PA measurement method in older people. Although, accelerometry is often considered as the gold standard for PA assessments, the results from this study show that accelerometry might not be the measure of choice when assessing exercise behaviour in the elderly, apart from walking activities. As the current recommendations for PA also include resistance exercises, accelerometry would be limited at accurately capturing all activities that participants may have engaged in. Although, walking has been shown to be one of the favourite activities for the elderly (Booth et al., 1997), other community programmes are encouraging an increase in any type of activity, such as gardening, household, daily routine activities. There are other issues with using accelerometers in the elderly, such as forgetting to wear them, or not attaching them correctly, which would result in loss of data. Self-reported measurement tools on the other hand are prone to over-reporting in the elderly likely due to misinterpretation of the questions (Heesch et al., 2010). When assessing PA in the elderly, these limitations of both, subjective and objective measures, need to be considered when making a choice which one to use. If the intervention is a walking intervention than accelerometers are indeed a good choice. If other activities are promoted as part of the intervention, self-report may be more relevant. It could be

assumed that intra-individual errors in reporting will remain the same for every time-point of assessment. Therefore, the level of PA might not be a reflection of the true PA level, but it will give an indication whether the participant reduced or increased PA. Thus, self-report has the value of monitoring within-person change and may be used as a motivational tool when providing feedback to the participant. A baseline measure can act as the participant's personal 'baseline' and can measure their personal progress based on that baseline measure. This might be more important to the participant as it provides personal feedback. However, this has limitations if we want to assess whether people are meeting the current weekly PA guidelines of moderate and vigorous intensity PA. I believe that it is important to provide personal feedback, and if self-reported PA can act as a personal motivator based on feedback, then it should be used in community exercise programs.

Similarly, fitness assessment has limitations for the use with the elderly. I noticed that a fitness assessment on the bicycle ergometer was more feasible than the assessment on a treadmill in an elderly population. There were no reports of participants being unable to complete the fitness test in the PARC study that used bicycle ergometers. But some MOVE participants were unable to complete the treadmill test, even though it was only a submaximal test. The 6-min walk test has been shown to be significantly correlated with peak VO_2 and might therefore be a better choice in a community setting (Ross et al., 2010). The efficacy of PA interventions at improving peak fitness is inconclusive (Foster et al., 2008). In an elderly population, age-related deconditioning should be considered when interpreting the results of fitness tests. In older people a decline of 0.5-1% per year of cardiopulmonary fitness has been reported (Milanović et al., 2013). For longer-term studies this may mean that no improvements will be detected, but we should regard the maintenance as fitness as a success of the intervention.

Lastly, I will briefly consider the use of behaviour change theory in exercise programmes. There is agreement that behaviour change interventions need to be underpinned by theory (Michie and Abraham, 2004). But whether behaviour change interventions are making efficient use of theory is not clear, limiting the evidence of theory's efficacy and decision of which theory to use. There is an abundance of behaviour change theories (Michie et al., 2014) but only a minority of these are being used to inform interventions (Painter et al., 2008). Moreover,

there appears to be a dearth of community-level theories being used in health behaviour change research (Painter et al., 2008). Therefore, more research should apply such theories, including SDT, in a community-level exercise programme.

Limitations, strengths, and future directions

The strengths of the studies were the use of a behaviour change theory and a detailed description of how the theory informed the development of the intervention. Furthermore, both studies (PARC and MOVE) included a 'true' follow-up without intervention strategies during that period. With this, we were able to investigate the long-term effects of the intervention on PA behaviour after all intervention components ceased and the participant relied on their own resources. The RCT design further added strength by reducing the risk of bias.

There are also some limitations to the studies described in this thesis. First, low recruitment rates limited the ability to produce statistical significance, thus the results have to be interpreted with caution. This further limited the ability to undertake meaningful statistical analysis of the association between PA levels and motivational regulations. Another limitation is that the researcher delivering the intervention also carried out all the assessments and data analysis. Only the VO_{2max} test was carried out by a blind assessor.

9.9. Future directions

Future research should also investigate psychological needs (autonomy, competence, relatedness) and motivational regulations as mediators of PA behaviour. Mediator analysis in a RCT setting has only been conducted in one study, but relatedness was not included (Silva et al., 2010a). The sample size in the studies of this thesis was too small to conduct meaningful mediator analysis. This will add further to the understanding of the mechanisms by which an autonomy-supportive intervention works in promoting PA behaviour. These associations will also need to be explored in the long-term to provide an understanding of the mechanisms that promote behaviour maintenance.

Furthermore, studies should also include an economic evaluation of interventions, because cost-effectiveness is important to evaluate the economic and clinical benefit of the intervention.

The components of this trial can be adapted for a larger trial. It should be considered whether the groups should be kept at small numbers, or increased in size. Larger group sizes have cost-effectiveness benefits, but might jeopardise other beneficial aspects of the dynamic of small groups. In regards to workshops based on MI, groups larger than 12 members are not recommended by the authors of the book "Motivational Interviewing in Groups" (Wagner and Ingersoll, 2012). Larger MI groups might start seeming like classes or meetings, and participants may feel vulnerable to share personal information with so many other members. This might pose a problem for a larger study. One way to overcome this is to split the groups and allocate participants with higher 'readiness for change' in one group and participants with lower 'readiness' in a different MI group.

In regards to recruitment, besides a multi-centre design as previously discussed in the relevant chapters, a research nurse might be more effective at recruiting patients. Recruitment to an exercise intervention with women treated for breast cancer increased by over 70% after three clinical researchers were hired to dedicate time for recruitment (Campbell et al., 2005).

9.10. Conclusion

The findings in this study suggest that an autonomy-supportive lifestyle intervention with supervised exercise sessions and counselling workshops is feasible and has the potential to evoke changes in PA levels and in behavioural regulations from a more external regulation to a more internal regulation in elderly people diagnosed with colonic polyps. Furthermore, the findings indicate that an intervention based on SDT could be successful in maintaining behaviour changes beyond the intervention. A larger RCT is needed to confirm these preliminary findings, and follow-up time should be extended beyond 12 months.

The findings of the study also suggest that a 3 month autonomy supportive lifestyle intervention with supervised exercise and PA counselling is feasible after CRC treatment. However, 3 months intervention time might not be sufficient in length to evoke changes in behavioural regulation but was effective at changing PA levels after the intervention and at 3 month follow-up. A larger-scale RCT with a longer intervention period and longer follow-up is needed to investigate whether a longer intervention will be more effective at evoking changes in behavioural regulation.

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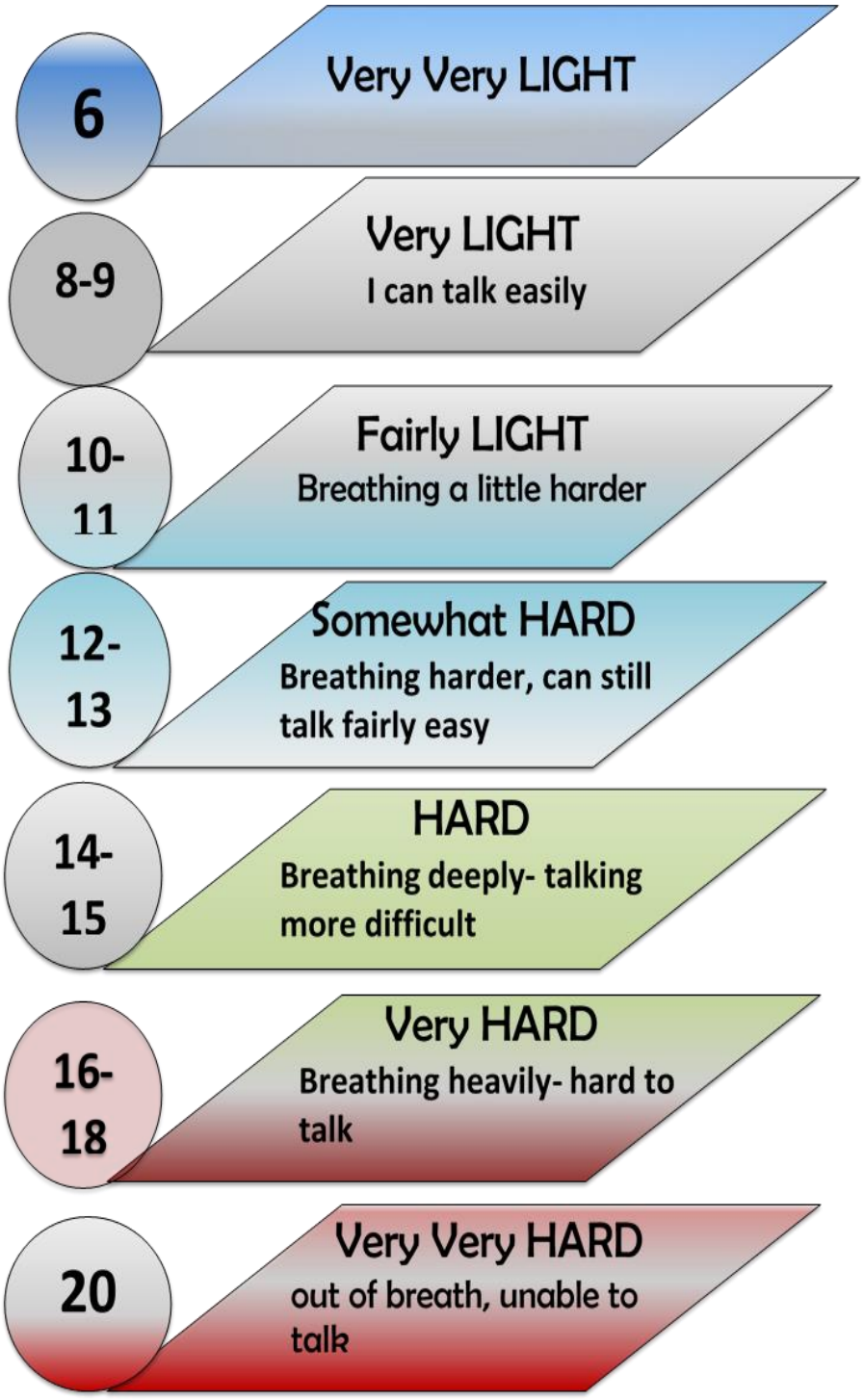
11. Appendices

Appendix 1- Borg Scale



Appendix 2- Workshop topics

PARC

WEEK	CONTENT AND TOOLS
2	Identifying benefits of PA; Identifying personal aims; increasing knowledge about current PA recommendations; Readiness ruler
4	Increasing knowledge about PA and polyps/ CRC; possible mechanisms of action; basics about PA; Self-monitoring; Social support; PA intensity monitoring worksheet
6	Review of PA intensity monitoring worksheet; Perceived pros and cons of more PA; Goal setting; Introduction to GP-referral scheme and completing application forms
8	Discussing goals set in previous week; Identification of barriers in achieving goals; Group suggestions of overcoming barriers; Committing to a strategy to overcome barriers; Identification of community PA programmes, nearby gyms, walking groups, etc.; PA resources
10	Review of previous week set goals and barriers; Assessment of importance and competence to be more active; Progress of GP-referral applications; Committing to registration with gym, walking group, or other personally identified and preferred mode of PA
12	Review of last three months of supervised exercise; review of home-based exercise; identification of strategies to continue exercise over next three months with less supervised exercise
14	Review of goals set from previous week; discussion barriers; adjustment of goals; behaviour strategies; Evaluation of progress since start of programme; perceived changes in fitness, weight, well-being, etc.;
16	Review of previous week's PA; Personal improvements and progress of becoming an individual exerciser; Long-term goals; identifying barriers and how to overcome them; Development of strategies and identifying prompts; Identifying situations of difficulties to maintain PA levels;
18	Evaluation of goal's; re-adjustment of goals; Sharing successful behaviour strategies; Perceived competence of exercising beyond the end of the supervised exercises;
20	Review of previous week's goals; Clear plan and strategies for future exercises after end of intervention; Barriers and solutions; Encouraging group visits at the gym;
22	Review of previous week's goals; re-evaluation of competence to exercise in the future; re-evaluate personal benefits;

24	Review previous week's goals; Evaluation of the intervention; Behavioural strategies and prompts; Re-evaluation of competence to continue exercise in the future; Sharing feelings about the end of the intervention;

MOVE

WEEK	CONTENT AND TOOLS
1	Identifying benefits of PA; Identifying personal aims; increasing knowledge about current PA recommendations; Readiness ruler;
2	Increasing knowledge about PA and CRC; possible mechanisms of action; basics about PA (FITT); Self-monitoring; Social support; PA intensity monitoring worksheet
3	Review of PA intensity monitoring worksheet; Perceived pros and cons of more PA; Goal setting; Barrier identification and solutions; Introduction to GP-referral scheme; Identification of community PA programmes, nearby gyms, walking groups, etc.; PA resources; Behavioural strategies; Assessment of importance and competence to be more active
4	Review of previous week's PA goals and barriers; Personal improvements and progress of becoming an individual exerciser; Long-term goals; Barriers and solutions; Development of strategies and identifying prompts; Identifying situations of difficulties to maintain PA levels; Evaluation of progress since start of programme; perceived changes in fitness, weight, well-being, etc.;
6	Review of previous week's goals; identification of strategies to continue exercise over next month with less supervised exercise; Barriers and solutions; Sharing successful behaviour strategies; adjustment of goals; Committing to registration with gym, walking group, or other personally identified and preferred mode of PA
8	Review of previous week's goals; Clear plan and strategies for future exercises after end of intervention; Barriers and solutions; Encouraging group visits at the gym; Re-evaluation of competence to exercise in the future; re-evaluate personal benefits; Sharing feelings about the end of the intervention

Appendix 3- BREQ-2

We are interested in the reasons underlying peoples' decisions to engage, or not engage in physical exercise. Using the scale below, please indicate to what extent each of the following items is true for you. Please note that there are no right or wrong answers and no trick questions. We simply want to know how you personally feel about exercise.

(1-19) Please circle one number on each line indicating how true each statement is for you.

		Not true for me	Sometimes true for me			Very true for me
1	I exercise because other people say I should	0	1	2	3	4
2	I feel guilty when I don't exercise	0	1	2	3	4
3	I value the benefits of exercise	0	1	2	3	4
4	I exercise because it's fun	0	1	2	3	4
5	I don't see why I should have to exercise	0	1	2	3	4
6	I take part in exercise because my friends/family/partner say I should	0	1	2	3	4
7	I feel ashamed when I miss an exercise sessions	0	1	2	3	4
8	It's important to me to exercise regularly	0	1	2	3	4
9	I can't see why I should bother exercising	0	1	2	3	4
10	I enjoy my exercise sessions	0	1	2	3	4
11	I exercise because others will not be pleased with me if I don't	0	1	2	3	4
12	I don't see the point in exercising	0	1	2	3	4
13	I feel like a failure when I haven't exercise in a while	0	1	2	3	4
14	I think it is important to make the effort to exercise regularly	0	1	2	3	4
15	I find exercise a pleasurable activity	0	1	2	3	4
16	I feel under pressure from my friends/family to exercise	0	1	2	3	4
17	I get restless if I don't exercise regularly	0	1	2	3	4
18	I get pleasure and satisfaction from participating in exercise	0	1	2	3	4
19	I think exercising is a waste of time	0	1	2	3	4

Appendix 4- Intention to Exercise

		Do not agree at all						Completely agree
3	I intend to exercise regularly over the next month	1	2	3	4	5	6	7
3 4	I intend to exercise regularly over the next 6 months	1	2	3	4	5	6	7

Appendix 5- Self-efficacy to exercise

With the next questions we want to know how confident you are right now that you could exercise for 30 minutes on most days of the week, if …?

		Not very confident										Very confident
20	The weather was bothering you	0	1	2	3	4	5	6	7	8	9	10
21	You were bored by the programme or activity	0	1	2	3	4	5	6	7	8	9	10
22	You were not exactly sure what exercise to do	0	1	2	3	4	5	6	7	8	9	10
23	You felt pain when exercising	0	1	2	3	4	5	6	7	8	9	10
24	You had to exercise alone	0	1	2	3	4	5	6	7	8	9	10
25	You did not enjoy it	0	1	2	3	4	5	6	7	8	9	10
26	You were too busy with other activities	0	1	2	3	4	5	6	7	8	9	10
27	You felt tired	0	1	2	3	4	5	6	7	8	9	10
28	You felt stressed	0	1	2	3	4	5	6	7	8	9	10
29	You felt depressed	0	1	2	3	4	5	6	7	8	9	10

Appendix 6- SF-36 (Quality of Life)

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. *Thank you for completing this survey!*

For each of the following questions, please tick the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one week ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one week ago	Somewhat better now than one week ago	About the same as one week ago	Somewhat worse now than one week ago	Much worse now than one week ago
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a <u>Vigorous activities</u>, such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐ 3
b <u>Moderate activities</u>, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐	☐ 3

c	Lifting or carrying groceries	☐	☐	☐ 3
d	Climbing several flights of stairs	☐	☐	☐ 3
f	Bending, kneeling, or stooping	☐	☐	☐ 3
f	Bending, kneeling, or stooping	☐	☐	☐ 3
g	Walking more than a mile	☐	☐	☐ 3
h	Walking several hundred yards	☐	☐	☐ 3
i	Walking one hundred yards	☐	☐	☐ 3
j	Bathing or dressing yourself	☐	☐	☐ 3

4. During the past week, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the <u>past week</u>, how much of the time have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the <u>amount of time</u> you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b <u>Accomplished less</u> than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Did work or other activities <u>less carefully than usual</u>	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. During the <u>past week</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. How much <u>bodily</u> pain have you had during the <u>past week</u>?

None	Very mild	Mild	Moderate	Severe	Very severe
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. During the <u>past week</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. These questions are about how you feel and how things have been with you <u>during the past week</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past week</u>…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	▼	▼	▼	▼	▼
a Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f Have you felt downhearted and low?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the <u>past week</u>, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

		Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a	I seem to get ill more easily than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Appendix 7- International Physical Activity Questionnaire- long version

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work,

and any other unpaid work that you did outside your home. **Do not** include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

Yes ☐

No ☐ ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the last 7 days as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, heavy construction, or climbing up stairs as part of your work?

Think about only those physical activities that you did for at least 10 minutes at a time.

_____ days per week

No vigorous job-related physical activity ☐ ***Skip to question 4***

3. How much time did you usually spend on one of those days doing vigorous physical activities as part of your work?

_____ hours per day

_____ minutes per day

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like carrying light loads as part of your work? Please do not include walking.

_____ days per week

No moderate job-related physical activity ☐ →

Skip to question 6

5. How much time did you usually spend on one of those days doing moderate physical activities as part of your work?

_____ **hours per day**

_____ minutes per day

6. During the last 7 days, on how many days did you walk for at least 10 minutes at a time as part of your work? Please do not count any walking you did to travel to or from work.

_____ **days per week**

No job-related walking ☐ → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days walking as part of your work?

_____ hours per day

_____ minutes per day

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the last 7 days, on how many days did you travel in a motor vehicle like a train, bus, car, or tram?

_____ days per week

No traveling in a motor vehicle ☐ → ***Skip to question 10***

9. How much time did you usually spend on one of those days traveling in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**

_____ minutes per day

Now think only about the bicycling and walking you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the last 7 days, on how many days did you bicycle for at least 10 minutes at a time to go from place to place?

_____ days per week

No bicycling from place to place ☐ → ***Skip to question 12***

11. How much time did you usually spend on one of those days to bicycle from place to place?

_____ **hours per day**

_____ minutes per day

12. During the last 7 days, on how many days did you walk for at least 10 minutes at a time to go from place to place?

_____ **days per week**

No walking from place to place ☐ → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days walking from place to place?

_____ hours per day

_____ minutes per day

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the last 7 days in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, chopping wood, shoveling snow, or digging in the garden or yard?

_____ days per week

No vigorous activity in garden or yard ☐ → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing vigorous physical activities in the garden or yard?

_____ hours per day

_____ minutes per day

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, sweeping, washing windows, and raking in the garden or yard?

_____ days per week

No moderate activity in garden or yard ☐ → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing moderate physical activities in the garden or yard?

_____ **hours per day**

_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, washing windows, scrubbing floors and sweeping inside your home?

_____ **days per week**

No moderate activity inside home ☐ → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing moderate physical activities inside your home?

_____ **hours per day**

_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the last 7 days solely for

recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the last 7 days, on how many days did you walk for at least 10 minutes at a time in your leisure time?

_____ **days per week**

No walking in leisure time ☐ → ***Skip to question 22***

21. How much time did you usually spend on one of those days walking in your leisure time?

_____ **hours per day**

_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like aerobics, running, fast bicycling, or fast swimming in your leisure time?

_____ **days per week**

No vigorous activity in leisure time ☐ → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing vigorous physical activities in your leisure time?

_____ **hours per day**

_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis in your leisure time?

_____ **days per week**

No moderate activity in leisure time ☐ → ***Skip to PART 5:***

TIME SPENT SITTING

25. How much time did you usually spend on one of those days doing moderate physical activities in your leisure time?

_____ **hours per day**

_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the last 7 days, how much time did you usually spend sitting on a weekday?

_____ hours per day

_____ minutes per day

27. During the last 7 days, how much time did you usually spend sitting on a weekend day?

_____ hours per day

_____ minutes per day

Appendix 8- Functional Assessment for Cancer Therapy

FACT-G

Below is a list of statements that other people with your illness have said are important. **Please circl or mark one number per line to indicate your response as it applies to the past 7 days.**

	PHYSICAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

FACT-C

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
C1	I have swelling or cramps in my stomach area	0	1	2	3	4
C2	I am losing weight	0	1	2	3	4
C3	I have control of my bowels	0	1	2	3	4
C4	I can digest my food well	0	1	2	3	4
C5	I have diarrhea (diarrhoea)	0	1	2	3	4
C6	I have a good appetite	0	1	2	3	4
C7	I like the appearance of my body	0	1	2	3	4
Q2	Do you have an ostomy appliance? (Mark one box)	☐ No		or	☐ Yes	
	If yes, please answer the next two items:					
C8	I am embarrassed by my ostomy appliance	0	1	2	3	4
C9	Caring for my ostomy appliance is difficult	0	1	2	3	4

FACT-F

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

Appendix 9- Psychological Needs Satisfaction for Exercise

PSYCHOLOGICAL NEED SATISFACTION IN EXERCISE SCALE

The following statements represent different experiences people have when they exercise. Please answer the following questions by considering how YOU TYPICALLY feel while you are exercising.

	False	Mostly False	More false than true	More true than false	Mostly True	True
1. I feel that I am able to complete exercises that are personally challenging	1	2	3	4	5	6
2. I feel attached to my exercise companions because they accept me for who I am	1	2	3	4	5	6
3. I feel like I share a common bond with people who are important to me when we exercise together	1	2	3	4	5	6
4. I feel confident I can do even the most challenging exercises	1	2	3	4	5	6
5. I feel a sense of camaraderie with my exercise companions because we exercise for the same reasons	1	2	3	4	5	6
6. I feel confident in my ability to perform exercises that personally challenge me	1	2	3	4	5	6
7. I feel close to my exercise companions who appreciate how difficult exercise can be	1	2	3	4	5	6
8. I feel free to exercise in my own way	1	2	3	4	5	6
9. I feel free to make my own exercise program decisions	1	2	3	4	5	6
10. I feel capable of completing exercises that are challenging to me	1	2	3	4	5	6
11. I feel like I am in charge of my exercise program decisions	1	2	3	4	5	6
12. I feel like I am capable of doing even the most challenging exercises	1	2	3	4	5	6
13. I feel like I have a say in choosing the exercises that I do	1	2	3	4	5	6
14. I feel connected to the people who I interact with while we exercise together	1	2	3	4	5	6
15. I feel good about the way I am able to complete challenging exercises	1	2	3	4	5	6
16. I feel like I get along well with other people who I interact with while we exercise together	1	2	3	4	5	6
17. I feel free to choose which exercises I participate in	1	2	3	4	5	6
18. I feel like I am the one who decides what exercises I do	1	2	3	4	5	6

Appendix 10- Bruce protocol

Stage	Speed (km/h)	Grade (%)	Duration (min)	HR
0	2.7	0	3	
0.5	2.7	5	3	
1	2.7	10	3	
2	4.0	12	3	
3	5.5	14	3	
4	6.7	16	3	
5	8.0	18	3	
6	8.8	20	3	
7	9.6	22	3	

Appendix 11-Survey questionnaires

11.1. EQ-5D Quality of life questionnaire

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

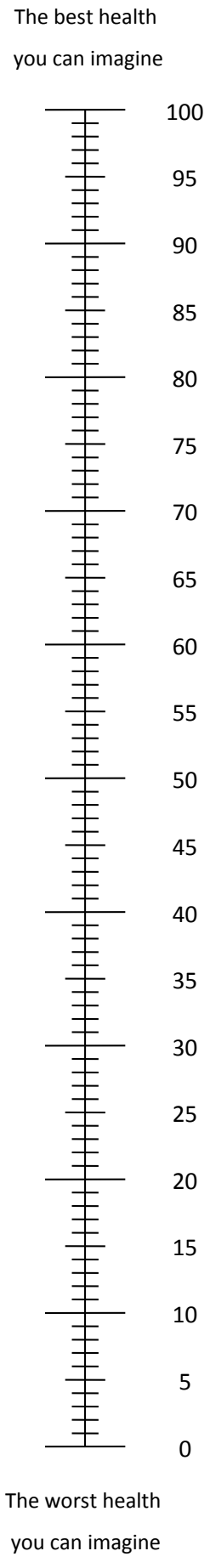
ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

We would like to know how good or bad your health is TODAY

- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY =



11.2. Reasons for non-participation

2. Do any of the following factors play a role in your decision making not to take part in the study?

Distance to the research site: Yes ☐ No ☐

Health: Yes ☐ No ☐

Time commitment: Yes ☐ No ☐

Other reasons: _____

11.3. Barriers to exercise

4. How much do you agree with the following statements in regards to exercise?	Strongly agree									Strongly disagree
I don't know what exercises to do	1	2	3	4	5	6	7	8	9	10
I don't know how much exercise to do	1	2	3	4	5	6	7	8	9	10
I don't have time to exercise	1	2	3	4	5	6	7	8	9	10
My health prevents me from exercising	1	2	3	4	5	6	7	8	9	10
I cannot afford the costs of exercising	1	2	3	4	5	6	7	8	9	10
I cannot get myself motivated to exercise	1	2	3	4	5	6	7	8	9	10
I don't have anyone to exercise with	1	2	3	4	5	6	7	8	9	10
There is nowhere to exercise in the area where I live	1	2	3	4	5	6	7	8	9	10
I don't feel safe exercising in my neighbourhood	1	2	3	4	5	6	7	8	9	10

11.4. Physical activity status

5. Would you describe yourself as:

very active ☐ moderately active ☐ somewhat active ☐ inactive ☐

11.5. Godin-Leisure-Time Physical Activity Questinonaire

6. During a typical 7-Day period (a week) how many times on the average do you do the following kinds of activities for more than 15 minutes?	Times per week	Minutes each time
Strenuous activities (heart beats rapidly) e.g. heavy garden work, digging, running, jogging, vigorous sports, fast swimming, fast bicycling		
Moderate activities (not exhausting) General gardening, vacuuming, washing windows, fast walking, easy bicycling, badminton, dancing		
Mild activities (minimal effort) e.g. easy walking, golf, bowling, yoga		

Appendix 12- Study Protocol PARC- Version 1

PROTOCOL

1. INTRODUCTION

1.1 Background to the study

In the UK, colon cancer (CC) is the second most common type of cancer by absolute incidence in males and females combined. Malignant neoplasms of the colon were responsible for 8248 deaths in England and Wales in 2010, of which 95% were in persons aged 60 or over (Office for National Statistics, 2011). The aetiology of CC follows the adenoma-carcinoma sequence model described by Fearon & Vogelstein (1990); whereby mutations can inactivate tumour suppressor genes and concurrently activate oncogenes associated with tumour development. This can lead to the formation of benign abnormal tissue, known as an adenoma. Adenomas usually take the form of polyps (small extrusions on the lining of the large intestine) which can eventually become cancerous. Since this seminal work, the model has been updated to account for the genetic and epigenetic disparities between CC types (Harrison & Benziger, 2011).

A strong body of evidence suggests that lifestyle factors influence cancer risk, and there is now convincing evidence that a physically active lifestyle is associated with reduced risk of developing colon cancer (Wiseman, 2008), a position which is substantiated by several systematic reviews in the field (Friedenreich *et al*., 2010; Samad *et al*., 2005; Slattery *et al*., 2003; Slattery *et al*., 2004). Furthermore, a recent meta-analysis of 52 case-control and cohort studies of the relationship between physical activity and CC estimated that regular physical activity confers a 24% reduction in risk (Wolin *et al*., 2009). In accordance with these observations, American Cancer Society (ACS) guidelines recommend a minimum of 150 min of moderate to vigorous physical activity per week to help reduce the risk of cancer, but one hour per day on at least 5 days per week is likely to bring added health benefits (Kushi *et al*., 2006). However, according to the 2008 Health Survey for England (HSE) self-report measures of physical activity, only 39% of males and 29% of females aged 16 or over are achieving the 150 min per week minimum, and according to accelerometry data, this is as low as 6% and 4% in males and females, respectively (NHS, 2010). Therefore, there is a need for effective lifestyle interventions which are aimed at reducing the risk of CC in populations who are more susceptible to developing the disease.

Research has shown that people recently diagnosed with an illness can be highly receptive to health promotional messages, with the illness forming a 'teachable moment' or a catalyst for lifestyle change (While, 2011). To date, one study (Hoff *et al*., 2001) has established whether informing patients classified as at moderate risk of CC after screening has provoked a lifestyle change. Their findings

suggest that after a 13 year follow up, those informed of the presence of a colon polyp had improved smoking habits and less BMI increase than those not informed.

Few studies have investigated the efficacy of behaviour change interventions in patients classified as being at elevated risk of CC after colonoscopy (Caswell *et al*., 2009, Emmons *et al*., 2005) or flexible sigmoidoscopy (Robb *et al*., 2010). These interventions aimed to decrease risk behaviours such as poor diet, alcohol consumption and inactivity, with a minimal-contact protocol. Only one study (Emmons *et al*., 2005) specified which theoretical model the behaviour intervention was based on. The duration of the studies varied from 10 weeks (Caswell *et al*., 2009) to 4 months (Emmons *et al*., 2005) and 6 months (Robb *et al*., 2010). Participants received printed materials or phone calls ranging from twice per month to once per month and there was no direct contact with the participants. No study was able to show significant improvements in physical activity levels. This might be due to the short duration of the studies or minimal amount of contact time with the participants. Clearly, more effective interventions for engaging patients at elevated risk of CC in regular physical activity are needed. Additionally, further studies of the barriers and facilitators to exercise are needed to understand how these factors interact to influence behaviour change in this patient group.

1.2 Study rationale

1.2.1 Intervention design

Given the low self-reported physical activity levels in elderly populations (NHS, 2010), physical activity interventions for this patient group need to evoke meaningful and sustained changes in physical activity behaviour to increase the potential for improvements in CC risk profile to occur. According to a recent systematic review of lifestyle interventions that targeted weight loss and higher physical activity levels, the effectiveness of an intervention increases when well-defined behaviour change techniques are used (Greaves *et al*., 2011). Increased contact time with the participant was also found to be a predictor of more positive behaviour changes. In accordance with these recommendations, a recent study (Silva *et al*., 2011) investigated the effects of a 1-year behavioural intervention with overweight women over three years of follow-up. Participants in the intervention group received 30 theory workshops aimed at increasing physical activity levels and energy expenditure. After one year, the intervention group achieved significantly higher levels of moderate and vigorous intensity exercise and weight loss in comparison with a control group who received general health advice only. More specifically, mean exercise levels and percentage weight loss in the intervention group were 300 min per week and -7.3%, as opposed to the control group (179min per week, -1.7%). The differences between groups were still significant after 3 years.

The intervention was based on a psychological model called the Self-Determination-Theory (SDT). According to this model, motivation can vary in level and orientation which means that the amount and

type of motivation can differ amongst people (Ryan and Deci, 2000). The more intrinsically regulated a motivation the more autonomously the behaviour is performed, which means the behaviour is carried out because of enjoyment. In turn, more extrinsically regulated motivations are performed with less autonomy which means the behaviour is controlled and performed because one was told to. People are more likely to maintain regular physical activity if the behaviour is intrinsically motivated. On the other hand, when physical activity behaviour is not yet maintained but in a stage of preparation or contemplation, then motivation regulation is more extrinsic (Thogersen-Ntoumani and Ntoumanis, 2006). These findings demonstrate that the effectiveness of an intervention is dependent on the motivation to perform a specific behaviour and they highlight the need to target motivation for a specific behaviour to promote long-term changes in that behaviour.

When implementing such a behaviour change intervention, it is important to understand its efficacy in relation to underlying determinants of behaviour change. Tools have been developed to measure key constructs influencing physical activity behaviour change. In addition, qualitative techniques can be used to gain deeper insights. An intervention that uses the SDT aims to implement changes in autonomy or self-determination, where a change from low autonomy to high autonomy is desired. This is because higher levels of autonomy are associated with greater adherence to a given behaviour over time, and this increases the likelihood for long-term maintenance of the adopted behaviour. It is therefore important to monitor the progress of this change to evaluate the effectiveness of the intervention. Authors Mullan *et al.* (Mullan et al., 1997) developed questionnaires to measure the level of autonomy with which a certain behaviour is performed. However, although autonomy is a predictor of physical activity behaviour, other variables, such as intention and self-efficacy, mediate between the two (Hagger and Chatzisarantis, 2009). Hence, in order to draw conclusions about the constructs that underlie the effects of the intervention, intention and self-efficacy need to be measured alongside measures of self-determination. Finally, as intention, self-efficacy to exercise and self determination to be physically active can be high and actual physical activity behaviour low, it is also necessary to assess the amount of physical activity that is performed over a defined period of time. Several physical activity questionnaires are available for this purpose.

Qualitative methods can also be used to gain a deeper understanding of the multidimensional factors influencing physical activity behaviour. In particular, narrative research allows light to be shed upon previous experiences and how they influence current decisions regarding physical activity behaviour (Carless and Sparkes, 2008). Buman *et al.* (2010) used a narrative interview approach to analyse barriers and facilitators to physical activity within the elderly. His findings accounted for how previous experiences can formulate intention and self efficacy and therefore constructs which could predict initiation and maintenance (McAuley *et al*., 2003). O'Brien-Cousins (1997) reported similar findings which established links between early life accomplishments and past success history, in relation to current self efficacy levels and confidence for physical activity participation.

Through the use of interviews and focus groups at the end of the 12 month intervention, more insight can be gained about personal experiences relating to the impact of the intervention not only with regards to health benefits and wellbeing but also social and psychological influences of taking part in the trial. Barbour (2000) suggested that many theories and health promotional strategies can be formed through the use of qualitative research. These gauge how personal experiences within interventions can influence health promotion messages in the future by drawing on individual accounts of most and least successful aspects. Issues surrounding the recruitment process and maintaining adherence can also be suggested, and prove invaluable when designing interventions of this kind in the future.

1.2.2 Impact of the intervention on CC risk markers

Many studies have attempted to elucidate how lifestyle factors – especially diet – modulate the pathways involved with cancer progression (Lund *et al*., 2011). Despite the relative wealth of evidence in favour of a physically active lifestyle, the mechanisms by which it dictates any changes in CC risk are largely unknown. To date, only one randomised controlled trial has examined the effect of exercise on physiological risk markers associated with CC in sedentary individuals, the findings of which were published in three papers (Abrahamson *et al*., 2007; Campbell *et al*., 2007; McTiernan *et al*., 2006). Although a 12 month exercise programme resulted in favourable changes in colonic cell growth patterns, especially in males who improved their aerobic fitness by > 5% (Abrahamson *et al*., 2007; Campbell *et al*., 2007), the effects upon important genetic/epigenetic markers, nuclear beta-catenin status and indices of chronic inflammation were not examined. Recent work has indicated that these markers are associated with CC stage and prognosis, and might serve as predictive tools in individuals at risk. Widespread aberrant DNA methylation, including a general loss of DNA methylation from the genome (global hypomethylation) together with CpG island (CGI) hypermethylation of tumour suppressor genes is a hallmark of advanced CC (Harrison & Benziger, 2011), and there is much potential in using CGI methylation status in genes known to be associated with colon carcinogenesis (e.g. *APC, WIF1, SFRP1, MGMT, p14, p16*) as indicators of risk (Hughes *et al*., 2012; Kim *et al*., 2010; Walther *et al*., 2009). Indeed, marked differences in CGI methylation exist in such genes between normal and neoplastic colon tissue (Belshaw *et al*., 2008), and increased aberrant DNA methylation is associated with poorer prognosis in colorectal cancer patients (Kim *et al*., 2010; Mitomi *et al*., 2010). Furthermore, negative nuclear beta-catenin/CTNNB1 status appears to be associated with improved disease-specific survival in colorectal cancer patients who undertake ≥ 18 MET hours/wk of physical activity, but not in individuals with a positive status (Morikawa *et al*., 2011). Similarly, disease free survival in stage III CC patients undertaking ≥ 18 MET hours/wk of physical activity was improved by 47% compared with their inactive counterparts (Meyerhardt *et al*., 2006).

Current research has also suggested that chronic, systemic inflammation – whilst known to be a feature of the neoplastic milieu – might predispose individuals to greater CC risk (Chan *et al*., 2011; Kim *et*

al., 2008), perhaps through aberrant cytokine-induced activation of signalling pathways associated with tumorigenesis (Terzic *et al*., 2010). Moreover, regular exercise is known to exert a potent anti-inflammatory effect (Petersen & Pedersen, 2005), and it is therefore possible that reductions in chronic inflammation achieved by an active lifestyle might confer decreased likelihood of CC initiation in populations at risk.

2. PURPOSE OF THE STUDY

The purpose of this study is to investigate the effects of a 12-month physical activity intervention on physical activity behaviour and biological markers of CC risk in individuals classified as being at elevated risk of developing further polyps following surveillance colonoscopy. The physical activity intervention will use self-determination theory (SDT) to create an autonomy-supportive environment, an approach that was recently shown to evoke greater physical activity levels and weight loss than general health education in overweight women (Silva *et al*. 2010). Secondary outcomes will explore the impact of the intervention on aerobic fitness, health-related quality of life and the underlying determinants of behaviour change (i.e. self-efficacy, intrinsically motivated regulation, etc). In addition, interviews and focus groups will be used to obtain narrative accounts of patient experiences, their perceived health benefits from participating in the intervention and the barriers and facilitators influencing adherence.

3. STUDY HYPOTHESIS

Patients randomised to the intervention group will have higher physical activity levels and improved CC risk profile in comparison to usual care controls after 12 months.

4. METHODS

4.1 Study design

The proposed study is a randomised controlled trial, with participants stratified for risk status (‘high’ or ‘intermediate’). Participants will be randomly allocated to either the physical activity intervention (Active Lifestyle Programme: ALP) (Fig 1) or the usual care control group (UC) (Fig 2). Participants randomised to UC will receive usual medical care but no specific lifestyle advice or exercise sessions. Outcomes will be assessed at baseline, and after 3, 6, 9 and 12 months (Table 2).

Fig 1. Study Design for Active Lifestyle Programme (ALP)

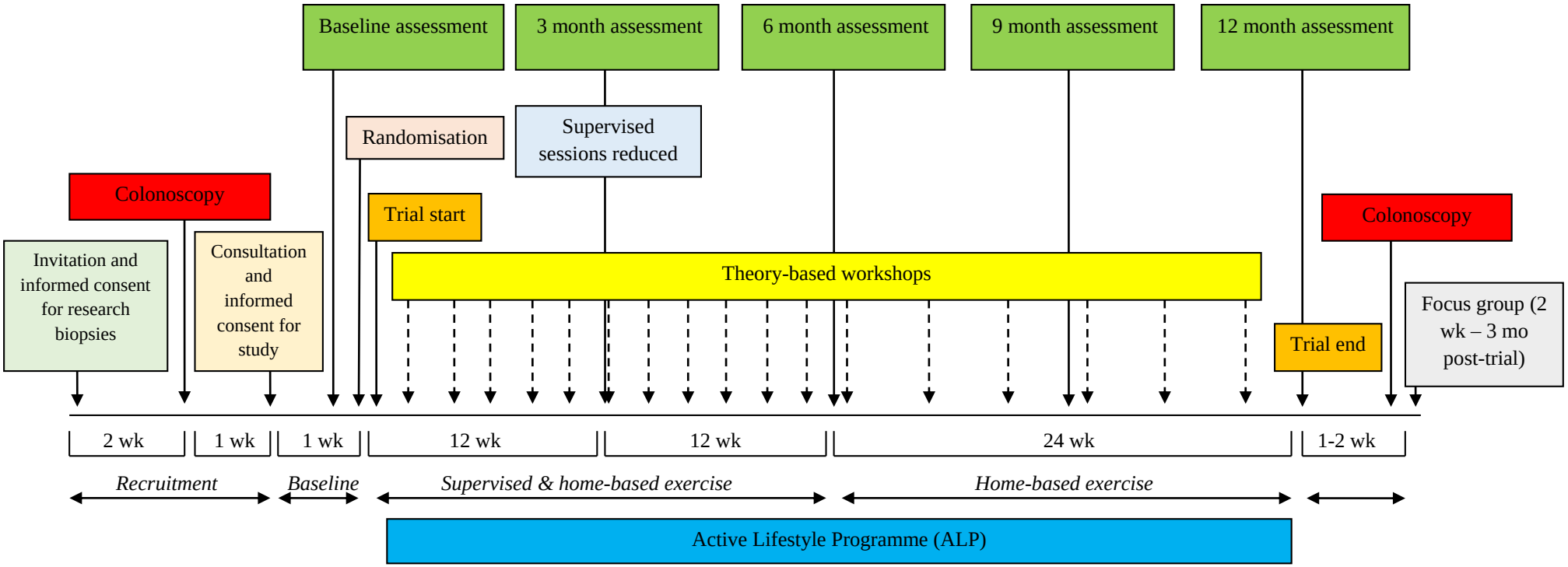
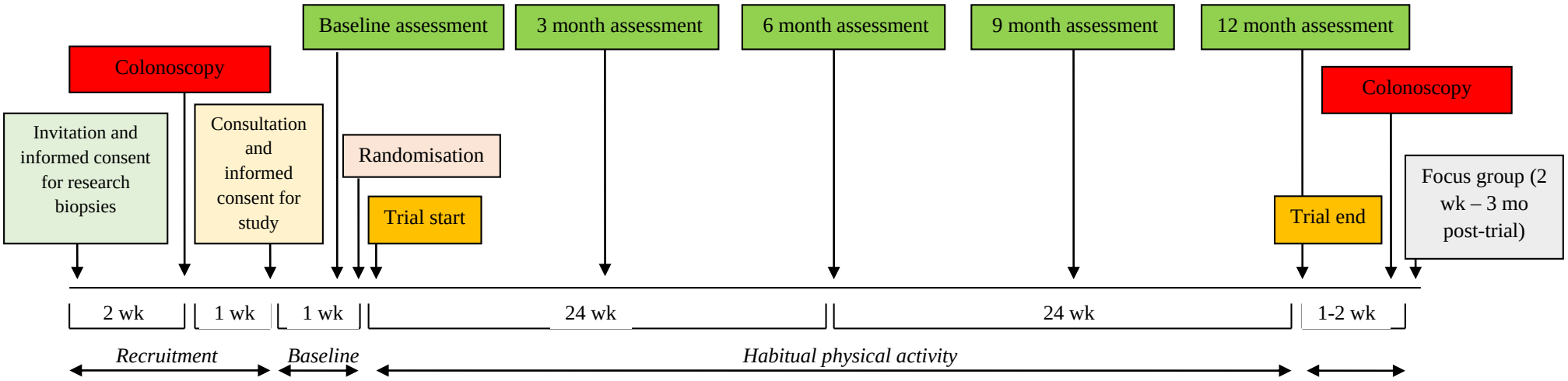


Fig 2. Study Design for Usual Care (UC)



4.2 Participants

Participants will be patients attending the Norwich and Norfolk University Hospital (NNUH) Gastroenterology Unit for a screening colonoscopy as part of the NHS Bowel Cancer Screening Programme. Only individuals who have a positive test result after a faecal occult blood test (FOBT) are referred for a screening colonoscopy at the NNUH. Those who are deemed 'intermediate' or 'high' risk for the development of further polyps as a result of the procedure will be eligible to take part in the study. Inclusion criteria are i) diagnosis of 'intermediate' to 'high' risk as a result of the screening colonoscopy; ii) aged 60 years and above and iii) physically able to partake in regular exercise. Exclusion criteria will include i) assignment into the 'low risk' category or diagnosis of colorectal cancer following the colonoscopy; ii) physical activity levels that meet the most recent American Cancer Society (ACS) guidelines for maintenance of health for at least the past 6 months; iii) presence or history of other co-morbid conditions which might preclude patients from safely undertaking regular exercise, including cardiovascular or pulmonary disease or stroke; iv) presence of other colorectal conditions (e.g. inflammatory bowel disease) or known familial colorectal cancer syndrome; v) chronic use of any treatments or alternative therapies that may affect the results of any study of colorectal tissue e.g. high corticosteroid, anticoagulant or laxative use, regular enemas, high dose vitamin or antioxidant supplements, etc.; vi) previous diagnosis of cancer; vii) inability to adequately understand written and spoken English, viii) presence of drug controlled type II diabetes mellitus and ix) current involvement in other ongoing research. Current health and demographic data will be captured from consenting participants using a bespoke questionnaire designed by the researchers (The UEA PARC health questionnaire; see Appendix 1). Data captured will include age, gender, ethnicity, medication profile (type of medications, dosage level and frequency), family history of colon cancer, co-morbidities, spouse present in the home, occupation, socioeconomic status (estimated using first half of participant's postcode), level of education, current involvement in ongoing research, alcohol consumption, smoking status and number of GP visits in the past year. The questionnaire will be administered again after 12 months to monitor any changes that occur during the trial.

4.3 Recruitment and informed consent

4.3.1 Recruitment via National Bowel Cancer Screening Programme

Patients attending the hospital for their pre-assessment (1-2 weeks prior to their screening colonoscopy) will be given a study invitation letter, a patient information leaflet and a consent form. The form will request their approval for the collection of five small research biopsies if they are classified as intermediate or high risk during the colonoscopy (See Appendix 2). On the day of their screening colonoscopy, patients will return their signed consent form if they are happy for the research biopsies to be taken, and the colonoscopist will be informed of the patient's willingness to participate in the study. A letter will also be sent to their GP outlining their interest in the study and providing contact details if they have any further questions (Appendix 3)

If the patient is identified as falling into a high or intermediate risk polyp group, five small research biopsies will be taken from the sigmoid colon by the colonoscopist and placed in RNAlater® formalin, Carnoy's fluid or frozen in dry ice for the subsequent collection by the research team. When the patient returns to the hospital for their results (approx 1-2 weeks later), those who consented to having research biopsies taken will be informed if this was carried out and whether they are eligible for the study. The contact details of eligible patients will be passed on to the researchers by the bowel cancer screening nurse subject to further consent (Appendix 4). Patients who consent to be contacted will be telephoned by the researchers within a week to organise an appointment at the exercise facility at The University of East Anglia. At the appointment, the researchers will explain the study and give the potential participant the opportunity to ask any questions before gaining full written informed consent (Appendix 5). During this meeting, participants will be given equipment for monitoring their baseline physical activity levels and a questionnaire booklet which includes measures of physical activity and behaviour change determinants (Appendix 6).

After randomisation, based upon an initial agreement of contact regarding the qualitative aspects of the research and baseline demographic data, approximately 10 participants from both the ALP and UC group will be sent a further information sheet detailing the content of the interviews at 1 and 12 months. These participants will be contacted a week later to arrange a date for their initial interview. At the interview a further consent stage will be established with specific qualitative criteria. The process will be repeated after the intervention for the focus group participants (Appendix 7). Health professionals within the gastroenterology unit at the Norfolk and Norwich University Hospital will be invited to attend a presentation introducing the study, including information about the focus group topic and what can be

expected of them if they agree to participate. Here Miss K Semper will give out 'Information about the Research – Focus Group, Health Professionals' (Appendix 7) and then gain permission from interested participants for their contact details to be passed on to the researchers. Within a week interested participants will be contacted and a date for the focus group arranged.

4.3.2 Recruitment via Big C charity

Posters and flyers will be posted at the Big C facility in Norwich which is located near the NNUH and on the Big C website (Appendix 8). These briefly introduce the topic of the research and what can be expected by the participant. Contact details of the researchers are printed on the posters. In the event that an interested potential participant contacts a researcher, the study will be explained fully to them via the phone and further questions will be answered. The research team will make the interested potential participant aware of the colon cancer screening programme or, if they are already enrolled in the programme, advise them to ask the specialist nurse at the NNUH when they are scheduled for their next colonoscopy appointment about the 'Active Lifestyle Programme'. Recruitment will then proceed as described above (4.3.1).

4.4 Randomisation

After baseline measures have been completed, participants will be randomised into the control or intervention group and stratified by risk status (intermediate/high). Randomisation will be completed using a bespoke programme based at the Institute of Food Research. Participants will be assigned a unique code which blinds the researchers as to their group allocation during analysis. A further code which details time of sampling for the repeated measures during the proposed study will also be used.

4.5 Usual Care (UC) Group

The UC group will not receive an intervention or any other form of advice in regards to lifestyle behaviours. However, they will have the opportunity to take part in a limited number of supervised exercise sessions and receive an intervention workbook at the end of the study. They will not receive any lifestyle advice or supervised exercise sessions until the end of the 12 months study period. There is the possibility for some participants in the UC group to be contacted from one of the researchers to be included in the qualitative interviews or focus groups.

Participants in the UC group will undertake the baseline measures and repeat these at the same time points as ALP. This will include fitness test, body composition, blood samples and all questionnaires at 6 and 12 months and some selected questionnaires at an additional two time points, at 3 and 9 months of the study.

4.6 Physical activity intervention (ALP)

All participants in ALP will attend a familiarisation session in the week before the trial starts. They will be introduced to the equipment available in the exercise facility (treadmill/rowing machine/cycle ergometer). The researchers will also demonstrate the various resistance/bodyweight exercises that the participants will be required to perform. These will include bicep curls, dumbbell flys, sit-ups and chest extensions (with Theraband). In the first 12 weeks of the study, participants will attend the exercise facility on 2 d/wk (time of day to be at the discretion of the researchers and participants) and complete a supervised exercise session. This will consist of a ten minute warm up, 30 minutes of aerobic exercise at 65-80% maximum heart rate (HR) as determined by the $\dot{V}O_{2\ max}$ test (it is acknowledged that some participants will be unable to exercise at 80% max HR for 30 min at the onset of the trial, so intensity will be adjusted accordingly to ensure a full 30 min bout is completed) and 30 min of resistance exercise using the exercises described above. Sessions will follow the principles of progression and overload such that participants continue to improve their fitness. On ≥ 3 days per week, participants will complete home-based exercise to complement these sessions. In the second 12 weeks of the study, supervised exercise at the exercise facility will take place on 1 d/wk only, and home-based exercise will take place on ≥ 4 d wk. For the remaining 24 weeks, participants will be expected to complete ≥ 300 min of moderate to vigorous exercise per week, spread over ≥ 5 days.

4.6.1 Physical Activity Workbook

To encourage exercise participation and maintain adherence, ALP will be provided with a bespoke physical activity workbook (the PARC workbook) designed by the researchers, which outlines suggestions for physical activity, and includes physical activity logs, progress monitors and contact details of the researchers. The participant will keep this workbook for the duration of the trial. Furthermore, ALP will be provided with pedometers, which will be used as a motivational tool to promote exercise (i.e. brisk walking) behaviour (Appendix 8).

4.6.2 Active Lifestyle workshops

Theory-based workshops will take place at the University of East Anglia every fortnight for the first 6 months of ALP and once a month for the remaining 6 months. The workshops will be based upon the Self-Determination Theory (Ryan & Deci, 1985) and will cover a range of topics including goal-setting and exercise barriers (Table 2). The workshops will be designed and delivered by Miss Liane Thomas. During the first 24 weeks of ALP, ALP will attend one workshop every two weeks after a supervised exercise session, which will last for approximately 30-45 min. This will continue for the remaining 24 weeks once per month, with participants attending the workshops without completing a supervised session beforehand (all exercise will be home-based by this point). An outline of the workshops is presented in Table 1.

Table 1. List of ALP workshop topics and schedule.

Week	Content
	Theory session
1	• Programme introduction • Key dates, follow-up testing • Benefits of exercise • Contra indication • Risk and safety of exercise • Exercise kit (shoes, bad weather kit)
	• Suggestions for home exercises with demonstration • How to use Therabands • Stretch exercises
3	• previous exercise experiences • Find gaps during the day to exercise What types of exercises would I enjoy?
	• Monitor exercise intensity ○ Exercise knowledge (training principles)
5	• Goal setting • Set SMART goals • The physical benefits of routine activities (e.g. gardening, housework, etc.)
	• Reflection on home exercising • Discuss barriers and how to overcome them • Personal goals evaluation and suggestions

	• Evaluation of exercise sessions
	  ○ Enjoyment
	  ○ Suggestions
	• Expectations

7	• Re-assess goals

	• Are you meeting your target exercise levels? • Do you have problems meeting your targets?
	• Discussion about feelings of last few weeks exercise regime. • How do you feel about exercising? • Discuss barriers with others and find own strategies to overcome these (how do others deal with barriers) • Compare goals achieved
	• How to involve friends and family • Discuss exercise opportunities in neighbourhood (parks, pavements, bike paths, gyms, etc)
9	• Re-evaluation of barriers and goals • Environmental constructing (building cues to exercise to remind to perform behaviour, suggest active programmes around the area, ...) • Exercise planning and building into daily routine • Planning strategies • How to overcome relapses • E.g. after holiday, injuries • Coping with environmental factors that may prevent exercise • How to adapt exercise plan to other unplanned changes in schedule
11	• Review barriers • Review goals • Reflect on the last few months of exercise • How do you feel? • Do you enjoy the activities you do? • Have you noticed benefits? • Achievements throughout the programme • Review exercises (types, time spent on it) and what has been learnt? • Make an action plan for home exercise and find other activity programmes in the area • How likely do you think, is it that you will follow the plan after the end of the study? • Where do you see difficulties
	• Final discussion of Barriers and goals • Future plans and strategies

4.7 Outcomes

An overview of the outcome measures can be seen in Table 2. All outcome measures will be repeated after 6 and 12 months. A sample of selected questionnaires will be repeated after 3 and 9 months in addition to this. To minimise bias due to perceived expectancy, all physiological samples collected will be coded so as to blind the researcher conducting the analysis (BS) as to the group allocation and time of sampling. The subjective nature of the self report instruments used for evaluation of the intervention is accepted and every effort will be made to minimise potential bias due to this dynamic. In particular, patients may over or under report their health

status depending on the trial arm to which they have been assigned - although randomised, it will be obvious to the participants which arm of the trial they are in. Baseline primary self-report assessments will however be completed by the participants before they are randomised. Due to the one-to-one participatory nature of the intervention, it will not be possible to blind study participants to their group allocation. However, analysis of outcome measures will be conducted by a researcher that is blind to group allocation. The Qualitative researcher, although aware of each participant's group randomisation upon interview, will have no additional contact with the purposefully selected participants throughout the 12 month intervention.

4.7.1 Primary outcomes

4.7.1.1 Physical activity

Objective free-living physical activity levels will be assessed over 7 days using accelerometry (ActiGraph®). The small unobtrusive accelerometer is worn on the hip and collects data on activity counts, step counts and total exercise energy expenditure. Self-reported physical activity will also be assessed using the International Physical Activity Questionnaire (IPAQ) (Friedenreich *et al*., 1998) and the Godin Leisure Time Exercise Questionnaire (Godin and Shephard, 1997). Both questionnaires are self-administered and use a 7-day recall period. The IPAQ is designed to measure four domains of physical activity: 1) Job-related; 2) Transportation; 3) House work; and 4) Recreation, sport and leisure-time. An additional question asks for the time spent sitting. Amount of exercise in MET-minutes per week is calculated by multiplying minutes and intensity of specific activity undertaken. The validity of the IPAQ has been rated as acceptable for the different activity domains (Hagstromer *et al*., 2006). The Godin Leisure Time Exercise Questionnaire is a short four-item questionnaire that assesses the number of times that strenuous, moderate or mild exercise was performed for more than 15 min over the last 7 days.

4.7.1.2 CC risk markers

Biopsies will be collected at initial surveillance colonoscopy (baseline) and after 12 months at their follow-up visit. Five small research biopsies of the sigmoid colon will be obtained during the screening colonoscopies. Two biopsies will be placed in fixative solutions (one in 10% formalin and one in Carnoy's fluid), two in RNAlater ® and one frozen on dry ice, for collection and transfer to the Institute of Food

Research. Samples will be stored at -80℃ until analysis. Biopsies will be analysed for global DNA methylation status by quantifying the methylation of the repetitive elements LINE-1, Alu and Satellite repeats, previously demonstrated to be suitable surrogate indices of global methylation, using a qPCR assay adapted from Iacopetta *et al*. (2007). Gene-specific CGI methylation status of a panel of genes previously shown to be involved in colon carcinogenesis and whose methylation status has also been demonstrated shown to be susceptible to environmental influences (Tapp *et al*. submitted) (e.g. *APC, WIF1, SFRP1, MGMT, p14, p16*) will also be determined using a quantitative methylation-specific PCR (QMSP) assay developed at the Institute of Food Research (Belshaw *et al*., 2008). RNA and protein expression regulated by these genes will be analysed by quantitative real-time polymerase chain reaction (PCR) and Western blotting, respectively. In addition, nuclear CTNNB1/beta-catenin status in colonic cells will be measured using immunohistochemical methods, which will detail its expression (none, weak, strong) and distribution (nucleus, cytoplasm, membrane). Markers of chronic inflammation (e.g. TNFα, IL-10) will also be investigated by multiplex ELISA. Mitotic and apoptotic figures and colonic crypt dimensions will be determined in microdissected crypts from Carnoy's fixed colon sections using the Feulgen's staining method established at the Institute of Food Research. Cross-validation of crypt cell proliferation and apoptosis rates will be obtained by immunohistochemical labelling of crypt sections for Ki67 and activated caspase 3. The phosphorylation and expression of regulatory proteins involved in signalling pathways known to be associated with colon cancer progression (e.g. ERK, AKT) will also be determined by Western blotting.

4.7.2 Secondary outcomes

4.7.2.1 Blood and buccal cell markers of CC risk

Venous blood will be obtained by venepuncture of the left or right antecubital vein by a trained phlebotomist. 2 x 5 ml of venous blood will be transferred into a plasma collection tube containing EDTA anticoagulant and gently agitated. Once collected, whole blood samples with EDTA will be refrigerated at 4℃. A further 2 x 5 ml of venous blood will be transferred into a serum collection tube and left to clot for 30 min at ambient temperature. Buccal smears will also be obtained. All samples will be subsequently transferred to the Institute of Food Research. Here, serum will be centrifuged at 2500 g at ambient temperature for 15 min, and the supernatant aliquoted into cryovials for storage at -80℃. Remaining whole blood will also be

stored at -80℃. The methylation status of DNA extracted from peripheral blood leukocytes and buccal cells will be analysed using the techniques detailed in section 4.7.1.2 above.

4.7.2.2 Anthropometry and cardiopulmonary fitness

Stature, body mass, body mass index (BMI) and waist-hip ratio will be measured using standard techniques. Cardiopulmonary fitness will also be assessed at baseline and after 6 and 12 months. Before the cardiopulmonary exercise test, participants will complete the Physical Activity Readiness Questionnaire (PAR-Q) (Thomas *et al*., 1992) (Appendix 10). This questionnaire is developed to determine the safety or risk of exercise for the participant by answering a series of health-related questions. Resting blood pressure and a 12 lead ECG will also be taken prior to the test. Participants will then perform a test of maximal aerobic capacity ($\dot{V}O_{2\,max}$) on an electronically braked cycle ergometer, which should last for approximately 8-12 min. The test starts with a 2 min freewheeling-period and intensity increases every 2 min by 25 Watts until exhaustion. During the test, a continuous ECG trace will be monitored by a medical professional, and the test will be stopped immediately should any abnormalities arise during the exercise bout. Once the participant has reached their $\dot{V}O_{2\,max}$ and is unable to continue, the test will finish and the participant allowed to 'freewheel' for as long as they deem necessary. Participants will then have the opportunity to shower and change and will be allowed to leave after their resting heart rate and blood pressure has been checked. This will be completed at baseline, and 6 and 12 months thereafter (Table 1).

4.7.2.3 Dietary analysis

Participants will complete a 4 day food record specifying any foods or liquids ingested, their approximate mass, and time of consumption. Completed records will be analysed for dietary macronutrient and micronutrient composition using the CompEat 5 (Nutrition Systems) software package. This will be completed at baseline and at, 3, 6, 9 and 12 months thereafter (Table 2).

4.4.2.4 Psychological measures and health related Quality of Life (QoL)

Participants randomised to the ALP will receive a questionnaire booklet (Appendix 6) which contains all self-report questionnaires and a 4-day food diary**.** This will be completed at home and returned at their next visit to the research facility. A researcher will give instructions on how and when to complete the questionnaires

and will check through them with each participant when they attend the research facility for other assessments. The assessment booklet will include the following questionnaires:

Behaviour Regulation for Exercise Questionnaire (BREQ)

The BREQ, designed by Markland and Tobin (Murcia et al., 2007), measures the continuum of motivation regulation, components of the Self-Determination Theory. It has been used widely in the sports and exercise domain. Questions are designed to measure amotivation, extrinsic, introjected, identified and intrinsic motivation for exercise. Nineteen items are rated on a scale from 1 ('not true for me') to 4 ('very true for me').

Short Form-36

The 36 item self-administered quality of life questionnaire was developed to be used in a generic setting with no target on a specific age group or disease. Numerous studies have used the SF-36 in a variety of clinical settings. Reliability has been tested extensively and results exceed the minimum standard of 0.70 advocated for group comparison measures. It consists of an 8-scale profile of physical and mental health scores: Physical Functioning, Bodily Pain, Role- physical, General- Health, Vitality, Social Functioning, Role Emotional, and Mental Health. Responses to each item are produced on a 5- Point- Likert Scale.

Self- Efficacy for Exercise (SEE)

The self-efficacy scale is a 9- item questionnaire assessing the participant's confidence to exercise under different situations such as pain, bad weather or being tired. On a scale from 0 (not very confident) to 10 (very confident) the participant assesses their confidence to exercise 30 minutes on most days of the week when confronted with such a situation. Items are developed specifically for an elderly population.

Intention to exercise:

This short two-item questionnaire assesses participant's intention to exercise regularly for the next month and for the next 6 months. Responses are rated from 1 (Do not agree at all) to 7 (Completely agree).

4.4.2.5 Qualitative analysis

Ten participants from both ALP and UC will be purposefully sampled and invited to take part in face-to-face interviews at 1 and 12 months. The purposive sampling frame will draw on priority criteria ensuring diversity in conceptually relevant characteristics of potential participants, to include: age, sex and baseline fitness ($\dot{V}O_{2\,max}$). Additionally, three focus groups will be administered at the end of the intervention with the ALP, UC and relevant health professionals (HP). For detailed Interview and Focus group designs see Appendix 10. Separate information sheets and consent forms (see Appendix 7) will be given to the trial participants at the end of the intervention phase, which will represent a separate consent stage for the focus groups at the end of the 12 month intervention. The main information sheet provided at the start of the trial will state that after the completion of the intervention participants may be asked to participate in a structured focus group. All qualitative measures will take place within the University of East Anglia, and will be audio recorded for analysis purposes – participants will also be made aware of this in the initial patient information sheet. All interviews and focus groups will take approximately 60 minutes. Interviews will also ideally be scheduled when other outcome measures need to be taken – for example at baseline and trial termination.

Interview 1 *(Start of Intervention)*

Aim: Narrative accounts to gain information regarding how various life experiences and attitudes towards physical activity shape beliefs surrounding a physically active lifestyle in the present day for each individual.

Other Objectives:

- Establish level of knowledge regarding the benefits of physical activity, especially within this specific population.

- Conclude if too little information is provided to this specific population regarding the health benefits of physical activity and gauge views as how best to administer this advice, and at what stage throughout adulthood

- Identify key barriers and facilitators to physical activity in this population and establish whether the risk diagnosis has provided a ‘teachable moment’ in these individuals.

Analysis: *Grounded Theory Approach* **-** Identify key concepts formed within the narrative accounts, and group these into categories with the final aim to create novel theories in order to better explain the participant of the research.

Interview 2 *(End of Intervention)*

Aim: Semi-structured interviews post intervention will be defined mainly upon emergent analysis from initial interviews to establish thoughts on the 12 month intervention and how attitudes towards physical activity may have changed.

Other Objectives:

- Compare experiences from the supervised and home based exercise interventions to establish a successful framework for future intervention.
- Establish whether this length of exercise intervention is sufficient enough to elicit a long term motivation to maintain physical activity.
- Assess the importance of group randomisation, effects of being placed in the control group.

Analysis: *Grounded Theory Approach* **-** Identify key concepts formed within the interviews, and group these into categories with the final aim to create novel theories in order to better explain the participant of the research.

Focus Groups *(End of Intervention)*

Aim: To compare and contrast differing experiences within the 12 month intervention and also cross compare issues regarding the recruitment and adherence to these sorts of studies with experienced health professionals.

Other Objectives:

- Hear thoughts on the intervention as a whole from both the exercise and control group in order to gain valuable insight for future intervention design.

Analysis: Broad thematic analysis will be used to analyse focus group date and identify emerging themes.

Table 2. Measurements taken from participant, their frequency and time of sampling

Type	Item	*Baseline*	*3 months*	*6 months*	*9 months*	*12 months*
Physiological	Colon tissue	✓	×	×	×	✓ (high risk only)
	Venous blood	✓	×	✓	×	✓
	Buccal smear	✓	×	✓	×	✓
Psychological	SF-36	✓	×	✓	×	✓
	SEE	✓	✓	✓	✓	✓
	BREQ	✓	✓	✓	✓	✓
	Intention	✓	✓	✓	✓	✓
Qualitative	Interview	✓	×	×	×	✓
	Focus group	×	×	×	×	✓
Habitual Physical Activity	Godin Leisure Time Exercise Questionnaire	✓	✓	✓	✓	✓
	IPAQ	✓	✓	✓	✓	✓
	Accelerometer(7 days)	✓	✓	✓	✓	✓
Diet	Food record (4 days)	✓	×	✓	×	✓
Fitness	Exercise capacity	✓	×	✓	×	✓
	12 lead ECG	✓	×	✓	×	✓
	Mass/BMI/Waist-hip ratio/body fat %	✓	✓	✓	✓	✓
	Heart rate/Blood pressure	✓	×	✓	×	✓

4.8 Statistical analysis

4.8.1 Sample size calculation

4.8.1.1 CGI methylation

The sample size was based upon the numbers required to demonstrate a clinically important change in aberrant CGI methylation and leisure-time physical activity as determined by the Godin Leisure-Time Exercise Questionnaire (Godin & Shephard, 1997). Previous work has demonstrated that aberrant CGI methylation in key genes is inversely related to the progression of sporadic CC (Grady & Carethers, 2008; Kim *et al*., 2010). Indeed, aberrant activation of the Wnt signalling pathway is a

common pathological feature of colon carcinogenesis. One reason for this is that the gene encoding the lipid binding protein Wnt inhibitory factor 1 (WIF1) that can inhibit this pathway is frequently methylated. Therefore, the statistical power for the present study is based on the assumption that exercise will i) significantly reduce the proportion of participants in whom the WIF1 gene is methylated in > 11% of alleles, and ii) reduce their WIF1 methylation profile by the equivalent of ten years of ageing. The 11% threshold was based upon data collected from the Biomarkers of Risk of Colorectal Cancer (BORICC; Food Standards Agency) study which indicated that 11% of participants aged between 47 – 53 have > 11% of WIF1 alleles methylated, compared with 33% in those aged from 57 – 63. To achieve a significant reduction ($P \leq 0.05$, 80% power) of WIF1 gene methylation from 33% to 11%, in participants with > 11% of WIF1 alleles methylated, it was calculated that n = 124 (i.e. 62 participants per group) is required. However, an attrition rate of 15-20% is to be anticipated based on former studies.

4.8.1.2 Leisure-time physical activity

Previous work in elderly colon cancer survivors has suggested that to demonstrate a meaningful increase in physical activity levels according to the Godin Leisure-Time Exercise Questionnaire (Godin & Shephard, 1997) after a 12 week exercise intervention (associated with significant improvements in functional fitness), at 90% power, alpha 0.05 and an effect size of 0.713, a total of 86 participants is required (43 per group). A total of 124 participants should thus be sufficient to demonstrate any changes in these outcomes.

4.8.2 Measuring effects

All quantitative data will be analysed by a researcher blinded to participant identity and group allocation (BS) using appropriate statistical tests. These will be performed on the 'R' Statistics package (R Core Development team, http://www.R-project.org) based at the Institute of Food Research. Ongoing assistance will be provided by the in-house statistics team at the Institute.

4.8.2.1. CGI methylation, inflammatory markers and protein phosphorylation /expression

Change in global CGI methylation (i.e. percentage of alleles methylated in all genes studied) and two-way analysis of variance (ANOVA) for treatment x time. Percentage change in the CGI methylation profile of specific genes will be detected

by n way analysis of covariance (ANCOVA) to determine the relative effects (if any) of covariates including age, group allocation, BMI etc. N way ANCOVA will also be used to detect differences (if any) in chronic inflammation for each individual marker and differences in phosphorylation and expression of signalling proteins involved in pathways associated with CC progression.

4.8.2.2 Colonic cell proliferation/beta-catenin status

Change in distribution of colonic cell apoptosis, mitosis and beta-catenin status pre and post intervention within groups will be assessed using the χ^2 test. In addition, the tests will be performed between ALP and UC at baseline and post-intervention to detect any differences in distribution between groups.

4.8.2.3 Questionnaire responses

Responses to questionnaires will be compared using Student's t test to detect differences between ALP and UC. Where data is non-normally distributed, a Mann-Whitney test shall be employed instead.

4.9 Project timetable

The project will take place over 2.5 years (30 months) including preparation and write up/ dissemination time. Participants will be recruited on a 'rolling' basis, so that as participants go through the trial, new ones will be recruited. The estimated time from the first participants beginning the trial to the final participants ending the trial is 18 months.

Appendix 13- Summary of amendments PARC

Amendment number	Summary
#1:	The amendment was created to allow the researchers to take consents for the biopsy procedures to facilitate recruitment. Before the amendment, only nurses were allowed to take consent.
#2	i) Incorporate all workshop material into the first 6 months of the study, instead of spreading intervention material over the follow-up period. ii) Change buccel and bowel tissue to be primary outcome measure
#3	Include patients who have undergone screening colonoscopy in the past 3 years instead of only patients who were newly diagnosed with polyps. These patients were approached via invitation letter.
#4	`To include patients with a 'low' risk polyp
#5	To include patients who were referred by their GPs to a screening colonoscopy and allow researchers to approach patients at the hospital
#6	There are was a mistake with the version number on the patient information sheet as a result from a previous amendment. This was rectified with this amendment.
#7	This amendment was for another PhD student, Kelly Semper, to allow her ask patients the reasons for not participating.
#8	An amendment to allow surveys to be sent to non-participants.

Appendix 14- PARC Study approval from Research Ethics Committee

NHS
Health Research Authority
NRES Committee East of England - Norfolk
Victoria House
Capital Park
Fulbourn
Cambridge
CB21 5XB

Telephone: 01223 597733
Facsimile: 01223 597645

16 May 2012

Sent by email 16 May 2012

Professor John M Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Room 2-8 Queen's Building
University of East Anglia
Norwich
NR4 7TJ
john.saxton@uea.ac.uk

Dear Professor Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**

Thank you for your letter of 16 April 2012, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair.

Confirmation of ethical opinion

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

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Notification(s) of no objection have been received from local assessors for the non-NHS site(s) listed in the table below, following site-specific assessment (SSA).

I am pleased to confirm that the favourable opinion applies to the following research site(s), subject to site management permission being obtained prior to the start of the study at the site (see under 'Conditions of the favourable opinion below').

Research Site	Principal Investigator / Local Collaborator
The University of East Anglia	Professor John M Saxton

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

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

Document	*Version*	*Date*
Advertisement	2	13 April 2012
Covering Letter from Professor John Saxton		17 February 2012
Evidence of insurance or indemnity Zurich Municipal		28 June 2011
GP/Consultant Information Sheets GP letter	1	14 February 2012
Interview Schedules/Topic Guides Interview Design - Active Lifestyle Programme and Usual Care Group	1	14 February 2012
Investigator CV Professor John Saxton		
Investigator CV Dr Nigel Belshaw (Supervisor 1)		
Investigator CV Mr Barnabas Shaw (PhD Student)		21 February 2012
Dr Caitlin Notley (Supervisor)		
Investigator CV Liane Thomas (Student)		21 February 2012
Investigator CV Kelly Semper (Student)		21 February 2012

Letter from Sponsor from Sue Steel, University of East Anglia		17 February 2012
Letter of invitation to participant	2	13 April 2012
Other: PARC - Physical Activity and Risk of Colon Cancer - Active Lifestyle Booklet	1	14 February 2012
Participant Consent Form: - Contact Details	1	14 February 2012
Participant Consent Form: Patient Consent Form	2	13 April 2012
Participant Consent Form: - Initial Biopsies	2	13 April 2012
Participant Consent Form: - Interviews	2	13 April 2012
Participant Consent Form: - Focus Group	2	13 April 2012
Participant Information Sheet: Patient Information Sheet	2	13 April 2012
Participant Information Sheet: - Interview One	2	13 April 2012
Participant Information Sheet: - Interview Two - Control Group	2	13 April 2012
Participant Information Sheet: Interview 2 - Exercise Group	2	13 April 2012
Participant Information Sheet: - Focus Group - Intervention	2	13 April 2012
Participant Information Sheet: - Focus Group - Health Professionals	2	13 April 2012
Protocol	2	13 April 2012
Questionnaire: Health Questionnaire - Medical Information	1	14 February 2012
Questionnaire: Health Questionnaire PARC - Physical Activity and Risk of Colon Cancer	1	14 February 2012
Questionnaire: Physical Activity Readiness Questionnaire (PAR-Q)	1	14 February 2012
REC application IRAS Parts A&B 93475/295463/1/647 and SSIF 93475/295467/7/463/132645/236289		20 February 2012
Response to Request for Further Information from Professor John Saxton		16 April 2012

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views

known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/EE/0106	**Please quote this number on all correspondence**

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

Yours sincerely

pp

Dr Robert Stone
Vice-Chair

Email: Anna.Bradnam@eoe.nhs.uk

Enclosures: "After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Mrs Sue Steel (Sponsor Contact)*
sue.steel@uea.ac.uk

Ms Kath Andrews, (NHS R&D Contact)
Norfolk and Norwich University Hospitals NHS Foundation Trust
kathryn.andrews@nnuh.nhs.uk

Appendix 15- Approval letters for amendments (PARC)

15.1. Amendment #1:

NHS
Health Research Authority

NRES Committee East of England - Norfolk
Victoria House
Capital Park
Fulbourn
Cambridge
CB21 5XB

Tel: 01223 597750
Fax: 01223 597645

12 September 2012

Professor John M Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Room 2-8 Queen's Building
University of East Anglia
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**Amendment #1 Substantial**
Amendment date:	**06 September 2012**
Amendment Summary:	**Informed consent for the biopsy procedure be taken additionally by key investigators Mr Barnaby Shaw and Mrs Liane Lewis in order to facilitate recruitment.**

Ethical opinion

None

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Notice of Substantial Amendment (non-CTIMPs) : Amendment #1 Substantial		06 September 2012

Covering Letter : From Barnabas Shaw		06 September 2012

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

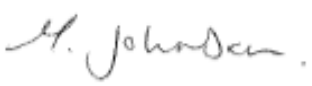
All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely



PP

Michael Sheldon (Chair)
Chair

E-mail: melanie.johnson@eoe.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: Professor John M Saxton: john.saxton@uea.ac.uk
Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust: kathryn.andrews@nnuh.nhs.uk
Mrs Sue Steel: sue.steel@uea.ac.uk

15.2. Amendment #2

NHS
Health Research Authority

NRES Committee East of England - Norfolk

Victoria House
Capital Park
Fulbourn
Cambridge
CB21 5XB

Tel: 01223 596906

17 September 2012

Professor John M Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Room 2-8 Queen's Building
University of East Anglia
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**Amendment #2 Substantial 06/09/2012**
Amendment date:	**10 September 2012**
	(1) Incorporate the workshop material fully into the first 6 months rather than over the 12 month period. (2) Given that a second biopsy will not be obtained from the intermediate-risk group (who constitute approximately 2/3 of our target population compared with high-risk, based on NNUH screening colonoscopy statistics for year 2011), we feel that analysis of changes of blood and buccal cell markers of colon cancer risk should be a primary outcome measure; as opposed to a secondary outcome measure as currently stated in the protocol.

Thank you for submitting the above amendment, which was received on 12 September 2012. I can confirm that this is a valid notice of a substantial amendment and will be reviewed by the Sub-Committee of the REC at its next meeting.

Documents received

The documents to be reviewed are as follows:

Document	Version	Date
Participant Information Sheet	Version 3	06 September 2012
Protocol	Version 3	06 September 2012
Notice of Substantial Amendment (non-CTIMPs)	Amendment #2 Substantial	10 September 2012

Notification of the Committee's decision

The Committee will issue an ethical opinion on the amendment within a maximum of 35 days from the date of receipt.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval for the research.

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely

Har Hari Kaur

Ms Har Hari Kaur
Assistant Committee Co-ordinator

E-mail: har.hari.kaur@eoe.nhs.uk

Copy to: *Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust*

Mrs Sue Steel

Professor John M Saxton
john.saxton@uea.ac.uk

15.3. Amendment #3

NHS
Health Research Authority

NRES Committee East of England - Norfolk
Victoria House
Capital Park
Fulbourn
Cambridge
CB21 5XB

Tel: 01223 596906

12 October 2012

Professor John M Saxton
john.saxton@uea.ac.uk
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Room 2-8 Queen's Building
University of East Anglia
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**Amendment #3 Substantial**
Amendment date:	**27th September 2012**
Amendment summary:	**Include participants who have undergone screening colonscopy in the past 3 years and meet inclusion criteria**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Letter of invitation to participant	Version 3	12 September 2012
Participant Information Sheet	Version 4	12 September 2012

Protocol	Version 4	12 September 2012
Notice of Substantial Amendment (non-CTIMPs)	Amendment #3 Substantial	27 September 2012

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely

P.P. Har Hari Kaur

Michael Sheldon (Chair)
Chair

E-mail: har.hari.kaur@eoe.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Email to: Professor John M Saxton
john.saxton@uea.ac.uk

Copy to: *Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust*

Mrs Sue Steel
sue.steel@uea.ac.uk

15.4. Amendment #4

NHS
Health Research Authority

NRES Committee East of England - Norfolk

Nottingham REC Centre
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

27 March 2013

Prof John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**93475/419101/13/537/15698**
Amendment date:	**27 February 2013**
IRAS project ID:	**93475**

The above amendment was reviewed on 11 March 2013 by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
GP/Consultant Information Sheets	2	01 November 2012
Participant Consent Form: Full study consent form	3	22 October 2012
Participant Consent Form: Biopsy Consent form	1	22 October 2012
Participant Consent Form: Biopsy Consent form	4	22 October 2012
Participant Information Sheet: Patient Information Sheet	5	22 October 2012
Protocol	4	22 October 2012
Covering Letter	Letter from Professor John Saxton	28 February 2013
Notice of Substantial Amendment (non-CTIMPs)	93475/419101/13/537/15698	27 February 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely

Dr Michael Sheldon
Chair

E-mail: leni.smith@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust*
Mrs Sue Steel

15.5. Amendment #5

Health Research Authority

NRES Committee East of England - Norfolk

Nottingham REC Centre
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

27 March 2013

Prof John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**93475/419102/13/644/17310**
Amendment date:	**27 February 2013**
IRAS project ID:	**93475**

The above amendment was reviewed on 11 March 2013 by the Sub-Committee in correspondence.

Ethical opinion
The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents
The documents reviewed and approved at the meeting were:

Document	Version	Date
Letter of invitation to participant	1 - Study Invitation Letter	07 January 2013
Participant Consent Form: Retrospective Biopsy Consent Form	1	16 January 2013
Participant Consent Form: Full study Consent form	1	07 January 2013
Participant Consent Form: Biopsy Consent form	1	07 January 2013
Participant Information Sheet: Retrospective Patient Information Sheet	1	16 January 2013
Participant Information Sheet: Patient Information Sheet	1	07 January 2013
Protocol	5	07 January 2013
Notice of Substantial Amendment (non-CTIMPs)	93475/419102/13/644/17310	27 February 2013
Letter of invitation to participant	1 - Retrospective Invitation Letter	16 January 2013

Membership of the Committee
The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval
All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance
The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely

pp: Dr Michael Sheldon
Chair

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust*
Mrs Sue Steel

15.6. Amendment #6

NHS
Health Research Authority

NRES Committee East of England - Norfolk

Nottingham REC Centre
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

27 March 2013

Prof John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Prof Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**93475/419103/13/362/17356**
Amendment date:	**27 February 2013**
IRAS project ID:	**93475**

The above amendment was reviewed on 11 March 2013 by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Participant Information Sheet: Patient Information Sheet - (for retrospective recruitment)	1	12 September 2012
Notice of Substantial Amendment (non-CTIMPs)	93475/419103/13/362/17356	27 February 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely

pp: Dr Michael Sheldon
Chair

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust*
Mrs Sue Steel

15.7. Amendment #7

NHS
Health Research Authority

NRES Committee East of England - Norfolk

Nottingham REC Centre
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

27 March 2013

Prof John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**93475/419104/13/887/17401**
Amendment date:	**27 February 2013**
IRAS project ID:	**93475**

The above amendment was reviewed at the meeting of the Sub-Committee held on 11 March 2013.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Questionnaire: Appendix 9 - Recruitment Questionnaire	1	17 January 2013
Participant Information Sheet: Patient Information Sheet	6	17 January 2013
Protocol	6	07 January 2013
Notice of Substantial Amendment (non-CTIMPs)	93475/419104/13/887/17401	27 February 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely

pp: Dr Michael Sheldon
Chair

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust*
Mrs Sue Steel

15.8. Amendment #8:

NHS
Health Research Authorit

NRES Committee East of England - Norfo
Nottingham REC Cer
The Old Cha
Royal Standard Pl
Nottingh
NG1 6

Tel: 0115 8839

31 December 2013

Prof John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Prof Saxton

Study title:	**A randomised controlled trial investigating the effect of a 12-month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer.**
REC reference:	**12/EE/0106**
Amendment number:	**9-18/11/2013**
Amendment date:	**02 December 2013**
IRAS project ID:	**93475**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Covering Letter	Letter from Prof. John Saxton	17 December 2013
Notice of Substantial Amendment (non-CTIMPs)	93475/541729/13/244/24065	02 December 2013
Protocol	6	18 November 2013
Letter of invitation to participant	Follow Up Letter - Version 1	18 November 2013
Questionnaire	1	18 November 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/EE/0106:	**Please quote this number on all correspondence**

Yours sincerely

Dr Michael Sheldon
Chair

E-mail: NRESCommittee.EastofEngland-Norfolk@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Kath Andrews, Norfolk and Norwich University Hospitals NHS Foundation Trust*

Ms Sue Steel

Appendix 16- PARC NHS Research and Development study approval

Our Vision
To provide every patient with the care we want for those we love the most

Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

Mr Barnabas Shaw
ENV 0.58
Faculty of Health
University of East Anglia
Norwich
NR4 7TJ

01 July 012

Research & Development Office
Level 3 East
Norfolk & Norwich University Hospitals NHS Foundation Trust
Colney Lane
Norwich
NR4 7UY

direct dial: 01603 287806
direct fax: 01603 289800
e-mail: rdoffice@nnuh.nhs.uk
website: www.nnuh.nhs.uk

Dear Mr Shaw

Re: **R&D Reference Number:** 2012GAST03S (38-02-12)
Project Title: A randomised controlled trial investigating the effect of a 12month active lifestyle programme on physiological risk markers and physical activity behaviour in those diagnosed with intermediate or high risk for colon cancer

I am pleased to inform you that the above project has been given full NHS permission for research at Norfolk & Norwich University Hospitals NHS Foundation Trust.

This NHS permission for research has been granted on the basis described in the application form, protocol and supporting documentation as listed below:

Document	Version No	Date
Protocol	2	13 April 2012
Interview Design – Active Lifestyle Programme and Usual Care Group	1	14 February 2012
Patient Information Sheet	2	13 April 2012
PIS: Interview One	2	13 April 2012
PIS : Interview Two - Control Group	2	13 April 2012
PIS: Interview Two - Exercise Group	2	13 April 2012
PIS: Focus Group – Intervention	2	13 April 2012
PIS: Focus Group - Health Professionals	2	13 April 2012
Consent Form : Contact Details	1	14 February 2012
Consent Form : Patient Consent Form	2	13 April 2012
Consent Form : Initial Biopsies	2	13 April 2012
Consent Form : Interviews	2	13 April 2012
Consent Form : Focus Group	2	13 April 2012
Letter of invitation to participant	2	13 April 2012
GP Letter	1	14 February 2012
Advertisement	2	13 April 2012
Questionnaire : Health Questionnaire - Medical Information	1	14 February 2012
Questionnaire : Health Questionnaire -PARC - Physical Activity and Risk of Colon Cancer	1	14 February 2012
Questionnaire: Physical Activity Readiness Questionnaire - PAR-Q	1	14 February 2012
Other: PARC - Physical Activity and Risk of Colon Cancer - Active Lifestyle Booklet	1	10 February 2012

The agreed total local recruitment target for your study is 124 participants.

The R&D Office will contact you in due course to monitor progress.

I have enclosed two copies of the Standard Terms and Conditions of Approval. Please sign both copies and return one copy to the Research & Development Department at the above address and keep the other in your study file. Failure to return the standard terms and conditions may affect the conditions of approval.

Please note, under the agreed Standard Terms and Conditions of Approval you must inform the R&D department of any proposed changes to this study and submit annual progress reports to the R&D department.

If you have any queries regarding this or any other project please contact Seema Gopinath, Research Facilitator, at the above address. Please note, the reference number for this study is **2012GAST03S (38-02-12)** and this should be quoted on all correspondence.

Yours sincerely

Professor Krishna Sethia
Medical Director

Professor Marcus Flather
R&D Director

Appendix 17- PARC supportive documents

17.1. Invitation letter

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

The Effects of a 12 month Active Lifestyle Programme on patients diagnosed as being at increased risk of developing further polyps as determined by colonoscopy.

Dear

Re: Invitation to participate in an Active Lifestyle Study: What effect does physical activity have on exercise participation and bowel health?

I am delighted to let you know about a new research study for people who are undergoing a colonoscopy. Consultants from the Gastroenterology Unit and health researchers from the University of East Anglia are working together to investigate how a structured exercise and educational programme affects exercise participation and bowel health.

This study will be asking some eligible participants to undertake a programme of exercise and attend exercise-related educational workshops. We hope to gain a better understanding of how active lifestyle programmes like this impact upon physiological markers of bowel health and health behaviours.

Please find enclosed a patient information sheet, which describes the study in more detail and answers the most frequently asked questions.

If you are interested in the study please bring the tear off slip in the bottom of this letter with you to your appointment. A member of the study team (Mr Barnabas Shaw, Miss Kelly Semper or Mrs Liane Lewis) will be present at the NNUH on the day of your colonoscopy to talk to you about the study should you be interested. This is entirely voluntarily and your treatment will not be effected should you decide not to meet one of the researchers.

Yours sincerely,

Mr. James Hernon

Consultant Surgeon, Norfolk and Norwich University Hospital.

……

The Effects of a 12 month Active Lifestyle Programme on patients diagnosed as being at increased risk for developing further polyps as determined by colonoscopy.

☐ Yes. I am interested in the above named study.

☐ No, I am not interested in taking part in the study

Name: _____

Telephone Number: _____

17.2. Patient information sheet

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

Patient Information Sheet

The Effects of a 12 month Active Lifestyle Programme on patients diagnosed as 'intermediate' or 'high' risk for developing further polyps by their screening colonoscopy.

We are inviting you to take part in our research study. Before you decide whether or not to take part we want you to understand why we are doing this research and what it will involve for you. This information sheet provides an overview of the study, and it should take about fifteen minutes to read. Please feel free to discuss the study with family and friends. If there is anything you are not clear about, the contact details of the researchers are provided at the end. We will happily go through the information sheet with you and answer any questions you have.

We have compiled a list of Frequently Asked Questions (FAQs) which cover the main aspects of the research:

What is the purpose of the study?

Recently, some evidence has accumulated which suggests that people who have exercised regularly throughout their life might be at reduced risk of developing certain types of cancer, in particular colon (bowel) cancer. However, at the present time, we do not know whether a physically active lifestyle can have a positive effect on biological markers associated with colon cancer risk. Also, we do not know how taking part in a programme like this affects exercise behaviour and attitudes towards exercising after colonoscopy screening.

Therefore, we are aiming to find out whether an active lifestyle programme, incorporating supervised exercise sessions and healthy living workshops over a 12-month period has a positive impact on bowel health and exercise behaviour in people diagnosed as being at 'intermediate' or 'high' risk as a result of their screening colonoscopy. We also want to investigate if changes in exercise habits can affect physical function and feelings of well-being.

Why have I been invited?

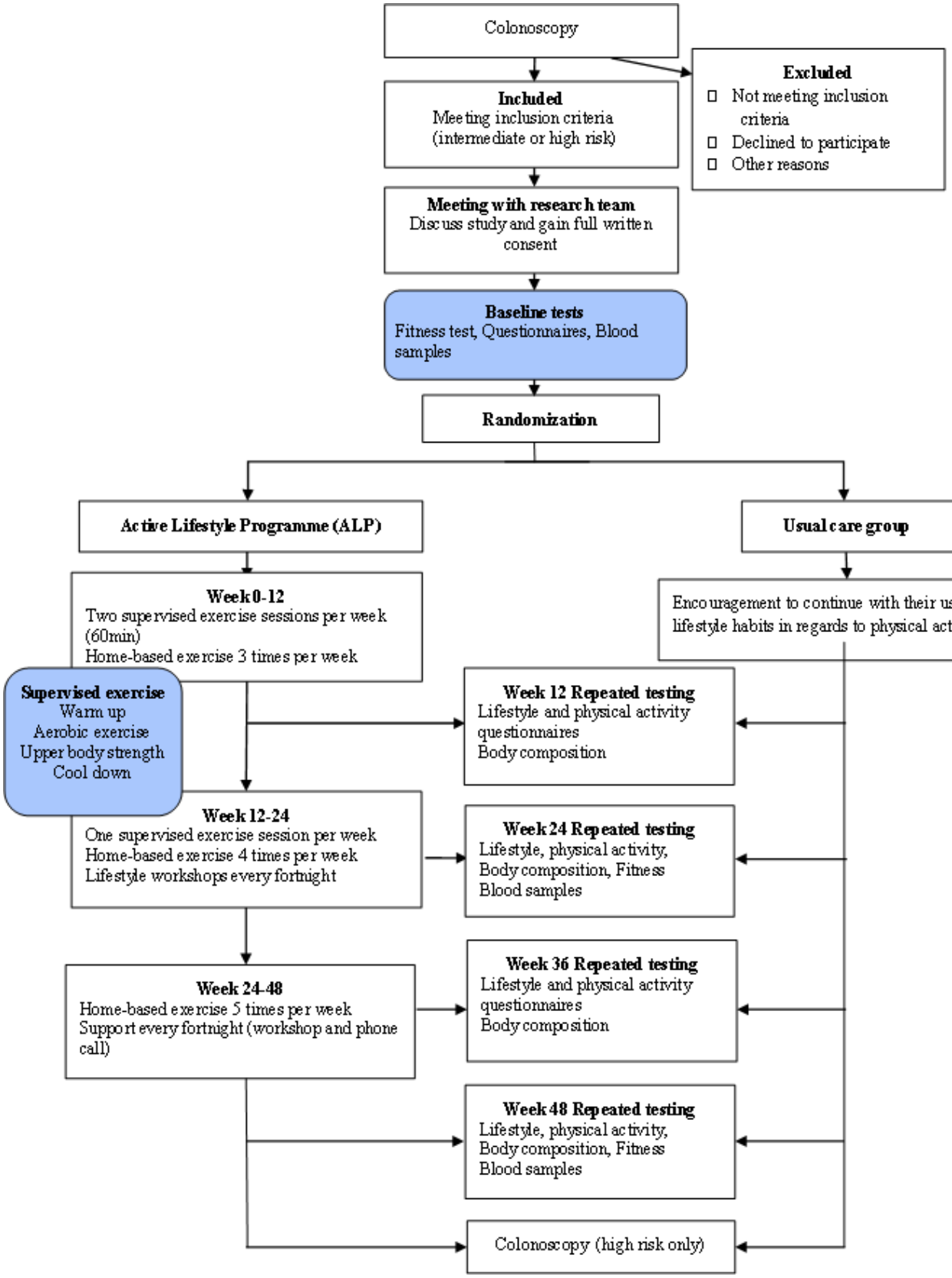
You have been selected as being a potentially suitable participant as you have presented to the Norfolk and Norwich University Hospital on the National Bowel Cancer Screening Programme. We are looking to recruit participants from this population subject to the outcome of your test.

Do I have to take part?

Your participation is entirely voluntary. If you decide not to take part, this will not affect the standard of care you receive from the hospital or any other health professional. You are also free to withdraw from the study at any time without giving reason.

What will happen to me if I take part/what do I have to do?

If you decide to take part and you meet our inclusion criteria (i.e. the surgeon identifies you as being 'intermediate' or 'high' risk for developing further polyps during the routine colonoscopy) you will have five small pinch biopsies taken from you colon, as well as any abnormal tissue that would be routinely removed. Once you have the results of your colonoscopy we will contact you to arrange a formal meeting with the research team at the University of East Anglia. If after the meeting you are still happy to take part, we will invite you to complete baseline tests. Afterwards, you will be randomly assigned to one of two groups; namely the Active Lifestyle Programme (ALP) or Usual Care (UC). You have an equal chance of being in either group. This is known as a randomised controlled trial, and we are running the study this way because we do not know which treatment is best. You will be involved in the study for 12 months, and the total length of the research will be 2 years. The figure below outlines all of the procedures involved:



The second colonoscopy at the end of the study only applies to those individuals diagnosed as 'high' risk at the first colonoscopy, which is routine. As before, the surgeon will take five further pinch biopsies as well as any abnormal tissue. We will monitor your physical activity levels, body composition, and diet, and ask both groups to complete questionnaires every 3 months. We will take venous blood

samples from you and ask you to complete a fitness test every 6 months. The principal difference will be that the ALP group will aim to achieve 300 min per week of moderate to vigorous physical activity for the duration of the study; whereas UC will maintain their normal lifestyle habits. To help achieve this goal, ALP will receive 36 personal training sessions at the University of East Anglia over 6 months. This will be complemented by 19 lifestyle workshops at the University which will run over 12 months.

Can I expect any payment/reimbursement of costs?

Unfortunately, we cannot offer any financial reward or cover any personal expenses. However, ALP will receive free personal training and lifestyle workshops, and we will make data pertaining to health such as body composition, cardiorespiratory fitness and diet analysis available to both groups at the end of the study.

What are the treatment alternatives?

Currently, there are no treatment guidelines for individuals diagnosed as being intermediate or high risk for developing further polyps, other than further screening colonoscopies.

What are the possible disadvantages/risks of taking part?

The potential for risks to occur will be minimised. We will make sure that you can safely complete the exercise sessions before you take part, so that the likelihood of anything untoward happening during the exercise will be minimal. Exercise protocols will be tailored to your needs and your heart rate will be monitored during the exercise. In the event that something does go wrong and you are harmed during the research study, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you might have grounds for legal action for compensation, but you could have to pay your legal costs.

Are there any side-effects of taking part?

If you haven't exercised for a while, and are part of the ALP group, physical activity might initially make you feel tired, and you could feel slightly breathless, but as you do it more regularly you will feel increasingly better.

What are the possible benefits of taking part in this study?

We cannot guarantee that you will benefit personally, but you will receive free fitness tests. The information which we will obtain might help improve medical care for patients at elevated risk like yourself.

What happens when the research study stops?

When the study finishes, we plan to publish the findings in a peer-reviewed scientific journal. We will not monitor you after your involvement in the study has finished. We will make data pertaining to health such as body composition, cardiorespiratory fitness and diet analysis available to both groups at the end of the study. If you are randomised to UC, you will be given the materials provided to ALP should you request them.

What if there is a problem?

In the event that something does go wrong and you are harmed during the research study, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you might have grounds for legal action for compensation, but you could have to pay your legal costs.

Will my taking part in the study be kept confidential?

The confidentiality of our patients and the data which this study will generate is of utmost importance. All data from this study will be anonymised with a unique code during the study so the researcher analysing your data will be blinded as to your identity, which group you are in and to information collected during the study. This is one of the clauses, which you will sign in agreement on the official consent form. Our procedures for handling, processing and storage of and destruction of data are compliant with the Data Protection Act 1998.

What if relevant new information becomes available?

We will inform you if relevant new information becomes available which might affect the way we treat you. We will also discuss whether we need to make any amendments with the trial steering committee, which is responsible for the conduct of the research.

What will happen if I do not want to carry on with the study?

You are free to withdraw from the study at any time without giving reason, and this will not affect the standard of care you receive from the hospital or any other health professional. Should you wish, we can also destroy any identifiable data/tissue samples that we have collected from you.

What if there is a problem?

If you have any cause to complain about any aspect of the way in which you have been approached or treated during the course of this study, the Patient Advice and Liaison Service is available to you. In order to use this service you can choose one of the following options:

Phone: 01603 289036
Email: PALS@nnuh.nhs.uk
Website: http://www.pals.nhs.uk/

Will my GP be notified?

With your consent, we will write and inform your family doctor that you are taking part in this study.

What will happen to any samples I give?

Any tissue samples that you provide will be transferred to the Institute of Food Research, where we will analyse them for indicators of bowel health. They will be stored there for the duration of the study. Responses to questionnaires, physical activity, diet and fitness data will be stored and analysed at the University of East Anglia for the duration of the study.

Will any genetic tests be done?

There are several genes which are known to be involved with the development of bowel cancer. These genes can be affected by ageing, which may in turn affect the

risk of developing the disease. We want to understand whether exercise can reverse the gene ageing process, and we will look for signs of this in the colon biopsies we obtain. We also would like to see whether any changes are reflected in other areas of the body, which is why we would like to analyse these genes in your blood and cheek cells. We will only analyse genes that are known to be implicated in bowel cancer, and we will *not* sequence your entire genome.

What will happen to the results of the research study?

We plan to publish the results of this study in a peer-reviewed scientific journal. However, you will not be personally identifiable from these results. In addition, the results from initial fitness testing and overall conclusions of the study will be available to you. Any further information will be available upon request. With your consent, we will anonymously store any leftover blood and tissue samples we collected from you at a NHS approved tissue bank for a period of 5 years. These samples might be used for future research into bowel health. You can still take part in the study even if you do not wish to have any leftover tissue stored in this way, in which case they shall be destroyed once the study has finished. All of these procedures will be compliant with the Human Tissue Act 2004.

Who is organising and funding the research?

The research forms part of a PhD programme funded by the University of East Anglia. The research is being conducted in collaboration with the Norfolk and Norwich University Hospital and the Institute of Food Research.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by Norfolk Research Ethics Committee.

Further information and contact details

If you have any specific questions about the study, we will be more than happy to answer them for you.

In the event of further questions please contact:

Mr Barnabas Shaw BSc. MSc. Email: B.Shaw@uea.ac.uk
Miss Liane Thomas BSc. Email: Liane.Thomas@uea.ac.uk
Miss Kelly Semper BSc. Email: K.Semper@uea.ac.uk
(Work phone numbers tbc)

Thank you for taking the time to consider participating in this study

Prof John Saxton (Project co-ordinator), Tel: 01603 593098, Email: john.saxton@uea.ac.uk

17.3. Biopsy consent form

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

Consent Form – Initial Biopsies

"The Effects of a 12 month Active Lifestyle Programme on patients diagnosed as'low' 'intermediate' or 'high' risk for developing further polyps by their screening colonoscopy."

Thank you for your initial interest to take part in our study. You will soon be undergoing your colonoscopy at the Norwich and Norfolk University Hospital.

Depending on the outcome of your colonoscopy, you may be eligible to take part in this research study. With your consent, and if you are eligible, the surgeon will take five further small biopsy samples from your colon for research purposes. These samples will be anonymised and transferred to the Institute of Food Research by the research team.

With your consent, we might store any leftover samples at a NHS approved tissue bank for future studies of bowel health after the study has finished for a period of 5 years. You can still take part in this study even if you do not consent to this tissue being stored, in which case the tissue will be destroyed after the study.

As the additional research biopsies to be taken are small in size (2-3 mm across), there is only a small risk that you will experience any adverse health effects from this procedure. Pinch biopsies carry a very small risk of bleeding or perforation (tearing) of the bowel, and this occurs in less than 1 in 1,000 cases.

Please initial box

I confirm that I have read and understood the above information ☐

I consent for further tissue samples to be extracted during my colonoscopy for analysis purposes. ☐

I consent for these samples to be transferred to the Institute of Food Research by the research team. ☐

I consent for any leftover tissue extracted to be anonymously stored at a NHS approved tissue bank for future studies of bowel health after the study has finished for a period of five (5) years. ☐

_____ _____

Name of Participant Date

Signature

_____ _____

Name of person taking informed consent Date

Signature

17.4. Study consent form

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

PATIENT CONSENT FORM

The University of East Anglia

The effects of a 12 month exercise intervention on patients diagnosed as being at increased risk for developing further polyps by their screening colonoscopy.

Patient Identification Number for this study:

Investigators: Consultant, Professor John Saxton, Students

Patient name:

1. **I confirm that I have read and understood the Patient Information Sheet Version ____ dated ____/____/____ for the above study. I** ☐

have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. **I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.**

3. **I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals of the research team, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.**
4. **I consent for tissue collected during the study (i.e. venous blood, cheek swab and colon tissue) to be transferred to the Institute of Food Research for analysis purposes**
5. **I agree to my G.P. being informed of my participation in the study.**

6. **I agree to take part in the above study.**
7. **I am aware that I may be contacted to be interviewed at 1 and 12 months.**

Name of Participant	Date	Signature
Name of individual taking consent (if not researcher)	Date	Signature
Researcher	Date	Signature

17.5. Letter informing GP of study participation

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

Dear

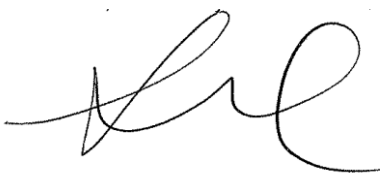
Re: patient name (xx/xx/19xx)

I am writing to inform you that xxxxx has consented to be contacted regarding his /her involvement in an exercise intervention based at the University of East Anglia, supported by the Norfolk and Norwich University Hospital.

The new project is aiming to identify the biological and psychological effects of a 12 month Active Lifestyle Programme on patients diagnosed as being at increased risk for developing further colon polyps at their screening colonoscopy. Alongside the 12 month exercise intervention, questionnaires to assess behavioural changes with regards to lifestyle factors will also be administered to each participant. As well as these procedures some participants may be asked to participate in interviews at the start and end of the intervention, and focus groups after trial completion to gain a more detailed account of personal experiences with both physical activity and the trial itself.

If you have any concerns or questions regarding your patient participating in this study please do not hesitate to contact a member of the study team on 01603 593098.

Yours Sincerely,



Appendix 18- MOVE study protocol version 1

A behavioural lifestyle intervention for colorectal cancer survivors

1. INTRODUCTION

1.1 Background to the study

In the UK, colon cancer (CC) is the second most common type of cancer by absolute incidence in males and females combined. Malignant neoplasms of the colon were responsible for 8248 deaths in England and Wales in 2010, of which 95% were in persons aged 60 or over (Office for National Statistics, 2011).

Evidence is emerging for a positive association between the amount of physical activity (PA) and survival from colon cancer. Data from a prospective cohort study with 832 stage III colon cancer patients showed that performing one hour of brisk walking on seven days of the week or equivalent PA accounted for a 49% lower risk of mortality from colon cancer compared to individuals not achieving this amount of PA. Furthermore, the risk for cancer recurrence was also reduced by 49% (Meyerhardt et al., 2006b). Similarly, results from a Norwegian study cohort demonstrated a 44% lower risk of death among most active patients compared to the least active (Nilsen et al., 2008). The cohort enrolled 59,369 participants of which 736 were diagnosed with colon cancer during the follow-up period. Data on PA was collected before a cancer diagnosis. Other benefits of PA for cancer survivors have been studied more extensively. There is now strong evidence for better Quality of Life (QoL) among physically active cancer survivors compared to non-active survivors. Other reported benefits in a systematic review were improved body composition, increased aerobic fitness and muscular strength, reduced fatigue, less anxiety, lower rates of depression and higher levels of self-efficacy (Speck et al., 2010). Given the evidence for the positive effects of PA on psychological and physiological outcomes, it is a concern that more than 50% of cancer survivors are not meeting the current minimum PA recommendation of 150 minutes of moderate activity per week (Blanchard et al., 2010). Past studies have addressed this issue with exercise and lifestyle interventions aiming to increase PA levels of this population. However, only short-term changes in physical activity behaviour are reported and there is a lack of long-term intervention studies. Interventions that are underpinned by a well-defined behaviour change theory could aid the uptake and maintenance of physical activity in the long-term. This highlights the need for future studies to

investigate the effects of interventions for promoting a sustained increase in PA and assessing the impact on health outcomes after curative treatment for colon cancer.

According to a recent systematic review (Greaves et al., 2011) of lifestyle interventions that targeted weight loss and higher physical activity levels, the effectiveness of interventions that use a well-defined behaviour change technique is improved. Increased contact time with the participant was also found to be a predictor of more positive behaviour change. In accordance with these recommendations, a recent study (Silva *et al*., 2011) investigated the effects of a 1-year behavioural intervention in overweight women over three years of follow-up. Participants in the intervention group received 30 theory workshops aimed at increasing physical activity levels and energy expenditure. After one year, the intervention group achieved significantly higher levels of moderate and vigorous intensity exercise and weight loss in comparison with a control group who received general health advice only. More specifically, mean exercise levels and percentage weight loss in the intervention group were 300 min per week and -7.3%, as opposed to the control group (179 min per week and -1.7%). The differences between groups were still significant after 3 years.

The intervention was based on a psychological model called the Self-Determination-Theory (SDT). According to this model, motivation can vary in level and orientation which means that the amount and type of motivation can differ amongst people (Ryan and Deci, 2000). The more intrinsically regulated a motivation the more autonomously the behaviour is performed, which means the behaviour is carried out because of enjoyment. Conversely, more extrinsically regulated motivations are performed with less autonomy, which means the behaviour is controlled and performed because one was told to. People are more likely to maintain regular physical activity if the behaviour is intrinsically motivated. On the other hand, when physical activity behaviour is not yet maintained but in a stage of preparation or contemplation, then motivation regulation is more extrinsic (Thogersen-Ntoumani and Ntoumanis, 2006). These findings demonstrate that the effectiveness of an intervention is dependent on the motivation to perform a specific behaviour and they highlight the need to target motivation for a specific behaviour to promote long-term changes in that behaviour.

2. Purpose of the study

The purpose of this study is to investigate whether a 3-month physical activity behaviour change intervention is effective for increasing the amount of daily PA in colon cancer survivors after completion of surgery and if positive behaviour changes are maintained 3 months after the intervention. The physical activity intervention will use self-determination theory (SDT) to create an autonomy-supportive environment. Secondary outcomes will explore the impact of the intervention on physical functioning, health-related Quality of Life, anxiety and depression, fatigue, body composition and the underlying determinants of behaviour change (i.e. self-efficacy, motivation regulation, etc.).

When implementing such a behaviour change intervention, it is important to understand its efficacy in relation to underlying determinants of behaviour change. Tools have been developed to measure key constructs influencing physical activity behaviour change. An intervention that uses the SDT aims to implement changes in autonomy or self-determination, where a change from low autonomy to high autonomy is desired. This is because higher levels of autonomy are associated with greater adherence to a given behaviour over time, and this increases the likelihood for long-term maintenance of the adopted behaviour. It is therefore important to monitor the progress of this change to evaluate the effectiveness of the intervention. Mullan et al (1997) developed questionnaires to measure the level of autonomy with which a certain behaviour is performed. However, although autonomy is a predictor of physical activity behaviour, other variables, such as intention and self-efficacy, mediate between the two (Hagger and Chatzisarantis, 2009). Hence, to draw conclusions about the constructs that underlie the effects of the intervention, intention and self-efficacy need to be measured alongside measures of self-determination. Finally, as intention, self-efficacy to exercise and self-determination to be physically active can be high and actual physical activity behaviour low, it is also necessary to assess the amount of physical activity that is performed over a defined period of time. Several physical activity questionnaires are available for this purpose.

3. Study hypothesis

3.1 Null hypotheses

Patients randomised to the intervention group will not improve their PA levels after 3 months and 6 months.

3.2. Alternate hypotheses

Patients randomised to the intervention group will improve their PA levels after 3 months and 6 months.

3.3 Other hypotheses

Higher levels of PA will be reflected in behavioural regulation. Individuals being more physically active will be more intrinsically motivated. People who have increased their PA levels will also have improved psychological and physical outcome measures compared to people who did not increase their PA levels.

4. Methods

4.1. Study design

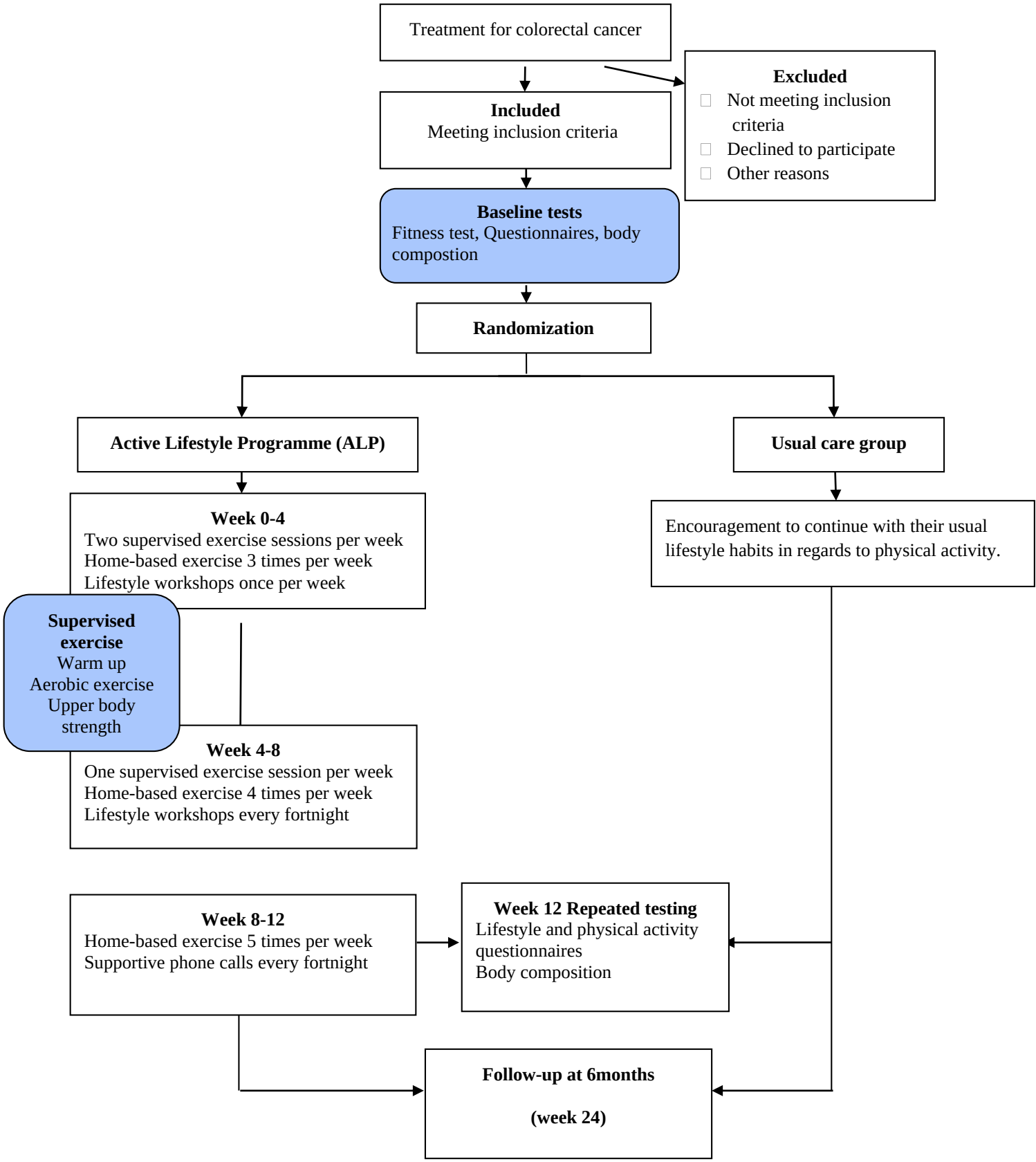
The study is a feasibility study with colorectal cancer patients after completion of treatment. Participants will be randomly assigned to either the control group or the intervention group. Participants in the intervention group will receive a physical activity intervention for 3 months which includes supervised exercise sessions, home-based exercise and a theory component. The control group will carry on with their usual medical care and be offered a few exercise sessions after the study has ended. Study outcomes will be assessed in both groups at the beginning of the study and after 3 and 6 months.

4.2. Participants

Participants will be patients from the Norfolk and Norwich University Hospital with a colorectal cancer as identified by the Colorectal Cancer Lead.

Inclusion: i) histologically confirmed diagnosis of colorectal cancer with Dukes stages A-C ii) completed cancer treatment within the last 24 months, iii) be able to understand spoken and written English, iv) score of 80 or more on the Karnofsky Performance Status Scale

Exclusion: i) already meeting general PA guidelines, ii) recent myocardial infarction iii) uncontrolled hypertension iv) a pacemaker v) or unstable angina.



4.3 Recruitment and informed consent

4.3.1 Recruitment via letter

The Colorectal Cancer Lead and chair of the Colorectal Multi-Disciplinary Team (MDT), Mr James Hernon, together with a Colorectal Specialist Nurse from the Colorectal Surgical Department at the Norfolk and Norwich University Hospital will identify potential patients from the hospital register. Potentially eligible patients will have had a diagnosis of colon or rectal cancer Duke's stage A-C within the last 3 months up to 3 years, who are being actively followed up by the Colorectal Surgical Department. Mr James Hernon will screen the identified patients for their eligibility and liaise with the responsible Colorectal Surgeon of the patient regards their possible involvement in the study. If the Colorectal Surgeon approves possible participation of the patient, the clinical staff will send out an invitation letter and a participant information sheet to the potentially eligible patients. This letter will contain details of the study and contact details of the specialist nurse and the researcher. The potential participant can call either the nurse or the researcher to find out more about the research and if interested to schedule an appointment with the researcher.

Patients who will have not responded to the initial invitation letter will be sent a second reminder letter after 4 weeks of sending the first letter. This letter will also be posted by the clinical staff from the Norfolk and Norwich University Hospital.

Patients who are interested in the study are invited for an information meeting at the University of East Anglia. During this meeting the study will be explained to the patient and questions answered before giving fully written consent to the study. The study facilities and equipment used during the intervention will be shown to the potential participant. If they remain interested in the study they will be given a general health and demographics questionnaire to determine eligibility. If the eligibility criteria are fulfilled, an appointment for baseline tests will be scheduled. Participants will be instructed to wear an accelerometer for 7 days to objectively assess free living PA. Questionnaires will also be given to the participants on this initial meeting.

4.3.2 Recruitment at hospital

Patients with a colorectal cancer diagnosis will present for a follow-up consultation at the Norfolk and Norwich University Hospital 3 months after their surgery. After the consultation the Colorectal Cancer Lead will ask the patient whether they are interested in speaking to a researcher about the study. The researcher will be present at the hospital in the event a patient is interested to talk about the study and

will provide the interested patient with a patient information sheet and communicate the purpose of the study briefly. If the patient remains interested after a brief introduction of the study, the researcher will take their contact details and ask whether the patient would like to be contacted in a few days after they had time to carefully read the patient information sheet. The researcher will give the patient a phone call and invite them to the University of East Anglia for an information meeting. Eligibility criteria will be assessed and fully written consent will be taken if the patient remains interested.

4.4 General procedures

After recruitment and written consent all participants, regardless of their group, will take part in baseline assessments. This will be repeated after 3 months and 6 months, which marks the end of the study.

There are two components of the baseline assessments. Firstly, participants will attend the exercise facility at the University of East Anglia for a physical assessment. This includes a variety of fitness tests for physical endurance and strength, and measures of body composition. Secondly, the participants will be given a questionnaire booklet containing a variety of questionnaires about their health status, current physical activity behaviour, self-efficacy, QoL, fatigue and motivation to exercise. The researcher will give instructions on how to answer the questions in the booklet and the participant will complete the questionnaire during their visit to the University of East Anglia. Further details of the outcome measures are given in section 4.8.

A brief health questionnaire assessing cardiovascular risk factors will be given only at baseline. Information about diagnosed cancer stage and type of treatment will be retrieved from medical records with the consent of the participant. This will be provided by the clinical staff at the NNUH and the researcher will not have direct access to these records.

4.5 Randomisation

Randomisation will occur after the baseline measures and participants will be informed immediately about their assignment. A computer programme will be used to generate the randomisation sequence.

4.6 Control group

The control group will continue with their usual care and not receive any form of advice. However, they will be offered supervised exercise for a limited period of time at the end of the study and they will be given an intervention workbook. Participants in the control group will undertake the same testing procedures (fitness test and questionnaires) as the intervention group and testing will take place at baseline, 3 and 6 months

4.7 Intervention group

The intervention comprises three components that will be carried out over a 3-month-period; 1) supervised exercise at a facility at the University of East Anglia, 2) home-based exercise on their own, 3) and a theory component.

During the first month participants will attend two supervised exercise sessions per week led by a trained exercise specialist and complete three additional home-based exercise sessions. A theory workshop will be held once per week before one of the supervised sessions.

The following month (month 2), supervised sessions will be held once per week and home-based exercise will increase to 4 days per week. Theory workshops will continue on a fortnightly basis.

During the last month of the intervention (month 3) participants will only perform home-based exercise on most days of the week. The researcher will call the participant every fortnight to discuss problems and progress throughout this last month of the intervention. This will form a transition period to prepare for the time after the intervention when exercise will only take place on their own with no supportive phone calls.

4.7.1 Supervised exercise programme

An outline of the programme is shown in Table 1. Supervised exercise sessions will consist of a ten minute warm up, 30 minutes of aerobic exercise at a moderate intensity of 10-15 according to the Rating of Perceived Exertion Scale (RPE-scale) and 30 min of resistance exercise. It is acknowledged that some participants will be unable to exercise at moderate intensity at the beginning of the intervention. Intensity and duration will be adjusted accordingly to individual needs. Resistance exercises will target large muscle groups using dumbbells and resistance bands.

For home-based exercises, the participants will be advised to repeat the exercises which they have learned during the supervised sessions. Each participant will be given a resistance band and an exercise DVD to take home to facilitate home-based exercising. Other suggested home exercises are walking, cycling, swimming, and the choice of several community programmes that offer aerobic classes, among other activities.

Furthermore, the participants will be provided with a pedometer, a small device that counts the daily number of steps taken. This will allow them to monitor their daily physical activity and will also function as a motivational tool.

4.7.2 Theory workshops

Theory-based workshops will take place at the University of East Anglia. This will be replaced by supporting phone calls in the last month (month 3) of the intervention. The workshops will be based upon the Self-Determination Theory (Ryan & Deci, 1985) and will cover a range of topics including goal-setting, social support, relapse prevention and overcoming exercise barriers. The workshops will be designed and delivered by Mrs Liane Lewis. Each workshop will take 30-45min.

Time in weeks	Supervised exercise per week	workshops	Home based exercise per week	Phone calls
1-4	2	1 x per week	3	0
4-8	1	Every fortnight	4	0
8-12	0	0	5	Every fortnight
12-24	0	0	0	0

Table Outline of the treatment in the intervention group

4.7.3 Physical Activity Workbook

To encourage exercise participation and maintain adherence, both intervention groups will be provided with a bespoke physical activity workbook designed by the researchers, which outlines suggestions for physical activity, and includes physical activity logs, progress monitors and contact details of the researchers. The participant will keep this workbook for the duration of the trial.

4.8 Outcome measures

All outcome measures will be tested at baseline and are repeated after 3 and 6 months.

4.8.1 Physical activity behaviour

Accelerometer

Objective free-living physical activity levels will be assessed over 7 days using accelerometry (ActiGraph®). The small unobtrusive accelerometer is worn on the hip and collects data on activity counts, step counts and total exercise energy expenditure.

International Physical Activity Questionnaire (IPAQ)

The IPAQ is a 7-day recall questionnaire designed to measure four domains of physical activity: 1) Job-related; 2) Transportation; 3) House work; and 4) Recreation, sport and leisure-time. An additional question asks for the time spent sitting. Amount of exercise in MET-minutes per week is calculated by multiplying minutes and intensity of specific activity undertaken. The validity of the IPAQ has been rated as acceptable for the different activity domains (Hagstromer *et al*., 2006).

Godin Leisure Time Exercise questionnaire

The Godin Leisure Time Exercise Questionnaire is a short four-item questionnaire that assesses the number of times that strenuous, moderate or mild exercise was performed for more than 15 min over the last 7 days.

4.8.2 Anthropometry

Stature, body mass, body mass index (BMI) and waist-hip ratio will be measured using standard techniques. All measures will be taken by a researcher at the University of East Anglia.

4.8.3 Psychological measures and health related Quality of Life (QoL)

A researcher will give instructions on how to complete the questionnaires and will check through them with each participant before returning the questionnaires. The assessment booklet will include the following questionnaires:

Behaviour Regulation for Exercise Questionnaire (BREQ)

The BREQ, designed by Markland and Tobin (Murcia et al., 2007), measures the continuum of motivation regulation, components of the Self-Determination Theory. It has been used widely in the sports and exercise domain. Questions are designed to measure amotivation, extrinsic, introjected, identified and intrinsic motivation for exercise. Nineteen items are rated on a scale from 1 ('not true for me') to 4 ('very true for me').

Psychological Need Satisfaction In Exercise Scale (PNSE)

Psychological needs (autonomy, relatedness and competence) are an important construct of the Self-Determination Theory. For a task to become internalised and not controlled by external factors, all three needs have to be satisfied. This questionnaire is a validated measure of the satisfaction of these needs with 18 question that can be rated on a 6-point Likert scale ('True' or 'False') (Wilson et al., 2006b).

The Functional Assessment of Cancer Therapy-Colorectal (FACT-C)

The FACT-C is a self-report questionnaire assessing QoL of colorectal cancer patients. This measure was designed to be used in research and clinical settings and can be used with colorectal cancer patients across all stages. It evaluates colorectal cancer specific concerns which are common to these patients. The questionnaire includes four functional areas (Physical well-being, social/family well-being, emotional well-being, and functional well-being) each of which has 6-7 items. An additional area addresses colorectal cancer specific concerns. These are rated on a scale from 0 ('Not at all') to 4 ('Very much').

The Functional Assessment of Cancer Therapy-Fatigue (FACT-F)

The FACT-F is a questionnaire designed for cancer patients to assess their treatment and disease related fatigue. Thirteen items are rated on a scale from 0 ('Not at all') to 4 ('Very much'). Lower scores represent less fatigue.

Health related quality of life (HRQOL) measured with the EORTC-QL30/29

The EORTC-QL is a questionnaire developed by the European Organisation for Research and Treatment of Cancer. This questionnaire is a self-administered and specifically developed for the use with cancer survivors in clinical trials. It measures disease and treatment related symptoms and physical, psychological and social

functioning. General quality of life is assessed with a 30 item questionnaire and an additional 29 item scale colorectal cancer specific symptoms.

Self- Efficacy for Exercise (SEE)

The self-efficacy scale is a 9- item questionnaire assessing the participant's confidence to exercise under different situations such as pain, bad weather or being tired. On a scale from 0 (not very confident) to 10 (very confident) the participant assesses their confidence to exercise 30 minutes on most days of the week when confronted with such a situation. Items are developed specifically for an elderly population.

Intention to exercise

This short two-item questionnaire assesses participant's intention to exercise regularly for the next month and for the next 6 months. Responses are rated from 1 ('Do not agree at all') to 7 ('completely agree').

4.8.4 Physiological measures

Chair sit-to-stand test

This test measures the muscle function of the lower body. It uses a chair and a stop watch. Aim of the test is to do as many 'sit-and-stands' as possible in 30 sec. The participant will be placed in a seated position on a chair and rise to a full standing position and return to a fully seated position immediately. This is repeated over 30 sec and the number of times the participant performed the task correctly will be recorded.

Aerobic endurance

A test of cardiorespiratory fitness will be performed on a treadmill. The test consists of 10 stages starting with a low walking speed and incline. Walking intensity will be increased every 3 minutes by increasing the walking speed and the incline of the treadmill. Heart rate and rate of perceived exhaustion will be monitored throughout the test. Endpoints of the test are perceived intensity of 'hard' as determined with the BORG-scale (scale of perceived exhaustion) and a heart of 85% of the predicted maximum.

Arm-curl test

This test is a measure of upper body muscle strength and endurance using dumbbells. Upper body strength is required in every-day tasks such as cleaning and shopping.

The participant is seated on a chair with the back in an upright position. A dumbbell of suitable weight for women and men will be chosen to perform biceps curls over a period of 30 sec. The number of curls performed in 30 sec will be recorded as the score of the test.

Grip strength

This test measures the maximum hand grip strength and represents the upper-limb strength. A dynamometer, a device that measures force, is gripped between the flexed fingers and the base of the thumb. The participant squeezes the dynamometer with maximum effort. Force applied will be displayed on the device.

4.9 Measuring effects

All quantitative data will be analysed by the researcher who is blinded to the identity of the participants using appropriate statistical software.

Parametric data will be compared using student's t-test to detect differences between the control and the intervention group. Where data is not normally distributed a Mann-Whitney test shall be employed. To compare data across different time points an ANOVA test will be applied.

Categorical data from questionnaires will be analysed using a X^2-test and ANOVA.

4.10 Project timetable

The project will take place over 1.5 years including preparation and write up/ dissemination time. Participants will be recruited on a 'rolling' basis, so that as participants go through the trial, new ones will be recruited. The estimated time from the first participants beginning the trial to the final participants ending the trial is 12 months.

Appendix 19- MOVE Research Ethics Committee Approval Letter

NRES Committee East of England - Norfolk
Nottingham REC Centre
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Telephone: 0115 8839368

16 April 2013

Prof John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Prof Saxton

Study title:	**Impact of a motivational active lifestyle programme on physical and psychological variables in colorectal cancer survivors**
REC reference:	**13/EE/0060**
IRAS project ID:	**114112**

Thank you for your letter of 8th April 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Ms Tracy Leavesley, NRESCommittee.EastofEngland-Norfolk@nhs.net

Confirmation of ethical opinion

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

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see

"Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

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

Document	*Version*	*Date*
Covering Letter	Letter from Professor John Saxton	04 February 2013
Evidence of insurance or indemnity	Zurich Municipal	15 May 2012
GP/Consultant Information Sheets	2	02 April 2013
Investigator CV	John Michael Saxton	05 February 2013
Investigator CV	Liane S Lewis	31 January 2013
Letter of invitation to participant	2	02 April 2013
Other: Reminder Letter	1	24 September 2012
Other: Consort Flow Diagram	1	24 September 2012

Participant Consent Form	1	24 September 2012
Participant Information Sheet	2	02 April 2013
Protocol	1	24 September 2012
Questionnaire: Health Questionnaire	1	24 September 2012
Questionnaire: Health Questionnaire Booklet	1	24 September 2012
REC application	114112/409999/1/892	01 February 2013
REC application	Non- NHS SSI - 114112/410000/7/551/172420/264334	16 January 2013
Response to Request for Further Information		
Sample Diary/Patient Card	Activity Log Book - Version 1	24 September 2012
Sample Diary/Patient Card	Active Lifestyle Booklet - Version 1	24 September 2012

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/EE/0060	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

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

Yours sincerely

Dr Michael Sheldon
Chair

Email:NRESCommittee.EastofEngland-Norfolk@nhs.net

Enclosures: "After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Mrs Yvonne Kirkham, UEA*

Ms Kath Andrews, Norfolk and Norwich University Hospital NHS Trust

Appendix 20-MOVE NHS Research and Development Approval

Our Vision
To provide every patient with the care we want for those we love the most

Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

Mr James Hernon
Department of Coloproctology and General Surgery
Norfolk and Norwich University Hospital
Colney Lane
Norwich
NR4 7UY

Research & Development Office
Level 3 East
Norfolk & Norwich University Hospitals NHS Foundation Trust
Colney Lane
Norwich
NR4 7UY

direct dial: 01603 287806
direct fax: 01603 289800
e-mail: rdoffice@nnuh.nhs.uk
website: www.nnuh.nhs.uk

18th April 2013

Dear Mr. Hernon

Re: **R&D Reference Number:** 2013GSUR01S (17-02-13)
Project Title: Impact of a motivational active lifestyle programme on physical and psychological variables in colorectal cancer survivors

I am pleased to inform you that the above project has been given full NHS permission for research at Norfolk & Norwich University Hospitals NHS Foundation Trust.

This NHS permission for research has been granted on the basis described in the application form, protocol and supporting documentation as listed below:

Document	Comments	Version No	Date
Protocol		1	24/09/2012
PIS		2	02/04/2013
Consent Form		1	24/09/2012
Letter of invitation		2	02/04/2013
GP Letter		2	02/04/2013
Activity Log Book		1	24/09/2012
Patient Letter	Reminder letter	1	24/09/2012
Questionnaire	Health Questionnaire	1	24/09/2012
Questionnaire	Health Questionnaire Booklet	1	24/09/2012
Active Lifestyle Booklet		1	24/09/2012
CONSORT diagram		1	24/09/2012
NHS R&D Form	114112/411682/14/883		
NHS SSI Form	114112/411685/6/656/171662/264740		

The agreed total local recruitment target for your study is 50 participants.

To support requirements of the National Institute of Health Research (NIHR) we will be monitoring and publishing outcomes of recruitment into your study. This includes benchmarking against a 70 day period from the time of receipt of a valid research application to this time of recruitment of the first patient for your study.

The date of receipt of a valid application for this study is 08/02/2013 and the benchmark of 70 days to recruit the first patient is 19/04/2013.

The R&D Office will contact you in due course to monitor progress against this benchmark.

Our Vision
To provide every patient with the care we want for those we love the most

Norfolk and Norwich University Hosp
NHS Foundatio

I have enclosed two copies of the Standard Terms and Conditions of Appro both copies and return one copy to the Research & Development Departm address and keep the other in your study file. Failure to return the star conditions may affect the conditions of approval.

Please note, under the agreed Standard Terms and Conditions of App inform the R&D department of any proposed changes to this study and progress reports to the R&D department.

If you have any queries regarding this or any other project please contact Lau Research Facilitator, at the above address. Please note, the reference numbe **2013GSUR01S (17-02-13)** and this should be quoted on all correspondence.

Yours sincerely

K. M. Andrew

Professor Marcus Flather
R&D Director

Appendix 21- MOVE supportive study documents

21.1. Participant invitation letter

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

A behavioural lifestyle intervention for colorectal cancer survivors

Dear

Re: Invitation to participate in an Active Lifestyle Study: The effects of a lifestyle intervention on physical and mental health in colorectal cancer survivors.

We have identified that you are potentially eligible for an active lifestyle intervention study to be carried out by researchers at the University of East Anglia in collaboration with the Colorectal Surgical Department at the Norfolk and Norwich University Hospital and we would like to extend an invitation to you to take part.

The project is a structured exercise and educational programme and aims to investigate whether such a programme can produce meaningful long-term effects on exercise participation, physical functioning and mental health in patients with a diagnosis of colorectal cancer.

The study will be asking eligible participants to undertake a 3-month programme of exercise and attend educational workshops. Efficacy of the intervention will also be assessed after the programme and 3 months later. Please take time to read the enclosed information sheet, which describes the study in more detail and answers the most frequently asked questions.

If you are interested in finding out more about the study and would like to meet one of the researchers please contact the Specialist Nurses, Jane McCulloch and Gek-Bee Cain, or the researcher Mrs Liane Lewis under the following numbers.

Mrs Jane McCulloch and Gek-Bee Cain
Tel: 01603289741.

Mrs Liane Lewis
Tel: 07933090197, *email:* liane.thomas@uea.ac.uk

Yours sincerely,

Mr James Hernon

21.2. Participant information sheet

Norfolk and Norwich University Hospitals NHS Foundation Trust

A behavioural lifestyle intervention for colorectal cancer survivors

Patient Information Sheet

Thank you for taking the time to read this information sheet. This document contains an overview of the study, our reasons for doing it, and answers some of the frequently asked questions that you might have and it should not take more than 15 minutes to read. Before you decide whether or not to take part we want you to understand why we are doing this research and what it will involve for you. Please feel free to discuss the study with family and friends. If there is anything you are not clear about, the contact details of the researchers are provided at the end. We will happily go through the information sheet with you and answer any questions you have.

What is the purpose of the study?

People who live with cancer often experience side-effects caused by the cancer or the treatment you received. These may include mental and physical fatigue, and a loss of physical functioning, which can all lead to a reduced quality of life. Evidence is emerging that physical activity may decrease the severity of these side-effects and help patients to regain their physical fitness at a faster rate. However, the majority of cancer survivors are not meeting the current physical activity guidelines.

Previous trials tested several strategies to improve people's physical activity behaviour but have not been successful in achieving a long-term behavioural change. New strategies are emerging which could prove to be more successful for changing patients physical activity in the long term.
Therefore, we are aiming to test an active lifestyle programme with people who have been treated for colorectal cancer, based on a behavioural model that has previously proven successful with people that were overweight. We want to find out, whether an active lifestyle programme lasting for 6 months, will improve physical activity behaviour and whether these changes are reflected in measures of physical functioning and behavioural variables.

Why have I been invited?

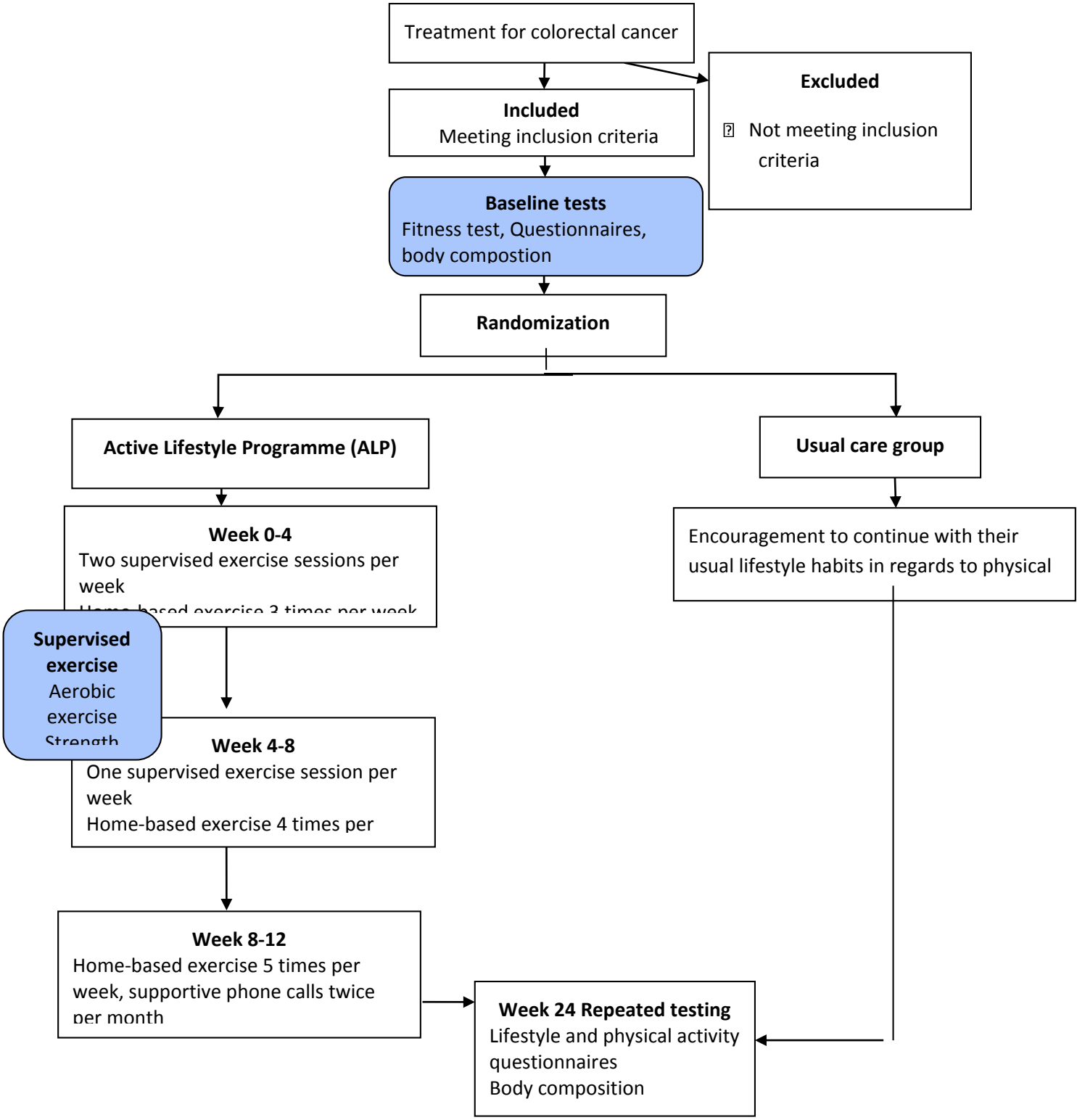
You have been selected by the Colorectal Surgical team at the Norfolk and Norwich University Hospital as being a potentially suitable participant because you have been diagnosed with colorectal cancer and completed treatment.

Do I have to take part?

Your participation is entirely voluntary. If you decide not to take part, this will not affect the standard of care you receive from the hospital or any other health professional. You are also free to withdraw from the study at any time without giving reason.

What will happen to me if I take part/what do I have to do?

If you decide to take part and you meet our inclusion criteria we will invite you to a meeting at the University of East Anglia to give you more details about the study and you will have the opportunity to ask questions. If after the meeting you are interested in taking part, you will sign a consent form agreeing you understood that participation is voluntary and that we will notify your GP about your participation. You will also agree that the researcher can request medical records about your diagnosis and treatment from the clinical staff at the Norfolk and Norwich University Hospital. Afterwards we will invite you to complete baseline tests. Afterwards, you will be randomly assigned to one of two groups; the Active Lifestyle Programme (ALP) or Standard Care (SC). You have an equal chance of being in either group. This is known as a randomised controlled trial, and we are running the study this way because we do not know which treatment is best. You will be involved in the study for 6 months. The figure below outlines all of the procedures involved:


Treatment for colorectal cancer
Excluded
Not meeting inclusion criteria
Included
Meeting inclusion criteria
Baseline tests
Fitness test, Questionnaires, body compostion
Randomization
Active Lifestyle Programme (ALP)
Usual care group
Week 0-4
Two supervised exercise sessions per week
Supervised exercise
Aerobic exercise
Encouragement to continue with their usual lifestyle habits in regards to physical
Week 4-8
One supervised exercise session per week
Home-based exercise 4 times per
Week 8-12
Home-based exercise 5 times per week, supportive phone calls twice per month
Week 24 Repeated testing
Lifestyle and physical activity questionnaires
Body composition

The baseline tests involve a series of questionnaires for assessing your regular physical activity levels and quality of life. We will also measure your body weight and height and your physical function.

These tests will be completed by both groups (ALP and SC) the beginning of the study, after 3 months and after 6 months. The principle difference between the groups is that the ALP group will be invited to attend the University of East Anglia for supervised exercise sessions and theory workshops and the SC group only has to attend the University to complete the bespoke tests.

Can I expect any payment/reimbursement of costs?

Unfortunately, we cannot offer any financial reward or cover any personal expenses. However, ALP will receive free personal training and lifestyle workshops, and we will make data pertaining to health such as body composition and cardiorespiratory fitness available to both groups at the end of the study. The SC will also be offered some exercise sessions and supportive exercise materials after the 6-month assessment.

What are the treatment alternatives?

Currently, there are no additional treatment guidelines to alleviate treatment side-effects.

What are the possible disadvantages/risks of taking part?

The potential for risks to occur will be minimised. We will make sure that you can safely complete the exercise sessions before you take part, so that the likelihood of anything untoward happening during the exercise will be minimal. Exercise protocols will be tailored to your needs and your heart rate will be monitored during the exercise.

Are there any side-effects of taking part?

If you haven't exercised for a while physical activity might initially make you feel tired, and you could feel slightly breathless, but as you do it more regularly you will feel increasingly better.

What are the possible benefits of taking part in this study?

We cannot guarantee that you will benefit personally, but you will receive free fitness tests. The information which we will obtain might help improve medical care for colorectal cancer survivors.

What happens when the research study stops?

We will not monitor you after your involvement in the study has finished. We will make data pertaining to health such as body composition, physical functioning and fitness analysis available to both groups at the end of the study. If you are randomised to UC, you will be given the materials provided to ALP should you request them.

What if there is a problem?

In the event that something does go wrong and you are harmed during the research study, there are no special compensation arrangements. If you are

harmed and this is due to someone's negligence then you might have grounds for legal action for compensation, but you could have to pay your legal costs.

Will my taking part in the study be kept confidential?

The confidentiality of our patients and the data which this study will generate is of utmost importance. All data from this study will be anonymised with a unique code during the study so the researcher analysing your data will be blinded as to your identity, which group you are in, and to information collected during the study. This is one of the clauses, which you will sign in agreement on the official consent form. Our procedures for handling, processing and storage of and destruction of data are compliant with the Data Protection Act 1998.

What if relevant new information becomes available?

We will inform you if relevant new information becomes available which might affect the way we treat you. We will also discuss whether we need to make any amendments with the trial steering committee, which is responsible for the conduct of the research.

What will happen if I do not want to carry on with the study?

You are free to withdraw from the study at any time without giving reason, and this will not affect the standard of care you receive from the hospital or any other health professional. Should you wish, we can also destroy any identifiable data that we have collected from you.

What if there is a problem?

If you have any cause to complain about any aspect of the way in which you have been approached or treated during the course of this study, the Patient Advice and Liaison Service is available to you. In order to use this service you can choose one of the following options:

Phone: 01603 289036
Email: PALS@nnuh.nhs.uk
Website: http://www.pals.nhs.uk/

Will my GP be notified?

With your consent, we will write and inform your family doctor that you are taking part in this study.

What will happen to any data I give?

Responses to questionnaires, physical activity, and fitness data will be stored and analysed at the University of East Anglia for the duration of the study. All collected data will be anonymised so that identification of the person to whom the data belongs is not possible.

What will happen to the results of the research study?

We plan to publish the results of this study in a peer-reviewed scientific journal and disseminate the results widely amongst doctors and patients. However, you will not be personally identifiable from these results. In addition, the results from

initial fitness testing and overall conclusions of the study will be available to you. Any further information will be available upon request.

Who is organising and funding the research?

The research forms part of a PhD programme funded by the University of East Anglia. The research is being conducted in collaboration with the Norfolk and Norwich University Hospital.

Who has reviewed the study?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by Norfolk Research Ethics Committee.

Further information and contact details

If you have any specific questions about the study, we will be more than happy to answer them for you.

In the event of further questions please contact:

Mrs Liane Lewis BSc.

Email: Liane.Thomas@uea.ac.uk

07933090197

Thank you for taking the time to consider participating in this study

Prof John Saxton (Project co-ordinator), Tel: 01603 593098, Email: john.saxton@uea.ac.uk

21.3. Reminder letter (sent out 2 weeks after first invitation letter)

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

A behavioural lifestyle intervention for colorectal cancer survivors

Dear

Re: Invitation to participate in an Active Lifestyle Study: The effects of a lifestyle intervention on physical and mental health in colorectal cancer survivors.

Recently, you have received a letter from us with information about a research project taking place at the University of East Anglia in collaboration with the Norfolk and Norwich University Hospital.

You may have not had time to read the information sheet which was enclosed in the previous letter. Therefore, we would like to remind you about the invitation to the study and ask you kindly to take a few minutes to read the information sheet. Please also let us know whether you would be interested to hear more about the study simply by contacting the researcher or specialist nurse.

Research projects such as this are important because the results may improve future follow-up treatments for colorectal cancer patients. This could lead to faster recovery from cancer therapy and quicker re-uptake of activity levels in regards to occupation and daily tasks.

If you are interested to hear more about the study or have any other questions you can contact Mrs Liane Lewis from the University of East Anglia or one of the specialist nurses named below.

Mrs Liane Lewis
Tel: 07933090197, *email:* Liane.thomas@uea.ac.uk

Mrs Jane McCulloch and Gek-Bee Cain
Tel: 01603 289741.

Yours sincerely,

Mr James Hernon
Consultant Gastroenterologist

21.4. Full study consent form

PATIENT CONSENT FORM

The University of East Anglia

A behavioural lifestyle intervention for colorectal cancer survivors

Patient Identification Number for this study:

Investigators: Consultant, Professor John Saxton, Student

Patient name:

1. I confirm that I have read and understood the Patient Information Sheet Version ____ dated ____/____/____ for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals of the research team, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I agree to my G.P. being informed of my participation in the study. ☐

5. I agree to take part in the above study. ☐

Name of Participant	Date	Signature
Name of individual taking consent (if not researcher)	Date	Signature
Researcher	Date	Signature

21.5. Letter to GP to inform about study participation of their patient

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

Dear Dr.

Re: Patient name (xx/xx/19xx)

I am writing to inform you that your patient (patient name) has consented to take part in an exercise intervention study based at The University of East Anglia, supported by the Norfolk and Norwich University Hospital.

The project is aiming to show positive effects of a 3-month active lifestyle intervention on physical function and quality of life in patients that received curative treatment for colorectal cancer. Furthermore, we are aiming to evoke meaningful long-term changes in exercise behaviour. Changes in physical activity behaviour and quality of life will be assessed using a variety of questionnaires.

If you have any concerns or questions regarding your patient participating in this study please do not hesitate to contact a member of the study team on 01603 59 3098.

Yours Sincerely,

Mr James Hernon

Consultant Colorectal Surgeon

Colorectal Cancer Lead Norfolk and Norwich University Hospital

Appendix 22

22.1. Summary of Amendments MOVE

Amendment number	Summary
#1:	The amendment was created to broaden the inclusion criteria. Instead of including only patients who completed treatment 24 months ago, we extended this to 3 y ears. This was implemented because the patient pool of potential participants was exhausted before the recruitment target was met.
#2	Survey- this amendment was implemented to be able to send surveys to patients who were not interested in the main trial

22.2. Approval letter from amendment #1

NHS
Health Research Authority

NRES Committee East of England - Norfolk
Nottingham REC Centre
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Tel: 0115 8839436

16 December 2013

Professor John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**Impact of a motivational active lifestyle programme on physical and psychological variables in colorectal cancer survivors**
REC reference:	**13/EE/0060**
Protocol number:	**N/A**
Amendment number:	**Amendment 1**
Amendment date:	**11 November 2013**
IRAS project ID:	**114112**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Participant Consent Form: Consent Form - Interview	1	10 October 2013
Participant Information Sheet: Information about the Research Interview	1	10 October 2013
Protocol	2	14 October 2013

Covering Letter	Letter from Professor John Saxton	18 November 2013
Qualitative Interview Design Sheet	1	14 October 2013
Notice of Substantial Amendment (non-CTIMPs)	114112/528294/13/332/23474	11 November 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

13/EE/0060:	**Please quote this number on all correspondence**

Yours sincerely

p p C Hallwell

Dr Michael Sheldon
Chair

E-mail: NRESCommittee.EastofEngland-Norfolk@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Kathryn Andrews, Norfolk & Norwich Univeristy Hospital NHS Trust*
Mrs Yvonne Kirkham

22.2. Approval letter from amendment #2

NHS
Health Research Authority

NRES Committee East of England - Norfolk

Nottingham REC Centre
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Tel: 0115 8839436

05 February 2014

Professor John Saxton
Professor of Clinical Exercise Physiology
University of East Anglia
School of Allied Health Professions
Queens Building Room 2.08
Norwich
NR4 7TJ

Dear Professor Saxton

Study title:	**Impact of a motivational active lifestyle programme on physical and psychological variables in colorectal cancer survivors**
REC reference:	**13/EE/0060**
Protocol number:	**N/A**
Amendment number:	**Amendment 2**
Amendment date:	**21 January 2014**
IRAS project ID:	**114112**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Covering Letter	Signed by Professor John Saxton	27 January 2014
Notice of Substantial Amendment (non-CTIMPs)	114112/556160/13/250/24517	21 January 2014
Protocol	3	16 December 2013
Letter of invitation to participant	Survey - Version 1	18 November 2013
Questionnaire: Survey Questionnaire	1	18 November 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

13/EE/0060:	Please quote this number on all correspondence

Yours sincerely

p p C Hallwell

Dr Michael Sheldon
Chair

E-mail: NRESCommittee.EastofEngland-Norfolk@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Kathryn Andrews, Norfolk & Norwich University Hospital NHS Trust*
Mrs Yvonne Kirkham

Appendix 23-TDier Checklist and CONSORT checklist

22.1 PARC TIDier Checklist

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	_____116	__Title of study provides the name intervention
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	__119-122	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	__106-115	___With reference to appendix 2_
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	_____106-115, and 122-126	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	_____128_____	_____
	HOW	106-115	
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	_____	_____
	WHERE	106, 123	
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	_____106, 123____	_____

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	_____106, 125-126	_____
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	____107-108	_____
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	124-125	_____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_____128__	_____
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	_____N/A____	_____

22.2. PARC- CONSORT Checklist

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	116
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	117
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	119-121
	2b	Specific objectives or hypotheses	122-objectives/aims
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	122
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	124-125,
Participants	4a	Eligibility criteria for participants	123
	4b	Settings and locations where the data were collected	106, 123

Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	106-115, 125-126
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	130- 135
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	N/A
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	126
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	126
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	126
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	126
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	127
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	132-
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	135-138
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	137
	13b	For each group, losses and exclusions after randomisation, together with reasons	139, 140, 141
Recruitment	14a	Dates defining the periods of recruitment and follow-up	125
	14b	Why the trial ended or was stopped	N/A

Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	142
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	137
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	140-158
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	167
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	160-168
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	160-168
Other information			
Registration	23	Registration number and name of trial registry	122
Protocol	24	Where the full trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	N/A

22.3. MOVE TIDier Checklist

TIDieR
Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	_____169	__Title of study provides the name intervention
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	__172-176	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	__106-115	___
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	_____106-115, and 176-179	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	_____106, 180_____	_____
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	106-115, 179-180_____	_____
	WHERE	106	
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	_____	_____
	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	_____106-115 179-178__	_____

	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	____107-108	_____
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	_____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_____180__	_____
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	_____N/A____	_____

22.4. MOVE CONSORT Checklist

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	169
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	170-171
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	172-176
	2b	Specific objectives or hypotheses	176-objectives/aims
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	176
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	176-177
	4b	Settings and locations where the data were collected	106, 176
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	106-115, 179
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	180-186

	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	N/A
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	179
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	179
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	179
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	179
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	179
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	186-189
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	187
	13b	For each group, losses and exclusions after randomisation, together with reasons	190, 191
Recruitment	14a	Dates defining the periods of recruitment and follow-up	177
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	192
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	187
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	191-206
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted	N/A

		analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	212
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	197-213
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	197-213
Other information			
Registration	23	Registration number and name of trial registry	176
Protocol	24	Where the full trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	N/A

Appendix 24 Study reports to participants- End of Study report

24.1. PARC Participant report

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

The Effects of a 6 month Active Lifestyle Programme on patients diagnosed as being at increased risk of developing further polyps as determined by colonoscopy.

Dear,

We would like to thank you for your time and interest in the study. You have made an invaluable contribution to research by making the time to attend research activities at the University of East Anglia for 12 months and we really appreciate all your commitment over this long study period.

The results that we got from the study have not only made a difference to research, but also led to the completion of a Doctorate for us three (Barnabas Shaw, Kelly Semper, and Liane Lewis). We want you to know that this would have not been possible without your help.

We have now completed all the analysis for the data that we collected and this letter is a little summary of the results. We have also presented some of the results at an International Conference in Austria.

If you have any questions about any of this, you are more than welcome to contact me on the following email: Liane.Lewis@surrey.ac.uk

Brief background why we did the study

We know that doing at least 150 minutes of moderate intensity physical activity each week is good for health. It is not only good for the heart, but it is also good to lower the risk of getting polyps in the bowel, and lower the risk that these polyps might turn into a cancer. Physical activity might help lower this risk by about 30%. That means, if you are active, there is a 30% lower chance that polyps will grow in your bowels, and that these polyps will turn into cancer.

What we do not know is how to motivate people do more physical activity if they are not very active at the moment.

That is why we did this study. We wanted to see if a certain style of exercise programme can help people become more active, and also help people to stay active. We think that motivation to be physically active is very important in adopting a more active lifestyle. So we were also interested how motivation changes over the study period.

What we did

You probably remember that we did all these tests at the beginning of the study. We looked at your activity levels at the moment, how fit you were, gave you a few questionnaires to see how healthy you feel at the moment, and measured a few things like your body weight and body fat content. We also asked you to carry one of those activity measures for one week.

Afterwards we put you into either the standard care group, or the exercise group. This was all decided by a computer programme, and we were not able to influence which group you were put in.

No matter which group you were in, we asked you to come to the University of East Anglia every 3 months for a full year to repeat all the measures we did at the beginning of the study.

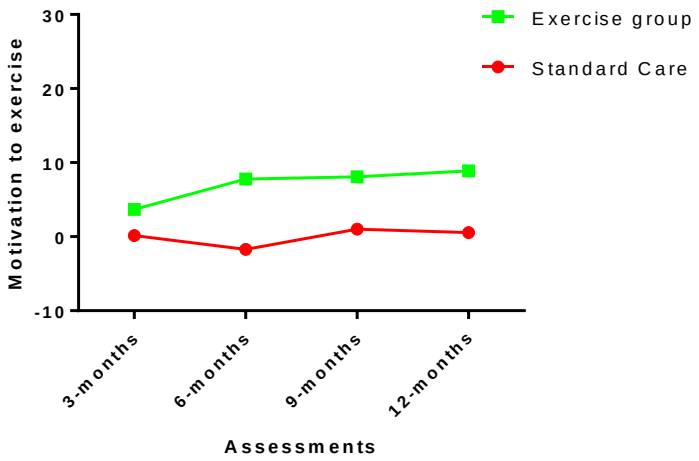
What we found

In total, we had 31 people joining this study, and you were one of them. There were 17 in the exercise group and 14 people in the standard care group (the one that did not take part in the exercises at the University).

Motivation

We found that people in the exercise group were more motivated to do exercise at the end of the intervention than the people in the standard care group. If you look at Graph 1 below, you can see the changes of motivation over the time of the study in relation to the beginning of the study. If the line goes up, that means that motivation got better. The green line is the exercise group and the red line is the standard care group. You can see that the exercise group had made larger improvements in motivation at 6 months than the standard care group. And you can see that this was similar at 12 months. That is good, because it means that Liane managed to get the people in the exercise group motivated in exercising and that they were still motivated to do exercise at 12 months after the beginning of the study.

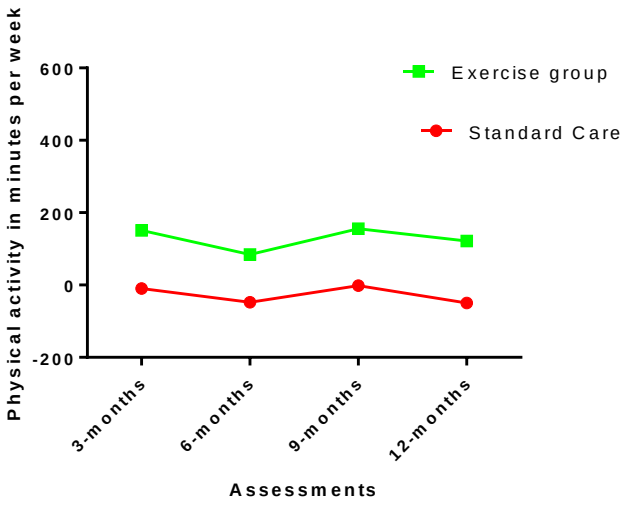
Graph 1



Physical activity

We also found that people in the exercise group started doing more physical activity in their leisure time than the standard care group. In Graph 2 below the lines show the change of minutes of physical activity each group has made throughout the study. Again, the green line is the exercise group and the red line the standard care group. You can see that at the end of the intervention, at 6 months, the exercise group did about 100minutes of physical activity more than they did at the beginning of the study. And the standard care group did actually less physical activity at 6 months compared to the beginning (because the dot is underneath the 0 value). And at 12 months this was very similar. Actually the exercise group did almost 200 minutes more exercise at the end of the study than they did at the beginning. And the standard care group did less than at the beginning of the study.

Graph 2



Fitness

We did notice that overall, the exercise group increased a bit in their fitness (from the bicycle test you did), and the standard care group decreased a little in their fitness throughout the study. But there was not a big difference between the groups, because some people in the standard group also increased their levels of fitness.

Quality of life

We did find that the exercise group felt a little better about their physical well-being after the intervention, but this was not very different to the standard care group.

Body composition

We also noticed that some people in the exercise group lost some weight, but not everyone did. Therefore, this was not very different to the standard care group.

We also found that the exercise group had a little bit less body fat at the end of the study than the standard care group. But the difference was not very big so we cannot really say that this was different between the groups.

What does this mean?

From the results we can say that the programme that Liane did was helpful in getting people more motivated to do more physical activity, but also helped them to actually do more physical activity. It is very important that people also still exercised more after the exercise sessions at the University stopped.

We are now able to test these findings in a bigger study where we will include a lot more people. Then more people can get the benefits of doing physical activity. If we can show that such programmes work, we hope that programmes like this will be routinely offered to people after they were diagnosed with a polyp, and to help them get the benefits of physical activity.

24.2. MOVE participant report

University of East Anglia

Norfolk and Norwich University Hospitals NHS Foundation Trust

A behavioural lifestyle intervention for colorectal cancer survivors

Dear,

We would like to thank you for your time and interest in the study. You have made an invaluable contribution to research by making the time to attend research activities at the University of East Anglia for 6 months and we really appreciate all your commitment over this long study period.

The results that we got from the study have not only made a difference to research, but also led to the completion of my Doctorate. We want you to know that this would have not been possible without your help.

We have now completed all the analysis for the data that we collected and this letter is a little summary of the results. We have also presented some of the results at an International Conference in Austria.

If you have any questions about any of this, you are more than welcome to contact me on the following email:

Liane Lewis: Liane.Lewis@surrey.ac.uk

Brief background why we did the study

We know from previous research that doing at least 150 minutes of moderate intensity physical activity per week can improve outcomes after a diagnosis of bowel cancer. Physical activity may lower the risk that the cancer comes back later in life by up to 50%. Studies have also shown that people who do at least 150 minutes of physical activity per week live longer after a diagnosis of bowel cancer.

We also know that people tend to do less physical activity after they had a diagnosis of cancer.

Therefore, in this study, we tried to develop an exercise programme that could help people become and stay more active. We think that motivation to be physically active is very important in adopting a more active lifestyle. So we were also interested how motivation changes over the study period.

What we did

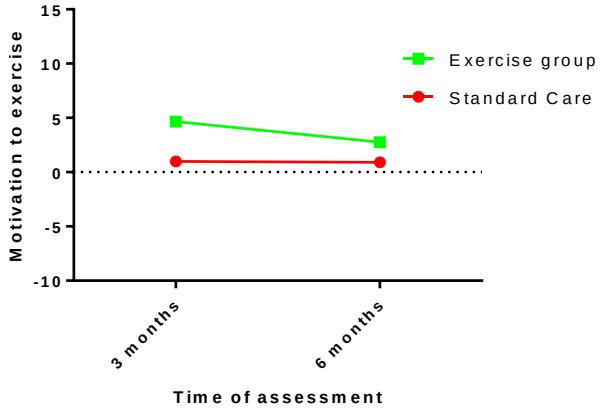
You probably remember that we did all these tests at the beginning of the study. We looked at your activity levels at the moment, how fit you were, gave you a few questionnaires to see how healthy you feel at the moment, and measured a few things like your body weight and body fat content. We also asked you to carry one of those activity measures for one week. Afterwards we put you into either the standard care group, or the exercise group. This was all decided by a computer programme, and we were not able to influence which group you were put in. No matter which group you were in, we asked you to come to the University of East Anglia every 3 months for 6 months to repeat all the measures we did at the beginning of the study.

What we found

In total, we had 28 people joining this study, and you were one of them. There were 14 in the exercise group and 14 people in the standard care group (the one that did not take part in the exercises at the University).

Motivation

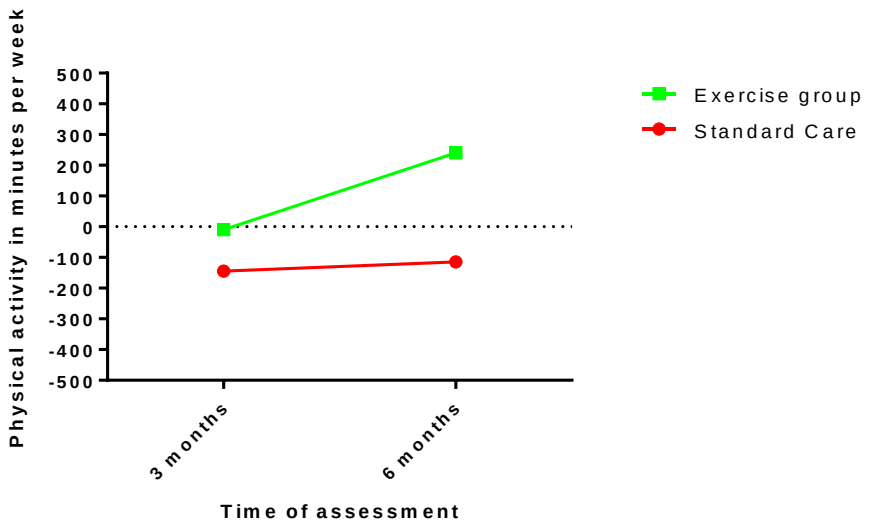
In Graph 2 below you can see the changes in motivation to exercise at 3 months and 6 months. The change is in relation to the beginning of the study. There was only a small change in motivation to exercise in the exercise group at both times we measured it throughout the study. The change was similar in both groups, that we did not observe a difference between them.



Physical activity

In Graph 2 below you can see the change in physical activity over the course of the study. We can see that at 3 months, immediately after the intervention ended, there were no changes in physical activity in either one of the groups. And at 6 months the exercise group did on average about 250 minutes of physical activity more than at the beginning of the study. And the standard care group did less physical activity at 6 months than at the beginning of the study.

Graph 2



Body composition

We found that people in the exercise group lost weight and body fat after the intervention at 3 months and at the end of the study at 6 months. The standard care group on the other hand, did increase their body weight and had more body fat at the end of the study. The exercise group lost about 1.4kg body weight and 0.3% body fat. And the standard care group lost about 0.2kg body weight but put on 1.3% body fat.

Strength and fitness

We did not find any differences between the exercise group and the standard care group in any of the measures that we did to test your fitness and strength.

What does this mean?

From the results we can say that the exercise programme was helpful in getting people to do more physical activity in the long-term (at 6 months). We are surprised that we did not see any changes in motivation to exercise in the exercise group. We are not very sure why this is, but we think that maybe the duration of the intervention was too short to make a difference in motivation. There is some research that suggested that an exercise programme might have to be at least 6 months long to help people make long-term changes. We are also surprised that we did not see any changes in strength. This might also be because the intervention was not long enough. More research needs to be done to find out what needs to be included in an exercise programme to make lasting changes in physical activity. If we can show that such programmes work, we hope that programmes like this will be routinely offered to people after a diagnosis of bowel cancer, and to help them get the benefits of physical activity.