Effects of a 6-month practical resistance training programme on muscle function and bone mineral density in adults with inactive or mildly active Crohn's disease: Study protocol for a randomised controlled trial

Section 1: Administrative Information

1.1a Trial registration

ISRCTN:11470370 DOI: 10.1186/ISRCTN11470370

1.1b Trial registration

Data Category	Information
Primary registry and trial identifying number	ISRCTN11470370
Date of registration in primary registry	11/12/2017
Primary sponsor	Northumbria University
Contact for scientific queries	Dr Garry Tew, Associate Professor or Exercise and Health Sciences
Public title	Resistance training in adults with Crohn's disease
Scientific title	Effects of a 6-month practical resistance training programme on muscle function and bone mineral density in adults with inactive or mildly active Crohn's disease: a randomised controlled trial
Countries of recruitment	United Kingdom- England
Health condition(s) or problem(s) studied	Inflammatory Bowel Disease- Crohn's disease (CD)
Intervention(s)	Group A: Usual care plus a 6-month practical resistance training programme Group B: Usual care only
Key inclusion and exclusion criteria	Inclusion • ≥16 years • Clinical diagnosis of CD for at least 4 weeks before screening visit

	• Inactive (<150 on Crohn's Disease Activity Index [CDAI]) or mildly active (150-219 on CDAI) CD assessed no greater than 4 weeks before screening visit • Faecal calprotectin (<250mcg/g) recorded no greater than 4 weeks before screening visit • Stable medications for at least 4 weeks before screening visit • Able to provide written informed consent and complete the study questionnaires • Able to travel to the research centre for assessment visits and exercise sessions <u>Exclusion</u> • Absolute contraindications to exercise testing and training as defined by the American College of Sports Medicine • Deemed unsuitable to undertake resistance exercise (assessed by gastroenterologist/ physician) • Planned major surgery within the first 6 months after randomisation • Female planning pregnancy within the first 6 months after randomisation • Pregnant • Current participation in >2 sessions/week of resistance exercise (self-reported) • Participation in another clinical trial for with concurrent participation is deemed inappropriate
Study type	Single-centre, two-arm, parallel group, randomised-controlled trial
Date of first enrolment	January 2018
Target sample size	Usual care plus a 6-month practical resistance training programme (n=25) Usual care only (n=25)

Recruitment status	Not yet recruiting
Primary outcome(s)	• Bone mineral density at the femoral neck, greater trochanter and lumbar spine (L2- L4) assessed using DXA at baseline and 6 months after randomisation • Muscle strength (N/kg_{FFM}) will be measured at baseline, 3 months and 6 months after randomisation. Lower limb strength (LS) and upper limb strength (US) will be assessed using an Isokinetic dynamometer system by measuring maximum voluntary isokinetic strength of the knee extensors on both legs and elbow flexors on both arms. Handgrip strength will be measured with a mechanical handgrip dynamometer, measures will be taken from the nondominant forearm to avoid training bias. • Muscle endurance will be determined at baseline, 3 months and 6 months after randomisation, lower extremity muscle endurance (LE) will be assessed using the 30-s chair stand test, upper extremity muscle endurance (UE) will be assessed using the 30-s arm bicep curl test

1.2 Protocol version: 2.0

Protocol Amendment:

Date	**Original**
18/12/2017	**1.1 Trial Registry:** Addition of the ISRCTN registration details
18/12/2017	**3.6 Participant Timeline:** Updated participant timeline to include the window of time assessments: 1) screening visit, 2) baseline visit; completed 4 weeks of the screening visit, 3)

	Randomisation, 4) Allocation of intervention; 1 week after randomisation exercise participants will commence the exercise sessions, 5) 13 week university follow-up; window of ±2 weeks for completion, 6) 26 week university visit and 26 week hospital visit; a window of +6 weeks for completion, 7) Exit interview and exercise consultation; a window of +6 weeks for completion. Added a paragraph, highlighting the aim of each visit and the window/ time frame in which the next should occur.
18/12/2017	**3.8 Recruitment:** Previous recruitment method was solely to approach patients in clinic, give them a recruitment pack and any interested patients could then make an appointment to attend a screening visit. Two additional methods of recruitment have been added: • Screening of the IBD BioResource, a database that contains patients who have consented to be contacted about future IBD studies and use of social media and social networking sites
28/01/2019	**3.5 Outcome Measures:** Feasibility and acceptability outcomes- to record exit interviews.

1.3 Funding

This study has received funding from PROcare LTD and the University of Northumbria at Newcastle. The University of Northumbria at Newcastle is responsible for the conduct of this study.

Breakdown of funding:

- PROcare LTD: 4 (four), 22.5-m rolls of latex-free resistance bands to the value of £500
- University of Northumbria at Newcastle: £1,000

  Consumables = £75

  1. Questionnaire licence fee for Inflammatory Bowel Disease Quality of life (£75)

  Equipment = £925

  1. Theraband equipment (£500)
  2. Skipping ropes, flat markers and gym mats (£225)
  3. Jamar hand-grip dynamometer (£200)

1.4 Investigator details

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Section 2: Introduction

2.1 Background and rationale

Crohn's disease (CD) is an immunologically mediated idiopathic chronic relapsing inflammatory disorder of the gastrointestinal tract (Sartor, 2006). The onset of this heterogeneous disease can occur at any age but typically peaks at 15 to 30 years and approximately affects one person in every 250 of the UK population (Crohn's and Colitis UK, 2015). However the incidence rates and prevalence of IBD has increased remarkably in recent years with over 10,000 new cases diagnosed every year, leading to an increased financial burden to the UK's National Health Service with projected annual costs to increase from £900 million to £1.5 billion by 2040 (Ghosh and Premchand, 2015; British Society of Gastroenterology, 2016). Despite extensive studies the aetiology of CD remains unknown and with no known cure symptoms such as fatigue, abdominal and joint pain, anaemia, blood loss and diarrhoea are managed and remission maintained with an array of medications or surgical interventions (Carter et al, 2004). Although pharmaceutical treatments are effective in controlling symptoms, these treatments are associated with undesirable serious side effects that continue to reduce a person's quality of life (Bilski et al, 2014). In addition, even when the disease is in remission 75% of patients are affected by impaired nutritional status, causing alterations in body composition such as depletion of fat stores, loss of muscle mass, bone substance and thereby decreased physical performance (Mijac et al, 2010). Moreover, these alterations are also highly associated to the development of extrainstestinal manifestations that occur beyond the intestinal tract such as musculoskeletal and dermatological disorders, liver disease and ocular, renal and pulmonary system involvement, which can be just as debilitating as the primary disease (Narula and Fedorak, 2008; Ott and Scholmerich, 2013).

Sarcopenia is a degenerative disease characterised by an involuntary loss of skeletal muscle mass and strength, contributing to poor physical performance and reduced quality of life (Greenland and Nair, 2003). Up to 60% of CD patients have depletion in muscle mass, reduced muscle function, strength and endurance in the upper and lower limbs in comparison to the healthy population, regardless of disease status (Geerling et al, 2000; Wiroth et al, 2005; van Langenberg, 2013). Interestingly, lower limb indexes: lower limb strength test (-24.6%, $p<0.001$), lower limb endurance test (-25.8%, $p<0.001$) and sit-up test (-25.1%, $p<0.001$) were significantly lower in the CD population (n=41) compared to the usual care control group (n=25) (Wiroth et al, 2005). Low lean mass and sarcopenia are highly prevalent in CD patients and are strong independent predictors for the development of osteopenia/osteoporosis (Bryant et al, 2015). Osteopenia and osteoporosis are skeletal disorders characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture (NIH, 2014). Up to 80% of CD patients have a

decreased bone mineral density (BMD), with 40-50% of these patients later going on to be diagnosed with osteopenia and a further 13-25% subsequently progressing to develop osteoporosis (Siffledeen et al, 2004). Resulting in individuals being three times more likely to sustain a fracture and skeletal complications compared to the general population (Mauro and Armstrong, 2007). Despite the high prevalence and the debilitating nature, these manifestations are not routinely assessed for in clinical practice and are only acknowledged when symptoms become apparent (Schneider et al, 2008).

To date, only a few small studies have assessed the impact of exercise on CD, examining the effects of low to moderate intensity continuous training programmes on physiological and psychological variables. Although exercise is not part of the treatment in CD patients, the perceived beneficial effects of exercise have been suggested to counteract some CD-specific complications by improving bone mineral density, immunological response, muscle mass and strength, fatigue, psychological health and overall quality of life (Buchman, 1999; Peters et al, 2001; Perez, 2009). While these preliminary studies are significantly limited by their small cohort size, observational design, no control group and lack of follow up there is growing evidence that resistance training may have a more profound effect on muscle strength and endurance and bone mineral density than aerobic exercise (Todd and Robinson, 2003; Vainionpaa et al, 2005). During resistance exercise the mechanical loading of the muscle increases the formation of myofibrils, thereby increasing muscle fibre thickness. The muscles then acting on the bone causes an anabolic effect resulting in osteogenesis, for this reason it is generally assumed that resistance exercise is the best treatment to elicit these physiological changes (Turner and Robling, 2004; Brotto and Johnson, 2014).

Despite this, no studies have explored the potential for resistance training to minimise or reverse decreased muscular performance within CD patients. Nevertheless, one randomised controlled trial has studied the impact of a low intensity resistance exercise programme on BMD in CD patients, focusing on the hip and lumbar regions only. At the conclusion of this 12 month study, the exercise cohort (n=53) showed a significant ($p>0.05$) improvement in BMD in the greater trochanter ($P=0.02$) and lumbar spine ($p=0.03$), reporting an average 8% increase in comparison to the control group (n=54). However, due to the cyclical nature of CD, only 52% of the exercise cohort managed to complete the twice weekly exercise programme over the year (Robinson et al, 1998). Although the study did show that a home-based muscular training programme is feasible in CD patients and is a potentially effective method for increasing BMD, further research addressing the compliance rates and examining the effect of more intense modes of exercise are needed.

2.2 Study objectives

Primary Objective

1. To investigate the effects of a 6-month practical resistance training programme on muscle function and bone mineral density in 50 adults with inactive or mildly active CD

Secondary Objectives

2. To investigate the possible benefits of a 6-month practical resistance training programme on fatigue, health-related quality of life and disease activity
3. To explore the patient acceptability and safety of a 6-month practical resistance training programme in adults with inactive or mildly active CD
4. To evaluate the feasibility of conducting a larger, multi-centre randomised-controlled trial of resistance training in adults with inactive or mildly active CD

Section 3: Methods, participants, interventions and outcomes

3.1 Study design

Single-centre, two-arm, parallel group, randomised controlled trial. After initial baseline assessments participants will be randomly assigned 1:1 to a 6-month practical resistance training programme plus usual care or a control group, who will receive usual care only. Study outcome measures will be measured at baseline, 3 and 6 months after randomisation. The study flowchart is shown in figure 1.

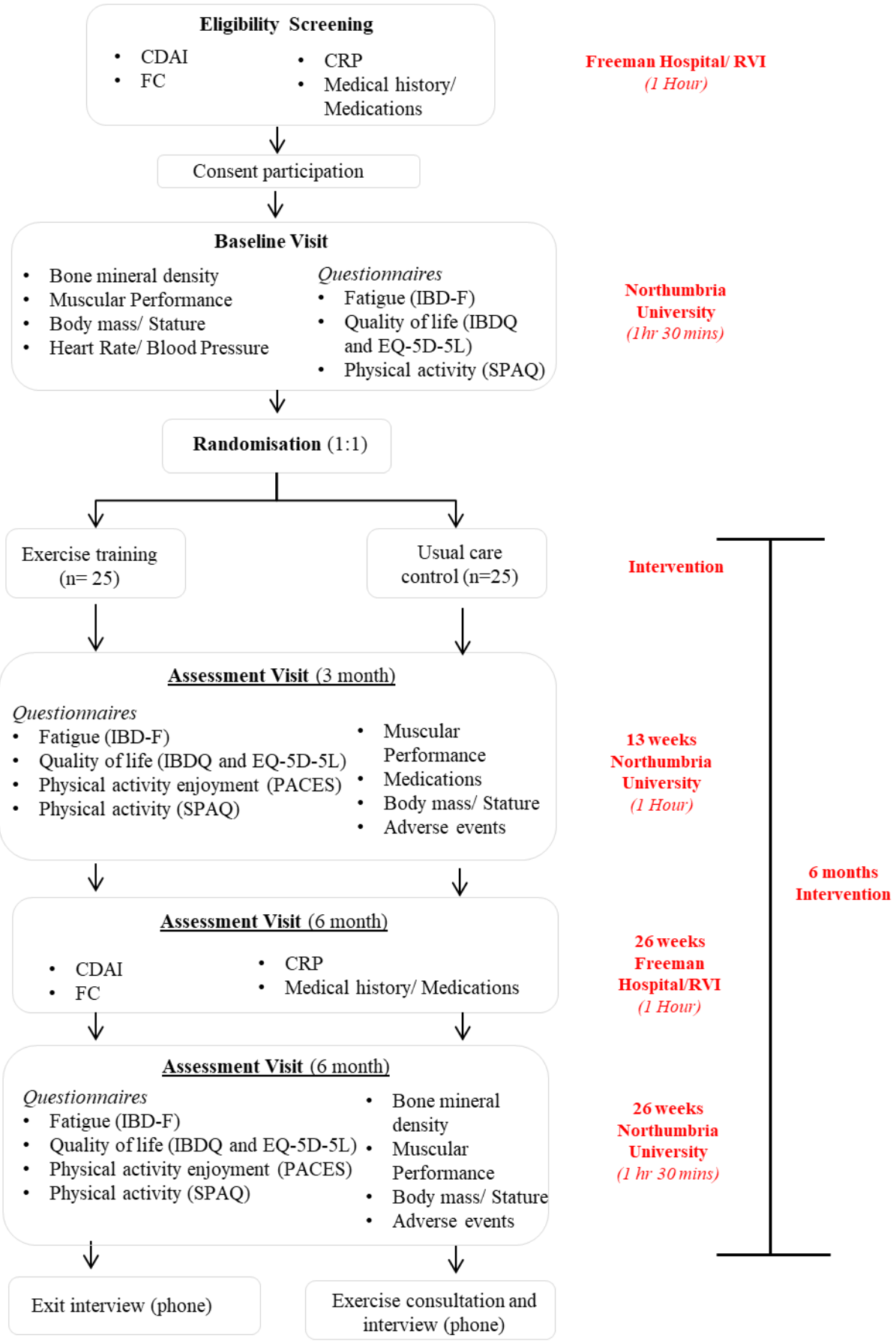

Figure 1. Study flow diagram

3.2 Study setting

Adults with Crohn's disease will be recruited from a clinical population within The Newcastle Upon Tyne Hospitals NHS Foundation Trust. Throughout the programme, participants will receive supervised resistance exercise sessions at Northumbria University to allow familiarisation and progression to the exercise programme. However, to promote long-term self-managed resistance training, the frequency of supervised sessions will be tapered over time, with an increasing emphasis on home based, unsupervised training (see section 3.4)

3.3 Eligibility criteria

Inclusion

Patients eligible for the trial must comply with all of the following at screening:

- ≥16 years
- Clinical diagnosis of CD for at least 4 weeks before screening visit
- Inactive (<150 on Crohn's Disease Activity Index [CDAI]) or mildly active (150-219 on CDAI) CD assessed no greater than 4 weeks before screening visit
- Faecal calprotectin (FC) (<250mcg/g) recorded no greater than 4 weeks before screening visit (Tew et al, 2017)
- Stable medications for at least 4 weeks before screening visit
- Able to provide written informed consent and complete the study questionnaires
- Able to travel to the research centre for assessment visits and exercise sessions

Exclusion

- Absolute contraindications or co-morbidities to exercise testing and training as defined by the American College of Sports Medicine (ACSM, 2017)
- Deemed unsuitable to undertake resistance exercise (assessed by gastroenterologist/physician)
- Planned major surgery within the first 6 months after randomisation
- Female planning pregnancy within the first 6 months after randomisation
- Pregnant
- Current participation in >2 sessions/week of resistance exercise (self-reported)
- Participation in another clinical trial for with concurrent participation is deemed inappropriate

3.4 Interventions

After baseline assessments participants will be randomly assigned 1:1 to a:

- Group A- 6-month practical resistance training programme plus usual care
- Group B- control group, usual care only

Group A- Supervised and unsupervised resistance exercise programme

Participants allocated to the resistance training group will be invited to complete three weekly supervised and unsupervised home based sessions for 60 minutes on non-consecutive days for 26 weeks. The supervised support sessions at Northumbria University will be tapered overtime:

1. 2 sessions a week for 2 weeks (week 1 and week 2) = 4 sessions
2. 1 session a week for 2 weeks (week 3 and week 4) = 2 sessions
3. 2 fortnightly sessions (week 5/6 and week 7/8) = 2 sessions
4. 4 monthly visits (week 9 onwards) = 4 sessions

Total= 12 supervised exercise sessions.

A maximum of three participants will be supervised per support sessions, which are expected to take place Monday to Sunday at the first convenience of the participant. These supervised sessions will provide participants with motivation and support regarding the exercise techniques, posture and body alignment. Heart rate and blood pressure will be recorded before and after the exercise programme.

Exercise Session

1. Warm up- 5 minutes - consisting of pulse raising dynamic exercises (60 seconds of: jumping jacks and mountain climbers, 45 seconds of boxer squat punch, cross over arm swings) and stretches (30 seconds of: forward and backward leg swings and big arm circles, 15 seconds of neck rolls and hip circles)
2. Jumping training- After initial rope skipping phase participants will progress to 2-3 sets of 10-15 multidirectional jumps.
3. Resistance training- 2-3 sets, 10-15 repetitions, 8-10 high intensity exercises targeting the upper body, lower body and midsection using a latex free resistance theraband. The latex free resistance therabands come in a range of precisely calibrated strengths and lengths depending on the requirements of the individual, allowing participants to reach an exercise overload effect regardless of initial fitness levels. They are light and easily stored and transported which simplifies the integration of an exercise programme into the lifestyle of the participant. Therabands have been shown to be easier on the joints and less likely to cause injury in comparison to using weights (Page and Ellenbecker, 2010; TheraBand, 2016).

Progression to the next level band will occur when the participant is able to complete the 3 sets of 10-15 repetitions easily, according to the Resistance Intensity Scale for Exercise (RISE) (Figure 3)

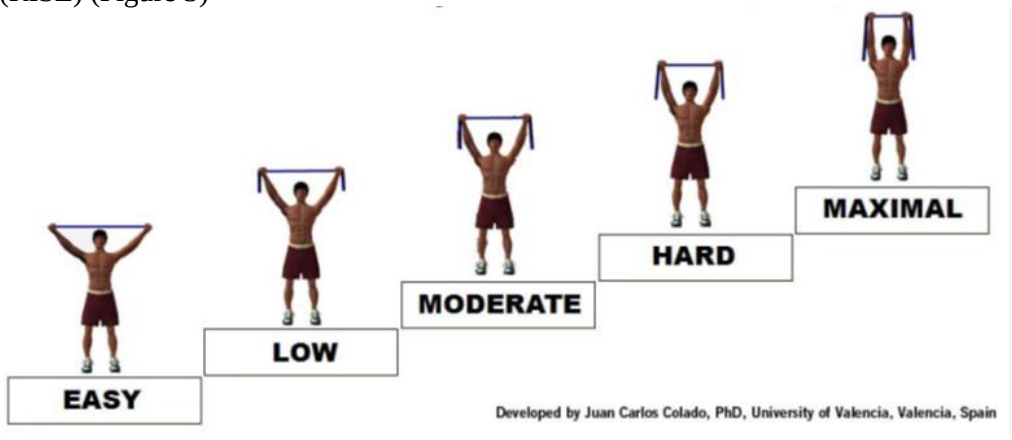

Figure 3. Resistance Intensity Scale for Exercise (RISE)

4. Cool down- 3 minutes- consisting of pulse lowering dynamic stretches (While walking up and down 30 seconds of: big arm circles, quad stretches and forward and backward leg swings and forward and backward lunges) and static stretches (15 seconds of: neck rolls, hamstring stretch, biceps stretch and cat back stretch)

Modifications and discontinuation

During the supervised sessions the appropriate training load will be progressed and determined using the 'Resistance Intensity Scale for Exercise', a validated tool to prescribe the appropriate intensity and progression of resistance training (Colado et al, 2014). Discontinuing the intervention criteria will include any participant who experiences a disease flare up requiring hospitalisation or a course of steroids, participant withdrawal that can occur at any time and for any reason, if the participant is unwilling/unable to comply with study procedures or if the investigator deems it unsafe. Participants will also be instructed to stop the training programme if they experience chest pain or any other distressing symptoms and to contact emergency services.

Compliance and adherence

Increasing self-efficacy, is a recognised and critical psychological determinant considered necessary for preparing the participant to adopt and maintain an exercise programme (Dijkstra *et al.*, 2003). Significant support has accumulated in favour of exercise interventions targeting increasing self-efficacy with the use of behavioural techniques such as goal setting, self-monitoring and social support (Bandura, 1997; Rovniak et al, 2002). These specific techniques have demonstrated an 80% improvement to adhering to exercise, maintenance of physical activity and lifestyle behavioural change post intervention in the general and clinical population (McAuley et al, 1993; Trost et al, 2002; Perri and Corsica, 2002). As inflammatory bowel disease (CD and ulcerative colitis) patients

have been shown not to meet recommend daily exercise guidelines or maintain incorporation of exercise into their lifestyle it is important to include these effective techniques to facilitate a transition in behavioural change (Mack et al, 2011; Chan et al, 2013; Tew et al, 2016). These strategies to improve and monitor adherence will be employed throughout the study:

- Goal setting- planning weekly specific, quantifiable and realistic goals following SMART guidelines
- Self-monitoring- objective and subjective measures- physical activity diary/ log to record self-managed training sessions and exercise participation
- Social support- Florence, a telehealth app that provides a motivational climate through the delivery of personalised motivation and text message reminders. All participants undertaking the exercise programme will receive an exercise and information programme booklet consisting of pictures and comprehensible text describing all elements of the programme and information on TheraBand care, travel information and contact information. All participants allocated to the control group will receive an information booklet consisting of travel information and reminders of assessment visits.

Rationale for choice of intervention

The main section of the programme will integrate high load resistance training exercises with high impact exercises to maximise the potential bone loading effects. These exercises were selected based on a recent meta-analysis which explored the effects of resistance training modes in 24 clinical trials on the preservation of bone mineral density. Results demonstrated that a combined resistance exercise protocol, integrating high load resistance training with high impact or weight bearing exercises, appeared more effective in preserving femoral neck (SMD = 0.411, 95 % CI = 0.176–0.645, $p = 0.001$) and lumbar spine (SMD = 0.431, 95 % CI = 0.159–0.702, $p = 0.002$) bone mineral density, compared to resistance training alone which only produced a nonsignificant positive effect (Zhao et al, 2015). In addition, similar training exercises have been shown to be safe and effective in other clinical populations such as diabetes, osteoarthritis and multiple sclerosis (Sabapathy et al, 2011; Latham and Liu, 2013).

Group B- Usual care group

This group will not receive any supervised exercise or be given any specific recommendations regarding exercise. However, once control participants have completed the 6-month assessment, they will be offered a one-to-one exercise consultation via telephone with the research assistant in which they will discuss the benefits of exercise training, barriers and facilitators to exercise, exercise guidelines, and personal goals and action plans. The aim of offering this consultation to control

participants is to help minimise the potential for resentful demoralisation that may occur through being allocated to this group (Torgerson and Sibbald, 1998).

3.5 Outcome measures

Primary outcomes

The primary measures that will be assessed:

- Bone mineral density (BMD)(g/cm2) will be determined at baseline and 6 months after randomisation using a Dual-energy X-ray absorptiometry (DXA) at the hip (femoral neck and greater trochanter) and lumbar spine (L2-L4).
- Muscle strength (N/kg_{FFM}) will be measured at baseline, 3 months and 6 months after randomisation. Lower limb strength (LS) and upper limb strength (US) will be assessed using an Isokinetic dynamometer system by measuring maximum voluntary isokinetic strength of the knee extensors on both legs and elbow flexors on both arms.
  For knee extension testing the highest five attempts will be recorded, with 1 minute rest between attempts. Peak values for the left and right leg will be averaged and used for analysis. For elbow flexion testing the highest three attempts, with 1 minute rest between attempts. Peak values for the left and right arms will be averaged and used for analysis. Handgrip strength will be measured with a mechanical handgrip dynamometer, measures will be taken from the nondominant forearm to avoid training bias.
- Muscle endurance will be determined at baseline, 3 months and 6 months after randomisation, lower extremity muscle endurance (LE) will be assessed using the 30-s chair stand test, upper extremity muscle endurance (UE) will be assessed using the 30-s arm bicep curl test (Jones and Rikli, 2002)

Secondary outcomes

- Quality of life will be measured using the Inflammatory Bowel Disease Quality of Life Questionnaire (IBDQ) and EuroQol five dimensions' questionnaire (EQ-5D-5L) at baseline, 3 and 6 months after randomisation
- Fatigue will be determined at baseline, 3 and 6 months after randomisation using the Inflammatory Bowel Disease Fatigue Scale (IBD-F)
- Body mass will be measured at baseline and 6 months using Avery Scales
- Stature will be measured at baseline and 6 months using a Stadiometer
- Disease activity will be measured at baseline and 6 months using the Crohn's Disease Activity Index (CDAI)
- Intestinal Inflammation will be determined by measuring faecal calprotectin at baseline and 6 months after randomisation

- Inflammatory markers in the body will be assessed through C-reactive protein (CRP), a blood test marker measured at baseline and 6 months after randomisation
- Physical activity habits will be determined using the Scottish Physical Activity Questionnaire (SPAQ) at baseline, 3 and 6 months

Feasibility and acceptability outcomes

Recruitment rates will be measured as rate of invited participants who are eligible and consenting and will be reported in a CONSORT participant flowchart. Acceptability of allocation procedures will be assessed by examining reasons for dropout in discontinuing participants and comparing attrition rates between the two study groups and between participants who did and did not receive their preferred allocation (assessed prior to randomisation). Suitability of measurement procedures will be evaluated based on completion rates and rates of missing data. Attrition rates will be established as discontinuation of intervention and loss to follow-up measurement for all groups. The acceptability of the exercise programme will be assessed using session adherence rates, measures of exercise enjoyment (PACES questionnaire at 3 and 6 months), and participant feedback via telephone interviews conducted after the 6-month assessment. Following obtaining consent specific to tape recordings, participant interviews will be recorded. The participant interviews will last up to 30 minutes and will cover perceived benefits and negative consequences from participating in the study, feedback regarding specific design features of the study (including the exercise protocol and assessment procedures), and perceptions of barriers and facilitators to intervention participation. The safety of exercise training will also be assessed by exploring rates of relapse at 3 and 6 months, reasons for dropout from the exercise programme, and the number and type of adverse events that occur in each group.

3.6 Participant timeline

Schedule of enrolment, interventions and assessments are demonstrated in the table below.

TIME FRAME			Within 4 weeks of Screening		Within 1 week of randomisation				±2 week window				±6 week window		±6 week window	
	PRE-EXERCISE				**STUDY PERIOD**										**POST-EXERCISE**	
	Enrolment	**Screening Visit- Hospital**	**Baseline Visit- University**	**Random isation (1:1)**	**Supervised Sessions- University**				**Assessment Visit- University**	**Supervised Sessions- University**			**Assessment Visit**		**Exit interview**	**Exercise consultation and interview**
													Hospital	**University**		
TIMEPOINT					Week 1-2	Week 3-4	Week 5-8	Week 9-12	Week 13 (3 months)	Week 14-17	Week 18-21	Week 22-25	Week 26 (6 months)			
Participant information sheet	X															
Eligibility screen- inclusion/ exclusion	X	X														
Disease Activity (CDAI and FC)	→	→											X			
Informed consent		X														
Participant ID number		X														
DATA COLLECTION																
Demographics		X														

Disease Variables (Medical history, medications)		X						X				X			
Stature: *Stadiometer*			X					X					X		
Body mass: *Avery Scales*			X					X					X		
Bone mineral density: *Dual-Energy X-ray Absorptiometry*			X										X		
Muscle strength: *Isokinetic Dynamometer and Handgrip dynamometer*			X					X					X		
Muscle Endurance: *30's chair stand test and 30's arm curl test*			X					X					X		
Fatigue: *(IBD-F)*			X					X					X		
Quality of Life: *(ED-5Q-5L and IBD-Q)*			X					X					X		
C-reactive Protein (CRP)		X										X			
Heart Rate and Blood Pressure			X		X	X	X	X	X	X	X				
Physical Activity Levels (SPAQ)			X					X					X		

Adverse event monitoring									X					X		
Physical activity enjoyment (PACES)									X					X		
INTERVENTION																
Exercise cohort plus usual care				X	X (4*)	X (2*)	X (4*)	X (1*)		X (1*)	X (1*)	X (1*)			X	
Usual care group only				X												X

* *Number of exercise sessions that week(s)*

Participants will be required to complete five assessment visits, a time frame for the participant is demonstrated in the table below.

- The screening hospital visit is designed to screen participants for eligibility and obtaining informed consent.
- The baseline university visit is to record baseline characteristics and measures. This visit must be completed within 4 weeks of the screening visit. After the baseline visit participants are randomised into one of two groups. A week after randomisation, participants in the exercise cohort will commence the thrice weekly exercise sessions for 26 weeks.
- The 13 week university visit is to follow-up with patients, record any changes, monitor any adverse events to the intervention and to assess any potential changes in the measures taken at baseline A window of $\pm$2 weeks will be allowed for the completion of this visit
- The 26 week university visit is to follow-up with patients, record any changes, monitor any adverse events to the intervention and to assess any potential changes in the measures taken at baseline and 13 weeks. The 26 week hospital visit is to follow-up with patients and assess patient safety through disease activity assessment: faecal calprotectin, blood markers of inflammation and CDAI. A window of $\pm$6 weeks will be allowed for the completing of the 26 week university visit and 26 week.
- The exit interview and exercise consultation will occur following the completion of both 26 week visits, a window of $\pm$6 week will be allowed for the completion of the telephone follow-up activities.

3.7 Sample size

We used the distribution based approach to calculate sample size because the minimum clinically important difference (MCID) has not been established for BMD measures in patients with Crohn's disease. We propose to use a superiority design to observe an effect size of 0.4 (i.e. a small-to-moderate effect); the effect size reported for hip BMD in a meta-analysis of combined resistance training interventions in post-menopausal women (Zhao et al., 2015). Using the sample size calculation methods of Borm et al. (2007), and assuming 80% power, a 5% alpha level (2-sided), and a correlation between pre and post hip BMD measures of r= 0.9, we will require 38 participants in total. After allowing for 20% attrition we need to recruit and randomise 50 participants (25 intervention, 25 control).

3.8 Recruitment

Adults with Crohn's disease will be recruited from a clinical population within The Newcastle Upon Tyne Hospitals NHS Foundation Trust. Recruitment posters advertising the research study will be placed in the waiting areas of the gastroenterology clinics and in examination rooms to stimulate interest and act as a reminder to staff. Methods of recruitment include:

1. Potentially eligible participants will initially be identified through the 'IBD Bio-resource database' at the Newcastle Centre of Bowel Disease Research, this database contains patients who have consented to be contacted regarding future trials they may be interested in. This database will be screened and potentially eligible participants will be identified and sent a recruitment pack before attending their routine gastroenterology appointment. This pack will contain: a recruitment letter, a participant information sheet, CDAI diary and example informed consent form. If interested in the study, patients will be asked to bring the CDAI diary recording parameters such as number of liquid stools, abdominal pain and general well-being over the last 7 days along with them to their appointment. If the inclusion/exclusion criteria appear satisfactory the participant will be asked to attend a screening visit either the same day as their gastroenterology appointment or to make an appointment at a time convenient.

2. Alternatively, potentially eligible participants will be approached by their gastroenterologist or a direct care team member when attending their routine appointment. Once informed about the study, participants will be given a recruitment pack containing: a recruitment letter, example informed consent form, CDAI diary and a participant information sheet informing them of the aims of the study, what is involved and any risks or benefits. Those wishing to participate in the study will be asked to wait 24 hours before contacting a member of the research team on the details provided. If the inclusion and exclusion criteria appear satisfactory an appointment will be made for potential participants to attend a formal

screening visit. Participants will also be asked to keep a disease activity diary, recording parameters such as number of liquid stools, abdominal pain and general well-being, for 7 days prior to their screening visit.

3. Crohn's disease patients will also be recruited through the use of social media tools and social networking sites, where details of the study will be uploaded and contact information regarding involvement will be provided. Interested participants will be asked to contact the study coordinator and a screening visit will be scheduled, the interested participant will also be asked to keep a disease activity diary for 7 days prior to this visit.

During this eligibility screening visit, the study will be explained in more detail and any questions will be answered. Participants will then be requested to sign an informed consent form, indicating they understand the study, what is involved and had the opportunity to ask questions. A direct care team member will then assess eligibility in more detail, involving objective and subjective measures of disease activity (Faecal Calprotectin [FC] and Crohn's Disease Activity Index [CDAI]). As a formality of routine gastroenterology appointments often faecal calprotectin and C-reactive protein are assessed, however if these measures have not been performed within the previous 4 weeks of the visit a stool and blood sample will need to be provided. Body mass, extrainstestinal complications, anti-diarrhoeal medication, haematocrit and a physical examination of abdominal mass will be assessed by a direct care team member. On the return of the intestinal inflammatory markers (FC) and calculation of CDAI scores, eligible participants will be telephone via the details provided and invited to book in for their baseline assessment measures. Participants who do not respond to recruitment attempts or who decline participation will not contacted further. Non-eligible participants will also be contacted to inform them that their participation will not be required.

Section 4: Methods- assignment of interventions

4.1 Randomisation and allocation

A researcher who is not involved in the recruitment process will use a free, online randomisation programme (www.randomization.com) to generate the randomisation sequence. Following baseline assessments, participants will be randomly assigned 1:1 to the intervention group or control group. Stratified block randomisation will be used. Stratification variables are sex (male/female) and disease activity (inactive/mildly active). Block size will be variable to ensure concealment.

4.2 Blinding

Due to the nature of the intervention, blinding the participants and intervention providers would be difficult or even impossible. Although both groups will be aware of the allocated arm, blinding is possible for the outcome assessors. Therefore, to reduce bias, participants will be asked not to inform

the outcome assessor (technician) of their intervention category and intervention providers will not be involved in taking outcome measurements.

Section 5: Methods- data collection, management and analysis

5.1 Data collection

Demographic information to inform analysis collected through self-reports will include age, gender, employment status and smoking history. Disease variables such as disease duration, current medication, comorbidities, previous use of glucocorticoids and surgical history will be established on the basis of medical notes. Clinical characteristics collected will include stature, body mass, BMI, bone mineral density, muscle performance, disease activity, fatigue, quality of life and exercise enjoyment.

Assessment of Bone Mineral Density

A dual-energy X-ray absorptiometry (DEXA) (Hologic Horizon W DEXA scanner) will be used to quantify bone mineral density (BMD). It will involve the participant lying flat on their back on an x-ray table for approximately 10 minutes. While remaining still, a large scanning arm will slowly be passed over the participant, emitting a narrow beam of low-dose radiation. A bone densitometry for both men and women uses a radiation dose of 0.01 mSv, equivalent to 3 days of natural background radiation (NBR). When comparing this measure to other procedures, the DEXA scan uses an extremely small amount of radiation in comparison to other radiological procedures: CT scan of the spine uses a radiation dose of 6 mSv comparable to 2 years NBR, CT scan of the abdomen and pelvis uses a radiation dose of 10 mSv comparable to 3 years NBR, X-ray at the lower gastrointestinal tract uses a radiation dose of 8 mSv comparable to 3 years NBR and a dental X-ray uses a radiation dose of 0.005 mSv comparable to 1 day NBR (International Commission on Radiological Protection, 2007). This simple, quick, non-invasive method was chosen as it requires no special preparation, causes the participant no physical harm and the participant is able to go home straight after (NHS, 2016). The reproducibility of DEXA is a key issue throughout this clinical research as changes in BMD are small and gradual. Various studies have suggested that DEXA is the 'gold standard' measurement tool for assessing bone mineral density, demonstrating a high degree of accuracy (coefficient of variation (%CV) whole body, 0.73%; lumbar spine, 0.92%; total proximal femur, 0.92%; total forearm, 0.69%) and high repeat measures (correlation coefficients ranging from 0.993 to 0.996 ($p<0.01$)) (Zack et al, 2002; Small et al, 2005; Humadi et al, 2010).

- Bone mineral density (BMD)(g/cm2) will be determined at baseline and 6 months after randomisation using a Dual-Energy X-ray absorptiometry (DEXA) at the hip (femoral neck and greater trochanter) and lumbar spine (L2-L4).

Assessment of Muscle Performance

An isokinetic dynamometer system (Biodex system 4 Pro) will be used to measure maximum voluntary isokinetic strength of the knee extensors on both legs and elbow flexors on both arms. For these clinical measurements muscles will function more safely and efficiently if warmed up, therefore participants will be required to perform a 10 minute cardio warm up concentrating on the areas that are going to be tested (Porcari et al, 2015). During the warm up participant information will be inputted into the computer and the dynamometer set up (individually adjusted for every patient). The participant will then be secured to the chair using the straps to stabilise them to minimise and prevent accessory movements of segments which would result in higher torque values. Practice attempts and demonstrations will be offered to participants to make them feel more comfortable about the procedure. For knee extension testing the highest five attempts will be recorded, with 1 minute rest between attempts. Highest peak values for the left and right leg will be used for analysis. For elbow flexion testing the highest three attempts, with 1 minute rest between attempts. Peak values for the left and right arms will be averaged and used for analysis. In order to make results more reproducible and consistent these tests will be performed in the same order every time. The isokinetic dynamometer is considered the gold standard measurement of muscle performance. In particular the Biodex system 4 has demonstrated the highest correlation coefficients for reliability, accuracy, validity and repeatability that remain unmatched. For the lower body, the peak torque, average peak torque and average power of the knee flexors and extensors all had values greater than ICC = 0.80, with the highest reliability observed at the peak torque of the knee extensor muscles (ICC = 0.99) (Maffiulett et al, 2007; Santos et al, 2013; Biodex, 2017). Similar results were observed for the upper extremity, with peak isokinetic elbow extension and flexion demonstrating values greater than ICC = 0.87 (Starsky et al, 2005; Bassan et al, 2015).

Grip strength, the result of forceful flexion of the finger joints with maximum voluntary force, will be determined using a calibrated handgrip dynamometer (JAMAR Hydraulic). Practice attempts and demonstrations will be offered to participants to make them feel more comfortable about the procedure. The participants elbow will be at a 90 degree angle from the side of their body and the base of the handgrip dynamometer will rest on the palm of the patient's nondominant hand, to avoid training bias. Maximum isometric effort will be maintained for 5 seconds, and the highest three attempts will be recorded, with 30 seconds rest between attempts. The Jamar handgrip dynamometer was selected due to its wide use in the clinical assessment of upper body strength, lack of invasive nature or laboratory testing and not requiring physician assessment (Bohannon et al, 2006; King, 2013). Results have demonstrated good reliability with intra-class coefficients ranging from 0.84 to 0.93 and when compared to certified standard weights excellent concurrent validity (r = 0.99) and strong concurrent validity with no significant difference (Niebuhr et al, 1994; Svens and Lee, 2005).

The 30-Second chair stand test will be used to measure lower limb muscle endurance (LE). A chair will be placed against the wall for stability, while the participant sits in middle of the chair, back straight, hands placed on their opposite shoulders and feet flat on the floor (Rikli and Jones, 1999). Prior to testing, a practice of the stand test will be conducted to ensure proper technique and adequate balance. The participant will then complete as many rises to full stand in 30 seconds. This clinical measure was selected due to its extensive use throughout literature and efficient nature in assessing lower limb muscle endurance in a short period of time. Its excellent test-retest reliability (r = 0.89), excellent criterion validity when compared to other assessments; leg press (r = 0.77, 95% CI = 0.64-0.85) and squat test (r = 0.71, 95% CI = 0.53-0.84) and excellent correlation to the 50ft walk test ICC = -0.64 (95% CI = -0.75 to -0.49) were also contributing factors (Jones and Rikli, 1999; Gill and McBurney, 2008; Gill and de Morton, 2012).

The 30-Second arm curl test will be used to measure upper limb muscle endurance (UE). The participant will be required to sit in the middle of the chair and hold the weight (5lbs for women and 8lbs for men) in their nondominant hand vertically down the side of the chair. They will then curl their arm up through a full range of motion, turning the palm up (flexion with supination), and gradually return to the starting position (Rikli and Jones, 1999). Prior to testing, a practice of the arm curl test will be conducted to ensure proper technique. The participant will then complete as many arm curls as possible in 30 seconds. This clinical measure was selected due to its high test-retest reliability (r =0.79), its ease and efficient nature in assessing upper limb muscle endurance in a short length of time (Jones and Rikli, 2002; Bhattacharya et al, 2016).

- Muscle strength (N/kg_{FFM}) will be measured at baseline, 3 months and 6 months after randomisation. Lower limb strength (LS) and upper limb strength (US) will be assessed using an Isokinetic dynamometer system by measuring maximum voluntary isokinetic strength of the knee extensors on both legs and elbow flexors on both arms. For knee extension testing the highest five attempts will be recorded, with 1 minute rest between attempts. Highest peak values for the left and right leg will be averaged and used for analysis. For elbow flexion testing the highest three attempts, with 1 minute rest between attempts. Peak values for the left and right arms will be averaged and used for analysis. Handgrip strength will be measured with a mechanical handgrip dynamometer, measures will be taken from the nondominant forearm to avoid training bias.

- Muscle endurance will be determined at baseline, 3 months and 6 months after randomisation, lower extremity muscle endurance (LE) will be assessed using the 30-s chair stand test, upper extremity muscle endurance (UE) will be assessed using the 30-s arm bicep curl test.

Assessment of Disease Activity and Inflammation

The Crohn's Disease Activity Index (CDAI) will be used to quantify disease activity for CD, by referring to disease symptoms exhibited over the last week. This standardised clinical index is comprised of 8 domains: number of liquid stools, abdominal pain ranging between none and severe, general well-being ranging between well and terrible, extracolonic features (arthritis, uveitis, erythema nodosum, peri-anal fissure, other bowel-related fistula and febrile), number of anti-diarrhoeals, abdominal mass ranging from none to definite, haematocrit and weight. After calculating the sum of results respondents will be categorised into four disease states, those in clinical remission (CDAI score <150), mildly active (CDAI score 150-220), moderately active (CDAI score 220-450) and severely active (CDAI score >450) (Best et al, 1976). The CDAI was selected due its extensive use throughout literature, its primary focus on the CD population and its use of subjective and objective measures. CDAI has also demonstrated acceptable reliability and validity, with a co-efficient of correlation between clinical assessment of disease activity and the CDAI of 0.7 and an intra-class correlation test determined by an ANOVA between total variance and components of this variance case was 0.66 (Summers et al, 1979; Sandlet et al, 1988; Yoshida, 1999).

Calprotectin, a calcium-binding protein biomarker will be measured to assess intestinal inflammation and risk of flare ups in CD patients. When the disease is active, due to the leukocyte shedding in the intestinal lumen this pro-inflammatory biomarker can be detected in the stool and the intensity of inflammation. Normal levels of FC in the general population are below 50µg/g, however within the CD population anything above 250µg/g is suggestive of an active disease. This non-invasive, simple and low cost indicator was selected as it prevents the need for unnecessary endoscopy procedures and histological assessment, which has been established to correlate well with calprotectin concentrations (Sipponen et al, 2008; Langhorst et al, 2008). FC has also demonstrated a strong correlation with 111-indium-labelled leucocytes, a measure that is considered the 'gold standard' in determining intestinal inflammation (Costa et al, 2003). A C - reactive protein (CRP) blood test marker will also assess the presence of inflammation. This substance is produced by the liver in response to inflammation, known as an acute phase reactant increasing when inflammation is present.

- Disease activity will be measured at baseline and 6 months using the Crohn's Disease Activity Index (CDAI)
- Intestinal Inflammation will be determined by measuring faecal calprotectin at baseline and 6 months after randomisation
- Inflammatory markers in the body will be assessed through C-reactive protein (CRP), a blood test marker measured at baseline and 6 months after randomisation

Assessment of Fatigue Levels

Fatigue will be measured using the IBD fatigue (IBD-F) self-assessment scale, by referring to symptoms experienced during the past two weeks (Czuber-Dochan et al, 2014). This standardised clinical index consists of three sections; the first section is comprised of 5 questions identifying the intensity and duration of fatigue, the second section is comprised of 30 questions assessing the impact of fatigue on daily activities and the third section identified causes of fatigue. Questions in section 1 and 2 are scored on 0-4 Likert scale, with the total possible score ranging from 0-120. After calculating the sum of results a score of 0 is indicative of no fatigue/ no effect on daily activities, a score of 1-60 is consider moderately fatigued/ moderate effect on daily activities and 61-120 is suggestive of severe fatigue/ severe effect on daily activities (Czuber-Dochan et al, 2014).

Due to its subjective and complex nature, fatigue can be difficult to define, understand and measure and thus poses a key obstacle in fatigue related research as no single 'gold standard' assessment measure can be developed that adequately captures the complexity of this debilitating and invisible symptom (Graff et al, 2011). While numerous fatigue assessment tools exist, the inflammatory bowel disease fatigue (IBD-F) patient self-assessment scale was selected due to its primary focus to the specific needs and experiences of IBD patients through asking questions based on the self-reports gathered from in-depth, cognitive interviews and questionnaires (Czuber-Dochan et al, 2014). Not only does this scale address the aims of the study, it is easy and clear to use (Mota and Pimenta, 2006; Eichhorn et al, 2010). In addition, it has also been identified as psychometrically robust with reliability estimates falling within statistically acceptable ranges (0.80 to 0.90), with a high degree of internal consistency (Cronbachs alpha >0.9) and good content validity, with acceptable test-retest stability (0.74) (Czuber-Dochan et al, 2014).

- Fatigue will be determined at baseline, 3 and 6 months after randomisation using the Inflammatory Bowel Disease Fatigue Scale (IBD-F)

Assessment of Quality of Life

Quality of life will be assessed using the EuroQol five dimensions questionnaire (EQ-5D-5L) and Inflammatory Bowel Disease Quality of Life Questionnaire- long version (IBDQ). The EQ-5D-5L consists of two parts: part 1 is comprised of five questions regarding mobility, self-care, usual activities, pain/discomfort and anxiety/depression, while part 2 uses a visual analogue (EQ VAS) to measure health status ranging from 0-100. Descriptive data that can be used to generate a health-related quality of life profile (EuroQOL, 2009). The EQ-5D-5L was selected due its extensive use throughout literature and simplistic and efficient nature in assessing quality of life (Bowling, 2005). It has demonstrated good test-retest reliability (r = 0.90) with kappa coefficients up to 0.61. Correlation coefficients with other measures of self-related health such as the 36 item short form health survey (SF-36) and the Health Utilities Index (HUI-3) indicated convergent validity (r = 0.64 and r = 0.69).

However, the EQ-5D-5L's lack of construct validity has been brought into question, with reports of health descriptions not correlating well with the participants actual health experiences (Insinga and Fryback, 2003). Therefore the IBDQ will be implemented to provide an additional screening method, which provides a valid and reliable measure of quality of life.

The IBDQ is comprised of 32 items into four dimensions: bowel and systemic symptoms, social impairment and emotional functioning. Scores ranging from 1 are indicative of poorest QOL to 7 which is consider best QOL, higher scores indicated better QOL (Guyatt et al, 1989). Whilst no 'gold standard' measurement tool for assessing quality of life in CD patients exists, the IBDQ was selected due to its ease, lack of invasive nature and its primary focus to the specific needs and experiences of IBD patients (Magalhaes et al, 2014). In addition it also showed to be homogeneous, with a Cronbachs alpha of 0.92, good test-retest reliability (0.76) and demonstrated a highly significant correlation with previous existing scoring systems, the 36 item short form health survey (SF-36) ($r= 0.86$, $p<0.0001$)(Hashimoto et al, 2003: Pallis et al, 2004: Verissimo, 2008).

- Quality of life will be measured using the Inflammatory Bowel Disease Quality of Life Questionnaire (IBDQ) and EuroQol five dimensions' questionnaire (EQ-5D-5L) at baseline, 3 and 6 months after randomisation

Data collection = 4 assessment visits for both interventions

5.2 Data management

All paper records, such as consent forms, completed questionnaires and clinical measurements will be stored in numerical order and kept secure in a locked cabinet at Northumbria University and in a patient's medical records at The Newcastle Upon Tyne Hospitals NHS Foundation Trust. To ensure quality data, all outcome data such as completed questionnaires will be checked manually by an investigator for completeness, clarity of answers and consistency before being entered electronically into Microsoft Excel. Data entry will involve labelling numeric codes (male = 1, female = 2), so data can be filtered and easier to understand. Checks after data entry will involve double data entry, carried out by two members of the investigatory team. These files will then be compared and any discrepancies checked against the original questionnaires and clinical measurement sheets.

Electronic data will be stored on a password-protected computer in accordance with university guidelines and the Data Protection Act (1998) and all data gathered during this research will be destroyed after 2 years following the conclusion of the study. Any identifiable information such as contact information will be destroyed/deleted as soon as possible. With exception of the healthcare professionals only the researcher will have access to any identifiable information which will be kept separate from any data that can identify the participant. In addition, for the safety of the participant if clinical measures are indicative of requiring treatment the patients named gastroenterologist will be

informed. A complete back up of the electronic database will be performed once a month, via a password protected hard drive, this storage device will be stored off-site. Incremental data back-ups will be performed on a daily basis. Passwords will be changed on a regular basis.

5.3 Statistical analysis

Analyses will be conducted in SPSS v22 using the principles of intention-to-treat. Significance tests will be two-sided at the 5% level. Descriptive statistics such as percentages, means + standard deviations will be used to present patient and disease-related characteristics. Continuous measures will be analysed using separate analysis of covariance models for months 3 and 6. These models will be adjusted for baseline value of the dependent variable, sex, and baseline disease status. Adjusted mean differences and 95% confidence intervals will be extracted from the models.

Section 6: Methods- harms

6.1 Harms

Adverse event reporting will be conducted in accordance with the Sponsor's Adverse Event Reporting Procedures. A clinical co-investigator will be responsible for determining the causality and seriousness of adverse events and ensuring that appropriate action is taken. Information about adverse events will be collected from the beginning of any study-related procedure. For the purpose of this study this is defined as the point at which written informed consent is given by the participant. The adverse event reporting period will stop at the participant's final trial contact, i.e. at the 6-month follow-up.

We will record all serious adverse events, as well as all non-serious adverse events that are either deemed to be related to participation in the research or result in withdrawal from an exercise programme or the study. Serious adverse events are defined as any untoward medical occurrence that fall in one of the following criteria: results in death; is life threatening; requires unplanned or prolonged hospitalisation; results in persistent or significant disability or incapacity, or; results in a congenital abnormality or birth defect. Non-serious events are defined as any untoward medical occurrence that does not fulfil any of the serious adverse event criteria.

Section 7: Ethics and dissemination

7.1 Research ethics approval, consent and confidentiality

The principle within research ethics is that the participant should not be harmed in any way by the research. To ensure the safety of the participant is protected the study will be submitted to Northumbria University Faculty of Health and Life Science Research Ethics Committee and the NHS Health Research Authority (HRA), which provides reviews of the application from the NHS Research Ethics Committees (REC) and the NHS Confidentiality Advisory Group (ADG). All data collected in

this study will be fully anonymised using numerical coding to maintain confidentiality. All paper records, such as completed questionnaires and clinical measurements will be stored in numerical order and kept secure in a locked cabinet at Northumbria University, in a patient's medical records and in a site file at The Newcastle Upon Tyne Hospitals NHS Foundation Trust. The site file will be placed and managed by a Research nurse within the NHS and will contain regulatory documentation, participant contact details, participant ID numbers, screening logs and consent forms. Electronic data will be stored on a password-protected computer in accordance with university guidelines and the Data Protection Act (1998) and all data gathered during this research will be destroyed after 2 years following the conclusion of the study. However, any identifiable information such as contact information will be destroyed/deleted as soon as possible. Only the principal investigator will have access to any identifiable information which will be kept separate from any data that can identify the participant. The results of the study will be used in the formation of a PhD thesis that will be examined as part of a postgraduate degree. Occasionally, some results might be reported in a scientific journal or presented at a research conference, however the data will always remain anonymous unless specific consent is obtained beforehand. Findings may also be shared with other organisations/ institutions that have been involved with the study.

Participants will be provided with a detailed information sheet regarding the aims of the study, what was involved, why they have been selected, withdrawal information, contact information of the researcher and any risks, discomforts or benefits involved. Once the participant has read and understood the participation information sheet, voluntary written informed consent will be gained. Although exercise testing has been demonstrated safe within the CD population (Narula and Fedorak, 2008; Bilski et al, 2014), due to the nature of the research risks assessments will be put in place with trained first aid members of staff available in the University premises. In addition, as recognised above the discussion of bowel movements and quality of life were addressed, aspects known to be sensitive and personal, therefore a participant debrief sheet with information regarding counselling services will be provided (Alarcon, 2009; Gray 2014).

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CRN Questions

1, Does the study take into account of the priorities, needs and realities of the NHS

Seeking to improve the health and well-being through alleviating complications and symptoms of Crohn's disease is the primary outcome of this research study. We aim to collaborate together in the interest and needs patients to promote, conduct and use this research to improve the current and future healthcare of the CD population. With shared principles, values and interests, the involvement of patients, clinicians and researchers is fundamental to contribute to the practice, theory and reality of incorporating new healthcare management options. Options that have the potential to improve quality of care that is safe, effective and efficient while strengthening and enabling patients to take control over their own condition.

Implementation of these findings will be broadcast to ensure stakeholders, NHS clinicians, Clinical Commissioning groups and most importantly patients are made aware of this research and its relevance to them to provide patients with additional management options. This study provides an essential step in the development of providing evidence based guidelines for individuals with this condition to improve health and care outcomes, the main priority of the NHS.

2, Is the study of clear value to the NHS

Inflammatory bowel disease (Crohn's disease and Ulcerative colitis) contributes to £900 million of the NHS budget. A figure that underestimates the impact this condition has upon the development of secondary complications both intestinal and extrainstestinal. Intestinal complications such as strictures, fistulae, bowel obstruction and perforation and extrainstestinal complications such as osteoporosis, sarcopenia, liver disease, bowel cancer and erythema nodosum.

There is significant pressure within the NHS to control expenditure, however with the incidence rates and prevalence of IBD increasing remarkably in recent years combined with its incurability, costs are expected to progressively increase over the next 10 years. Current therapies for Crohn's disease are often palliative rather curative, focusing on controlling symptoms and maintaining remission. However, while the aetiology and prevention of Crohn's disease remains unknown secondary complications such as osteoporosis (low bone mineral density) and sarcopenia (loss of muscle mass and strength) can be prevented,

managed and treated with weight bearing exercises. Although exercise is not part of routine treatment in CD patients, the perceived beneficial effects of exercise have been suggested to counteract some CD-specific complications by improving bone mineral density, immunological response, muscle mass and strength, fatigue, psychological health and overall quality of life.