# EXERCISE TRAINING IN YOUTH WITH INFLAMMATORY BOWEL DISEASE

# THE SAFETY AND FEASIBILITY OF EXERCISE TRAINING FOR YOUTH WITH INFLAMMATORY BOWEL DISEASE: AN EVALUATION OF FITNESS, FUNCTION AND PERCEPTIONS TOWARD PHYSICAL ACTIVTY

By

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TITLE: The safety and feasibility of exercise training for youth with inflammatory bowel disease: an evaluation of fitness, function and perceptions toward physical activity

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## ABSTRACT

As of 2012, 233,000 Canadians were reported to be living with inflammatory bowel disease (IBD), 2.5% of which were <18 years of age. In Ontario, the incidence of pediatric IBD is ~11.8 per 100,000 population, which is one of the highest rates in the world. Youth with IBD experience numerous health problems secondary to their diagnosis, including poor fitness and lower lean mass. The extent to which youth with IBD can respond to an exercise training program designed to improve fitness remains unknown. The aim of this thesis was to assess the safety, feasibility and physiological efficacy of an exercise training program for youth in remission from IBD. Additionally, we attempted to understand the barriers and facilitators to physical activity in this population.

A total of 104 patients were approached to participate in this study, 18 demonstrated interest and 11 consented to participate. Ten youth (nine males, age: 15.4±1.2 years) with IBD completed the study. Participants trained three times per week (2d in lab, 1d at home) for 16 weeks. Training sessions lasted 30 to 60 minutes, and consisted of a customized combination of aerobic and resistance exercises. Fat mass and lean mass were measured via Dual Energy X-ray Absorptiometry. Isometric and isokinetic torque of elbow flexion and knee extension were evaluated using an isokinetic dynamometer system. Peak oxygen consumption ($VO_{2peak}$) and peak mechanical power ($W_{peak}$) were determined using the McMaster All-Out Continuous cycling test. Barriers and facilitators to physical activity were measured via qualitative interviews pre-training. Body

composition, muscle strength and aerobic fitness variables were measured at baseline, after 8 weeks, and after 16 weeks of training. Participants completed 89.1±5.2% of lab training sessions and 55.0±26.5% of home training sessions. There were significant increases in whole body lean mass ($p<0.001$), isokinetic knee extension strength ($p<0.05$) and $W_{peak}$ ($p<0.001$) over the course of the training program with small, moderate and large effect sizes respectively. All participants were in remission post-training, demonstrated small deviations in features of disease activity and reported no adverse events with training. Participants described similar barriers and facilitators to physical activity, to those of the general public, such as lack of access to facilities and peer support, respectively. Additionally barriers and facilitators unique to individuals with this condition were identified including the physical burden of disease (e.g., episodic abdominal pain) and creating modifications to activities to facilitate accessibility. Our results demonstrate that exercise training in youth in remission from IBD is safe, feasible and has the capacity to counteract a broad range of secondary symptoms such as deficits in lean mass, muscle weakness and aerobic deconditioning. Youth with IBD should be encouraged to exercise on a regular basis. Results from this study will inform the design of a larger, randomized controlled trial.

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| | |
|---|---|
| AT | Aerobic training |
| APHV | Age at peak height velocity |
| BMI | Body mass index |
| CD | Crohn's disease |
| CF | Cystic fibrosis |
| DXA | Dual energy x-ray absorptiometry |
| FM | Fat mass |
| GI | Gastrointestinal |
| $HR_{max}$ | Maximal heart rate |
| IBD | Inflammatory bowel disease |
| JIA | Juvenile idiopathic arthritis |
| LBM | Lean body mass |
| PCDAI | Pediatric Crohn's disease activity index |
| PHV | Peak height velocity |
| PUCAI | Pediatric ulcerative colitis activity index |
| RT | Resistance training |
| $SV_{max}$ | Maximal stroke volume |
| UC | Ulcerative colitis |
| $VO_{2peak}$ | Maximal oxygen uptake |
| $W_{peak}$ | Peak mechanical power |
| WC | Waist circumference |

# CHAPTER 1: LITERATURE REVIEW

## 1.1 Introduction

There are approximately 5900 Canadian children <18 years of age with inflammatory bowel disease (IBD) (Rocchi et al., 2012). The prevalence of IBD among Canadian children and youth has risen steadily over the past 20 years and has recently been reported to be one of the highest in the world (Rocchi et al., 2012). Unfortunately there is no cure for IBD; thus, for the thousands of children and their families whose lives are complicated by this debilitating condition, strategies for disease management are essential. One commonly reported strategy for adults with IBD is exercise. Indeed, adults with IBD who engage in regular exercise can improve health-related fitness, quality of life, and overall well-being, without negative effects on disease symptoms (Loudon, Corroll, Butcher, Rawsthorne, & Bernstein, 1999; Ng, Millard, Lebrun, & Howard, 2006).

In a study by Ploeger et al. (2011), aerobic and anaerobic fitness were measured in pediatric patients with IBD who were in remission. They found that patient values were 15 to 25% lower than healthy reference values (Ploeger et al., 2011). Recognizing the intuitive link between fitness and physical activity, we objectively assessed habitual physical activity levels using accelerometry. We found that patients were accumulating less than half the minutes of moderate to vigorous physical activity than were being achieved by a control group of youth without IBD, tested at the same time of year (Timmons BW, *unpublished findings*). These troubling results suggest that inactive lifestyles are in place early

for youth with IBD and support the need for additional study of fitness and physical activity in these patients. Moreover, our new findings raise an important question about promoting physical activity among children and youth with IBD and learning what constitutes safe exercise.

To date*, there are no published studies reporting the effects of exercise training in pediatric patients with IBD.* To address this deficit in knowledge we conducted the current study with the aim of assessing the safety, feasibility and physiological efficacy of a 16-week exercise training program in youth with IBD. In addition, we utilized qualitative methodology to enhance our understanding of the barriers and facilitators to regular physical activity in this population.

### *1.1.1 Epidemiology of IBD*

The prevalence of inflammatory bowel disease (IBD) in Canada is among the highest in the world (Benchimol et al., 2009; Bernstein et al., 2006; Fedorak, Wong, & Bridges, 2010; Rocchi et al., 2012). As of 2012, ~233,000 Canadians were reported to be living with IBD and 10,200 new cases were diagnosed each year (Rocchi et al., 2012). While IBD can be diagnosed at any age, onset typically occurs in young adulthood (25-30 years) (Kim & Ferry, 2004). Nonetheless, approximately 20-30% of IBD cases in Canada are diagnosed in childhood (Kelsen & Baldassano, 2008), the average age of diagnosis being 10-12 years (Heyman et al., 2005). The prevalence of IBD in Canadian children and youth has increased dramatically in the last 20 years and in Ontario, is currently rated as an area with one of the highest incidences in the world (Rocchi et al., 2012). The

incidence of IBD in Ontario is 12 per 100000, and 6-7 and 4-5 per 100,000 for pediatric CD and UC respectively. In addition to a high prevalence of IBD in Canada, the economic burden is substantial. Combining direct and indirect sources, the cost of IBD amounts to $2.8 billion per year; approximately $12,000 attributable to each IBD patient (Rocchi et al., 2012). Taken together, IBD has proven to be a significant public health issue.

### *1.1.2 Clinical Presentation and Course of IBD*

IBD is a chronic inflammatory condition comprised of two subtypes, Crohn's disease (CD) and ulcerative colitis (UC). Both are characterized by high levels of inflammation along the gastrointestinal (GI) tract; however, they differ according to location and nature of inflammation. CD can occur at any part of the GI tract and affects the entire thickness of the GI wall, whereas UC is restricted to the mucosa of the colon and rectum (Kelsen & Baldassano, 2008). The origins of IBD remain idiopathic; however the most accepted hypothesis suggests that the combination of genetic predisposition and environmental factors may increase the susceptibility of experiencing a chronic inflammatory reaction along the GI tract (Kelsen & Baldassano, 2008).

A complex of abdominal pain, diarrhea, poor appetite and weight loss are characteristic of CD (Griffiths, 2004). Impaired linear growth and delayed sexual maturity may precede the development of intestinal symptoms and dominate the presentation. Conversely, the universal hallmark of UC is bloody diarrhea and impaired linear growth is rarely present at diagnosis (Griffiths, 2004). IBD is

characterized by variable periods of remission and exacerbation. CD is heterogeneous in nature and varies in severity among children. In a five year follow-up, approximately one-third of patients with CD were reported to have mild symptoms and another one-third troublesome exacerbations, but while in a state of remission nonetheless (Griffiths, 2004). The remaining one-third reportedly experience chronically active steroid-dependent disease, but half of these patients benefit significantly from resection and then a sustained remission. 70% of children with UC have been reported to enter remission within 3 months of initial diagnosis and in 45-58% of patients, their disease remained inactive over the first year after diagnosis. For most pediatric UC patients, disease was characterized by exacerbations and complete clinical remissions, while 10% had continuous symptoms in any year follow up (Griffiths, 2004). Given that the majority of pediatric patients with IBD experience remission, targeting interventions during this period of time is crucial.

### *1.1.3 Management of IBD*

IBD is a lifelong disease without a cure. Current treatment focuses on resolving symptoms during a flare up (induce remission) and preventing the recurrence of disease symptoms (maintenance) (Rocchi et al., 2012; Thayu et al., 2007). Therapies to induce remission include corticosteroids or exclusive enteral nutrition (EEN), whereas amino-salicylates or immunomodulators are used to maintain remission (Day, 2012). In addition to medical therapy, many children with IBD require surgical intervention. Close attention must be paid to growth and

nutritional status. As such, weight and height should be monitored regularly, in addition to height velocity and pubertal status. Further, providing attention to the psychosocial aspects and consequences of patients with IBD are equally as important (Day, 2012). Peer-support activities play an important role in the overall management of children with IBD.

## 1.2 Secondary Complications of IBD

IBD is not limited to the GI tract, as the disease expresses itself in various extraintestinal manifestations such as altered body composition, reduced muscle strength and impaired aerobic capacity, among others. An overview of studies examining physical fitness in youth with IBD is presented in **Appendix 1.**

### *1.2.1 Altered Body Composition*

There is a general consensus in the literature that lean body mass (LBM) is reduced in children with IBD compared to healthy controls (Bechtold et al., 2010; Boot, Bouquet, Krenning, & de Muinck Keizer-Schrama, 1998; Burnham et al., 2005; 2004; Sentongo, Semeao, Piccoli, Stallings, & Zemel, 2000; Thayu et al., 2007; Werkstetter et al., 2011; 2012). In a cross-sectional study, Sentongo et al. (2000) demonstrated that boys and girls with CD, compared to healthy controls, had an average of 3.5 and 2.9 kg less LBM respectively. Moreover it has been noted that LBM is significantly reduced irrespective of disease duration and diagnostic category (Bechtold et al., 2010). Children and youth with IBD exhibit sex-based differences in body composition. In newly diagnosed children with CD, FM and LBM were lower in girls compared to boys (Thayu et al., 2007).

Furthermore, girls presented with lower FM and LBM compared to healthy controls; whereas, boys primarily preserved their FM and had deficits in LBM (Thayu et al., 2007).

Results of longitudinal studies of body composition are equivocal. In one study, 42 children with CD did not improve their whole-body LBM during the 2-year observational study period, however BMI normalized, which may have been due to gains in FM (Sylvester et al., 2009). In comparison, Dubner et al. (2009) demonstrated significant improvements in calf LBM and FM during a 12-month observational study period in children and youth with CD. Most recently, Thayu et al. (2010) reported significant improvements in whole-body LBM and FM in boys and girls with CD over a 12-month observation period and continued gains over a long-term follow up (LTFU) (median: 43 months post diagnosis, range: 24-63 months). Compared to healthy controls, these boys with CD had a comparable LBM and significantly greater FM (Thayu et al., 2010). The girls with CD had deficits in LBM at LTFU compared to healthy controls, whereas FM was comparable (Thayu et al., 2010).

There are several proposed mechanisms to explain the altered body composition in youth with IBD. Firstly, an increased production of pro-inflammatory cytokines, e.g. TNF-α, can decrease myogenesis and induce muscle cell atrophy in vitro (Burnham et al., 2005). Inflammation may also decrease appetite, resulting in reduced caloric intake and anorexia, and impair nutrient absorption and utilization, resulting in malabsorption and nutrient deficiencies

(Bechtold et al., 2010; Burnham et al., 2005; Sylvester et al., 2009). Prolonged use of glucocorticoids has been shown to increase body fat and have catabolic effects on lean body mass (Burnham et al., 2005). Finally, a reduction in physical activity levels may detrimentally affect lean mass, while increasing fat mass (Burnham et al., 2005).

There is a compounded effect of disease onset when a child is in a vulnerable stage of growth and development (Bechtold et al., 2010). Average age of diagnosis of IBD in children is 12 years, with the majority being diagnosed between 6 and 17 years, which corresponds to a period of rapid and substantial gains in body mass. Specifically, the age of peak velocity of total body LBM in boys is 13.75 ± 0.97 years and 12.19 ± 0.96 years in girls (Bar-Or & Rowland, 2004). Reductions in LBM can have detrimental effects on physical function, increase the risk of infection and compromise peak bone mass accrual (Thayu et al., 2007; 2010). In addition, lack of muscle strain on developing bone may impair bone mineral accrual (mechanostat theory), which ultimately may increase the risk of fracture and osteoporosis in adulthood (Bechtold et al., 2010). Thus interventions to preserve or increase LBM are of the utmost importance.

### *1.2.2 Reduced Muscle Strength*

Both newly diagnosed youth with IBD and those in remission, have demonstrated reduced grip strength compared to healthy controls, which was reflected in reduced LBM (Werkstetter et al., 2012) and muscle cross sectional area (Bechtold et al., 2010; Werkstetter et al., 2011). Werksetter et al. (2010)

reported that while grip strength was significantly lower in newly diagnosed children with IBD compared to those with longstanding disease, the former group experiences a higher rate of catch-up over time. This highlights an important opportunity to introduce interventions to increase muscle strength at the point of diagnosis, to fully maximize strength benefits. Strength performance was assessed in adults in remission from CD (Wiroth et al., 2005). Maximal isometric strength and endurance of the leg extensors was lower in CD patients compared to healthy controls. In addition CD patients were significantly slower to complete a 12-repetition sit-up test (Wiroth et al., 2005).

Similar to LBM, reductions in muscle strength in youth with IBD may be due to any one or a combination of disease pathology (increased inflammatory cytokines) (Bechtold et al., 2010), secondary effects of standard treatment options (prolonged glucocorticoid usage) (Wiroth et al., 2005), malnutrition and hypoactivity, that spiral into a cycle of deconditioning and detraining.

Reduced muscle strength has important implications for children with a chronic disease. Muscle strength is related to one's ability to participate in activities of daily living independently, e.g. ability to move freely without assistance, and subsequently overall quality of life (Farpour-Lambert & Blimkie, 2008). De-conditioning leading to the reduction of muscle strength may lead to further disability and decrease future recreational physical activity options (Bar-Or & Rowland, 2004). In general, muscle strength increases joint stability and thereby minimizes risk of musculoskeletal injuries (Farpour-Lambert & Blimkie,

2008). Strength may also be an enabling factor, which facilitates development of persistent physical activity habits in youth and establishes a positive attitude towards exercise, which may increase the likelihood of carry over into adulthood (Farpour-Lambert & Blimkie, 2008). Given that youth with IBD demonstrate reduced muscle strength compared to their healthy peers, strategies must be devised to help these youth experience the benefits that are associated with greater muscle strength.

### *1.2.3 Impaired Aerobic Capacity*

Only a single study has assessed aerobic fitness – a key indicator of exercise capacity – as a primary outcome in youth with IBD (Ploeger et al., 2011). Ploeger et al. (2011) reported that measures of aerobic capacity ($VO_{2peak}$ and $W_{peak}$) were significantly lower than reference values from healthy youth (~75% of predicted). These findings are in accordance with previous studies of aerobic capacity in adults with IBD (Brevinge et al., 1995; Loudon et al., 1999). An additional study in youth with Crohn's disease only, confirmed lower fitness levels in these patients compared to healthy controls (Nguyen et al., 2013; Ploeger et al., 2012).

Reduced aerobic fitness in youth with IBD may be explained in part by low hemoglobin concentrations (Ploeger et al., 2011). In addition, a lower exercise capacity may be related to elevated resting levels of inflammatory cytokines, which are commonly seen in IBD. TNF-α, a key cytokine in the pathogenesis of CD, is associated with muscle atrophy, which can lead to lower

levels of aerobic capacity in various inflammatory diseases (Roubenoff, 2003). Medication such as glucocorticoids, may contribute to reduced aerobic capacity, given its catabolic effect on lean body mass (Schakman, Gilson, Kalista, & Thissen, 2009). Finally, low levels of physical activity increase the risk of entering a detrimental cycle of deconditioning (Bar-Or & Rowland, 2004). Impaired aerobic capacity is a concern as it increases the risk of future health consequences, such as cardiovascular disease (Carnethon et al., 2003), diabetes, osteoporosis and obesity.

### 1.3 Barriers and Facilitators for Physical Activity

Children and youth with IBD have demonstrated lower exercise capacity and reduced levels of physical activity compared to their healthy peers (Ploeger et al., 2011; Werkstetter et al., 2012). Further adolescence is a period of time where physical activity steadily declines and behaviours established during this time are likely to track into adulthood (Plotnikoff, Costigan, Karunamuni, & Lubans, 2013). Little is known as to why these youth are inactive or how to facilitate physical activity. Whether barriers and facilitators to physical activity are similar between healthy children and those with a chronic disease remain relatively understudied, but would provide valuable insight when prescribing exercise as a therapeutic intervention.

Several studies have assessed the correlates of physical activity in healthy youth, which provide insight into the barriers and facilitators they may experience. In a review by Bauman et al. (2012), individual, social and environmental

correlates and determinants of physical activity were examined in healthy children and adolescents. Individual determinants included psychosocial factors such as self-efficacy and perceived ability to be active (Bauman et al., 2012). Family and general support were identified as a correlates and in terms of environmental facilitators for physical activity, they reported factors such as walkability, traffic, and access or proximity to recreational facilities (Bauman et al., 2012). Barriers and facilitators for physical activity in healthy youth may also be of relevance to children with IBD at times when disease symptoms are not dominating.

The voices of youth with IBD regarding barriers and facilitators to physical activity are missing from the literature. That being said, several studies have assessed barriers and facilitators to physical activity in children with other chronic diseases. In a study by Moola et al. (2012), children with cystic fibrosis (CF) exhibited both positive and negative perceptions toward physical activity. Positive perceptions were experienced in the context of family support, mastery of skill, enjoyment and a sense of hope (Moola, Faulkner, & Schneiderman, 2012). Whereas negative perspectives included the detrimental impact of CF on physical activity, belief that physical activity is not important, perceived lack of parental support and an overall sense of despair (Moola et al., 2012). Finally all participants experienced physical activity in the context of reduced time; due to time-consuming daily treatments and the life-limiting nature of CF, children with CF reportedly have less time available to them in relation to their peers.

Youth with other chronic illnesses have reported that experiences such as bullying, social stigma, poor inclusion, and lack of access to physical activity opportunities, hinder regular physical activity participation (Goodwin & Staples, 2005; Moola, McCrindle, & Longmuir, 2009). Moreover, the inability to keep up with able-bodied peers may increase perceptions of abnormality among youth with chronic illnesses (Moola, Faulkner, Kirsh, & Kilburn, 2008). Unpleasant physical symptoms have also been expressed as deterrents to physical activity (Swisher & Erickson, 2008). Given that there is no information on perceptions towards physical activity in youth with IBD, information from children with other chronic disease may provide insight into the disease-related limitations or facilitators for physical activity and exercise in this population. Children with a chronic disease may find it more difficult to be physically active because they face unique challenges that encourage the adoption of a sedentary lifestyle. It may be that the daily burden of disease makes participation in physical activity difficult, as these children can often experience fatigue, lengthy treatments and a number of co-morbidities (Wilkes et al., 2009). Children with a chronic condition may also be restricted due to real or perceived limitations imposed by their disease (van Brussel, van der Net, Hulzebos, Helders, & Takken, 2011). Perceived limitations generally stem from parents who see their children as vulnerable or 'at risk' (Wilkes et al., 2009) and subsequently restrict them to sedentariness.

A single study of adults with IBD, surveyed respondents regarding their exercise habits, including possible barriers and facilitators to exercising (Robbins, Poullis, & Rogers, 2013). Barriers and facilitators described were both general and IBD-specific in nature. General barriers included lack of time and financial constraints, whereas disease-specific barriers included lack of toilet access, health concerns and pain preventing exercise (Robbins et al., 2013). When asked if exercise affected their IBD, 72% of respondents reported that it made them feel better as opposed to 22% who reported it made them feel worse. Perceived benefits of exercise included, improved general wellbeing, boosted energy levels, improvement in IBD symptoms and weight control (Robbins et al., 2013). Information from adults with IBD may provide insight into the perceptions of youth with IBD with respect to participation in physical activity and exercise. Furthermore, this information is important to consider when designing physical activity interventions for individuals with IBD. Minimizing general and disease-specific barriers in combination with promoting health benefits may optimize engagement in physical activity in this population.

Although there have yet to be studies assessing the barriers and facilitators to physical activity and exercise in youth with IBD, one study has qualitatively examined the lived experience of youth with IBD. Symptoms common among youth with IBD include abdominal pain, and diarrhea, which may make physical activity participation uncomfortable and encourage avoidance (Nicholas et al., 2007). Additionally, children with IBD have described feeling stigmatized as

anorexic due to weight loss or embarrassed due to weight gain as a result of prolonged steroid use (Lowe, Kenwright, Wyeth, & Blair, 2012). Feeling different from their peers and experiencing daily physical symptoms may reduce interest and subsequently participation in physical activities for youth with IBD.

The social cognitive theory (SCT) postulates that behavior change is dependent on an interaction between personal factors, factors related to the behavior itself and environmental factors (Bandura, 1986; 1997). Examples of personal factors may include previous physical activity experiences and outcome expectations. Green space and safe neighbourhoods are examples of environmental factors. Finally, an enjoyable activity that produces desired benefits is an example of behavioural factors. This concept has been termed reciprocal determinism such that these factors may affect or be affected by the other components that comprise the SCT. An important component of the SCT is self-efficacy, or confidence in ones abilities to successfully perform a particular behavior. Social cognitive theory helps to explain health behaviours such as physical activity and creates a framework to use when designing interventions to increase physical activity. Research has shown that theory-based interventions are more effective than antheoretical approaches (Plotnikoff et al., 2013).

The exploratory nature of qualitative methodology may help illuminate why youth with IBD are inactive, in spite of the well-known health benefits associated with physical activity. Qualitative investigations of youth's perceptions toward physical activity have not been well studied, thus the voices of youth with

IBD are absent in the literature. Understanding the reasons youth with IBD are inactive and how to facilitate physical activity by developing interventions that incorporate their social lives and their worlds is an advantage of the descriptive and client-centered approach that is qualitative research (Moola et al., 2012).

## 1.4 Exercise Training in Healthy Youth

### *1.4.1 Resistance Training*

Historically, resistance training (RT) was not recommended for prepubertal children for reasons related to insufficient testosterone for adaptations, risk of injury, and damage to growth plates (Behm, Faigenbaum, Falk, & Klentrou, 2008; Malina, 2006). These myths have since been refuted by scientific evidence and RT has been accepted as safe and effective in all phases of maturity if performed under supervised conditions, with proper technique, a gradual progression and adequate warm up and cool down (Behm et al., 2008; Malina, 2006). A meta-analysis by Falk and Tenenbaum in 1996 reported RT-induced strength gains of 13-30% in pre-adolescent children following RT program of 8-20 weeks. This was recently reaffirmed by Behringer et al. (2010), who reported an effect size of 1.12 ($p$<0.001), indicating that strength training is effective in childhood and youth. They also reported that trainability of muscular strength increases with age and maturation. Nevertheless, regardless of maturational age, children and adolescents are capable of increasing muscle strength (Behringer, Heede, Yue, & Mester, 2010). In a study by Pfeiffer and Francis (1986), significant gains in muscle strength were observed across all maturity groups in

response to RT, but not in a control group **(Table 1)**.

**Table 1.** Change in isokinetic elbow flexor and knee extensor strength after 9 weeks of RT, 3 times/week.

| | **Elbow flexion (120°/s)** | **Knee Extension (120°/s)** |
|---|---|---|
| **Prepubertal** | +28.7% | +16.7% |
| **Pubertal** | +13.9% | +13.2% |
| **Postpubertal** | +10.5% | -1.0% |

Muscle strength and endurance have been shown to improve significantly with resistance training beyond what is expected with normal growth and maturation (Behm et al., 2008). In a review by Malina (2006), 22 studies agreed that RT 2-3 times per week resulted in significant gains in muscle strength in childhood and adolescence and that few injuries were reported. In some cases, training-induced improvements were more evident in older boys, greater in lower vs. upper body strength and with 2 days/week compared to 1 (Malina, 2006).

Strength gains in children are comparable to those seen in adolescents and adults but not gains in muscle size. Strength gains in childhood are mainly attributed to neurological adaptations, such as increased recruitment and activation of muscles involved in specific tasks (Behm et al., 2008). These adaptations are believed to occur in the early phases of training (Ramsay et al., 1990). In pubescent children, strength gains are largely explained by hypertrophy due to greater levels of circulating androgenic hormones (Ratel, 2011).

Current recommendations for RT prescription include exercising 2-3 times/week on non-consecutive days, beginning with 8-12 exercises, targeting the upper body, lower body and midsection (Behm et al., 2008; Faigenbaum et al., 2009). Initially 1-2 sets of 8-15 repetitions with a low to moderate load (about 60% 1-RM) are recommended, focusing on correct technique and safety. The prescription should also include a dynamic warm up and cool down with less intensive exercises and static stretching (Behm et al., 2008; Faigenbaum & Myer, 2010). Health benefits associated with RT include increased bone mineral density, muscle strength and endurance and maintenance of LBM in pre- and post-adolescent youth (Behm et al., 2008). Given the improvements in strength and health benefits associated with resistance training in healthy children, it is important to assess whether these benefits may be applied to youth with a chronic disease, such as IBD.

### *1.4.2 Aerobic Training*

Aerobic training is defined as exercise that involves whole body endurance activity, that is sustained for a sufficient length of time and at a sufficient intensity in order to improve cardiorespiratory fitness (Armstrong & Barker, 2011). Few studies have assessed responses to aerobic training in youth over the age of 13 years. Two controlled studies reported modest increases (~9%) in $VO_{2max}$ (ml/kg/min) in adolescent boys and girls following training, despite a large difference in the training volume between studies (Armstrong & Barker, 2011). Changes in $VO_{2peak}$ with training can be attributed to cardiac output,

specifically increased maximal stroke volume ($SV_{max}$), as opposed to maximal heart rate (Armstrong & Barker, 2011). Eriksson and Koch (1973) observed a 12% increase in blood volume and 17% increase in $VO_{2peak}$ in nine, 11-13 year olds following a 4-month training program. They attributed the increase in $VO_{2peak}$ to an increase in $SV_{max}$.

Recently Armstrong and colleagues proposed recommendations, which were endorsed by the International Olympic Committee (ICC), to increase $VO_{2max}$ in children and adolescents (Armstrong & Barker, 2011). They suggested that aerobic training should include both interval and continuous exercises using the large muscle groups. Frequency of training should be 3-4 times per week for 40-60 min per session for a minimum of 12 weeks. Additionally, the intensity of the sessions should be in the range of 85-90% of $HR_{max}$ (Armstrong & Barker, 2011).

The benefits associated with aerobic training are evident in healthy children, however the extent to which they can be seen in youth IBD post-training, remains to be studied. Understanding the physiological adaptations to aerobic training in this population in combination with exercise recommendations for healthy children will provide the basis for designing exercise training programs and guidelines in children with chronic disease.

**1.5 Exercise Training in Children with a Chronic Inflammatory Disease**

Unfortunately there is no cure for IBD, thus treatment must focus on managing disease symptoms and preventing extraintestinal manifestations. Physical activity is an attractive, non-pharmacological, and non-invasive

intervention that can attenuate the physical and psychosocial health deficits encountered by children with chronic disease. The benefits of regular exercise have been shown in several other chronic inflammatory disease groups. Patients with CF with high levels of aerobic fitness have a higher life expectancy (Nixon, Orenstein, Kelsey, & Doershuk, 1992) and better quality of life measures (Orenstein, Nixon, Ross, & Kaplan, 1989). Exercise training programs consisting of moderate intensity, continuous exercise can be tolerated by children with CF (Orenstein & Higgins, 2005); however, it has been acknowledged that this type of exercise prescription is unlikely to be sustained due to poor acceptability (i.e., the children did not enjoy this type of exercise) (Gulmans et al., 1999). In contrast, exercise training consisting of short bouts (e.g., 10-15 sec) of higher intensity exercise performed intermittently achieved similar physiological benefits but was viewed as more enjoyable by the participants (Klijn et al., 2004), suggesting a higher probability that this type of exercise would be sustained in everyday life.

For children with JIA, physical *inactivity* was historically prescribed – the rationale being that inflammatory conditions were considered best treated by rest (Bar-Or & Rowland, 2004). The evidence now reinforces the importance of health-related fitness in children with JIA. It is also interesting to note that functional ability in children with JIA is more closely correlated with anaerobic fitness than aerobic fitness (Takken, van der Net, & Helders, 2003), given than anaerobic activities (short bursts of high intensity) reflect the natural activity patterns of healthy children (Baquet, Stratton, Van Praagh, & Berthoin, 2007).

Although exercise training has not yet been explored in youth with IBD, studies in other pediatric chronic inflammatory disease groups provide rationale for, and guide the design of, the current exercise intervention in children and youth with IBD. Furthermore, given that there are no general exercise guidelines for youth with chronic diseases, those created for healthy children are often used and modified according to the abilities of the specific study population. Durstine et al. (2000) proposed that it is likely that the threshold intensity for improving aerobic capacity is reduced in patients with a chronic disease compared to healthy children thus has recommended a training intensity of 10-60% of peak oxygen uptake, which corresponds to a HR of about 66% of $HR_{peak}$ (Habers, van Brussel, Langbroek-Amersfoort, van Royen-Kerkhof, & Takken, 2012). Given the lack of exercise guidelines for youth with a chronic disease, important modifications must be made to recommendations targeted at healthy children in order ensure safety and optimize engagement in these vulnerable populations.

**1.6 Exercise Training in Adults with IBD**

Despite the lack of exercise training studies involving youth with IBD, at least six studies have assessed the effects of prolonged exercise training in adults with IBD (Candow, Rizvi, Chilibeck, & Worobetz, 2002; Elsenbruch et al., 2005; Gupta, Khera, Vempati, Sharma, & Bijlani, 2006; Loudon et al., 1999; Ng et al., 2006; Robinson et al., 1998), while one study has examined the response to acute, submaximal exercise (D'Incà et al., 1999). Studies examining the effects of exercise training in adults with IBD have mainly involved patients in remission or

with mildly active disease **(Appendix 2)**. Moderate exercise, such as walking, yoga and resistance training has been shown to improve bone mineral density, fitness, strength and quality of life and reduce stress. Importantly, all studies reported improvements in physiological and psychological outcomes without exacerbation of disease symptoms. Furthermore, D'Inca et al. (1999) reported that participants in remission from IBD who had performed acute exercise had not relapsed 6 months following exercise. It is encouraging that even light intensity physical activity appears to positively influence a number of health outcomes. It may be that patients with IBD experience such low levels of fitness and PA that even modest increases can have substantial benefits.

Few studies in adults with IBD have reported adherence to exercise training programs. Adherence was the lowest in a randomized control trial investigating the effects of a 12-month, home-based, low-impact exercise program on bone mineral density (BMD) in adults with Crohn's disease. The study reported a 52% adherence rate, with only 26% of participants completing the exercise regimen as prescribed (Robinson et al., 1998). Although adherence was poor, when participants were contacted at six months following the study, 50% had reported continued participation in exercise two to six times per week (e.g. aerobics, walking, aquacise, and cycling) (Loudon et al., 1999). Furthermore, higher adherence rates were observed in group-based and individual walking programs (Loudon et al., 1999; Ng et al., 2006).

Taken together, research has shown that low-to-moderate intensity exercise has beneficial effects on both physiological and psychological health in adults with IBD, without causing disease exacerbation. It remains unknown whether or not youth with IBD experience these same effects in response to exercise.

**1.7 Responses to Acute Exercise in Youth with Crohn's Disease**

Unfortunately, there have been no studies assessing the response to prolonged exercise participation in children and youth with IBD. However, two recent studies have evaluated the effect of acute exercise on inflammation and substrate utilization in adolescents with Crohn's disease (Nguyen et al., 2013; Ploeger et al., 2012).

First, Ploeger et al. (2012) measured the effects of acute bouts of moderate intensity continuous exercise (MICE) and high intensity intermittent (HIIE) on key markers of inflammation and growth relevant to children with CD. Except for monocytes in response to MICE, all markers exhibited exercise-induced responses that were similar to controls. Neither type of exercise increased TNF-α, which is thought to play a key role in the growth failure of children with CD (Shamir, Phillip, & Levine, 2007), and has been associated with muscle atrophy (Roubenoff, 2003). Results from this study suggested that youth with CD could engage in different types of exercise without a significant acute exacerbation of inflammation.

Second, Nguyen et al. (2013) measured substrate utilization during an hour of submaximal exercise in patients with CD and healthy controls. Whole body fat oxidation rate was lower in children with CD and they relied more heavily on carbohydrates (CHO), with an approximately 10% greater contribution to total energy expenditure. There were no differences in plasma insulin, free fatty acids, and glucose between groups. Results from this study suggest that adolescents with CD have impaired fat metabolism during exercise and rely more heavily on CHO to meet the energy demands of submaximal exercise.

It is important to note that the aforementioned studies in the pediatric CD population were based solely on acute exercise, and very little is known about the effects of chronic exercise on these variables. Nevertheless, these findings may serve to inform important considerations in designing a training program for youth with IBD. Specifically, these studies suggest that youth with CD can engage in two different types of acute exercise without experiencing an abnormal inflammatory response that may lead to exacerbation of the disease. Additionally, given the impaired fat metabolism and greater contribution of CHO to total energy yield observed in CD compared to controls, glycogen replenishment may be a necessary component of post-exercise nutrition so as to avoid further impairments in growth.

**1.8 Objectives**

Youth with IBD experience numerous health problems secondary to their diagnosis, including poor fitness and deficits in lean mass. Although these health

problems are known to respond to regular exercise, currently, there is no information on safe and effective exercise for these patients. Therefore, the objectives of this thesis were to:

1. Evaluate the safety and feasibility of a 16-week exercise training program in youth with IBD.
2. Assess the efficacy of a 16-week exercise training program in youth with IBD via changes in physiological health outcomes such as body composition, muscle strength and aerobic fitness.
3. Explore the barriers and facilitators for physical activity in youth with IBD using a social cognitive framework.

**1.9 Hypotheses**

We hypothesized that:

1. Over the course of the 16-week exercise training program, positive changes in physiological health outcomes would occur without exacerbation of disease symptoms.
2. 16 weeks of combined aerobic and resistance exercise training would result in increases in lean body mass, muscle strength and aerobic fitness in youth with IBD.
3. Barriers toward physical activity might include disease-specific physical symptoms, negative self-image and lack of opportunity (Nicholas et al., 2007). Facilitators toward physical activity might include social support, disease-

friendly environments and introduction to activities that do not exacerbate disease symptoms.

# CHAPTER 2: METHODS

## 2.1 Participants

Patients with IBD aged 10 to 17 years were recruited from the Centre for Child and Youth Digestive Health at McMaster Children's Hospital. Eligible participants were in remission from IBD, based on the pediatric Crohn's disease activity index (PCDAI) or the ulcerative colitis activity index (PUCAI) and/or physician confirmation (Hyams et al., 1991; Turner et al., 2007). Patients were excluded if their GI physician did not think they should be involved in an exercise program due to medical reasons or if they already engaged in resistance training ≥ 3 times per week. There were no restrictions on medication use in this pilot study. Informed consent and assent was collected from parents or guardians and participants. This study was approved by the Hamilton Integrated Research Ethics Board (HiREB).

## 2.2 Feasibility

Feasibility was defined as the ability to recruit and enroll participants in a 16-week exercise training program over a 12-month period. In addition we assessed retention and compliance to the exercise training program.

### *2.2.1 Satisfaction*

Participants engaged in a qualitative interview post-training to evaluate level of satisfaction with the exercise training program and identify areas for change. In this way, participants' own perspectives could guide the development

of future exercise interventions and guidelines. Participants were asked the following questions:

1. Which parts of the training program did you enjoy and what did you like about them?
2. What parts of the training program did you not enjoy and what about them did you not like?
3. Which parts of the training program would you recommend improving and how should we go about making these improvements?

**2.3 Safety**

The PCDAI and PUCAI were calculated before and after completion of the study to assess changes in disease activity **(Appendix 3, 4)**. Disease activity for patients with an ostomy pouch (n=3) was assessed by a physician pre- and post-training, as the PCDAI and PUCAI cannot be used for these individuals. Every two weeks participants completed a questionnaire that assessed a combination of variables from the PCDAI and PUCAI **(Appendix 5).** These questions measured numerous non-invasive variables that can be indicative of a disease flare up. Finally, we tracked adverse events such as musculoskeletal injuries or hospitalizations over the course of the study. An exit criterion was defined as any participant who experienced a disease flare up that required hospitalization and initiation of steroids.

**2.4 Study Design**

Over the course of 18 weeks, each child was asked to attend **(Appendix 6)**:

1. Three *evaluation sessions*: before training ("pre"), after 8-weeks of training ("mid") and within seven days of the final training session ("post"). Each evaluation session consisted of laboratory testing of anthropometrics, body

composition, muscle strength and aerobic fitness. Each session was approximately three hours in duration.

2. Two *training sessions* per week at *McMaster University* lasting 30-60 minutes per session. Each session consisted of a combination of aerobic and resistance exercises led by the primary investigator and study volunteers.
3. One *training session* per week *at home* lasting 30-60 minutes per session. Each session consisted of a combination of aerobic and body weight/band resistance exercises performed independently, with parental supervision if available.

**2.5 Evaluation Sessions**

Evaluation sessions took place in the Children's Exercise & Nutrition Centre at McMaster Children's Hospital and the exercise room in the Department of Kinesiology in the Ivor Wynne Center. The session began with an assessment of anthropometrics, followed by a DXA scan, and muscle strength tests. Participants were then given a 30-minute rest period before an assessment of aerobic fitness. At the pre- and post-training evaluation sessions participants engaged in a qualitative interview during the 30-minute rest. Finally, in the pre-training evaluation session participants were brought to the exercise room in the Ivor Wynne Center for familiarization with the exercise equipment.

***2.5.1 Assessment of Anthropometrics***

Standing height and sitting height were measured to the nearest 0.1 cm using a stadiometer (Harpenden wall-mounted Stadiometer 2109, CMS Weighing

Equipment, Ltd, London, United Kingdom). Weight was measured to the nearest 0.1 kg using a digital scale (Mott electronic scale, model LC 2424, 20-g accuracy, Santa Rosa, California). Waist circumference (WC) was measured 4 cm above the navel using a standard anthropometry tape. Body mass index (BMI) was calculated as weight/height$^2$. Height, weight and BMI percentiles were calculated using the Centers for Disease Control growth charts (Kuczmarski, Ogden, & Grummer-Strawn, 2000) and WC percentiles were calculated using reference values from 11- to 18- year-old Canadian children (Katzmarzyk, 2004). Each participant completed a self-assessment of secondary sex characteristics according to the method of Tanner – pubic hair development for boys or breast development for girls (S. J. Taylor et al., 2001). Sitting height and chronological age were used to estimate years from peak height velocity (PHV) which was used as a marker of biological development (Mirwald, Baxter-Jones, Bailey, & Beunen, 2002).

### *2.5.2 Assessment of Body Composition*

Body composition was assessed using dual energy x-ray absorptiometry (DXA). Whole body DXA scans were performed in a supine position on a Hologic QDR 4500A scanner (Hologic Inc., Waltham, MA, USA). Accompanying software (Version 12.3) was used to determine total body fat mass and lean body mass.

### *2.5.3 Assessment of Muscle Strength*

An isokinetic dynamometer system (Biodex IV, Biodex, Shirley, N.Y.) was used to measure isometric and isokinetic strength of the dominant knee

extensors and elbow flexors. Participants were secured to the chair to minimize activation and movement of muscles not being tested. For knee extension testing, the knee joint was positioned at 90°. For elbow flexion testing, the shoulder was positioned at 90° flexion, upper arm resting on the armrest and the elbow at 90° flexion. The dynamometer was individually adjusted for each participant such that the tested joint axis of rotation was aligned with the pivoting axis of the dynamometer. Verbal encouragement and visual feedback of the torque were provided during the test. All tests were administered by the same investigator.

Isometric strength testing began with a specific warm-up (3 maximal voluntary contractions). Following a short rest, participants performed three, 5-s maximal voluntary contractions, each separated by a 30-s rest. Isokinetic strength was measured at three angular velocities: 1.04 rad·s$^{-1}$ (60°·s$^{-1}$), 2.09 rad·s$^{-1}$ (120°·s$^{-1}$), and 3.14 rad·s$^{-1}$ (180°·s$^{-1}$). The range of motion of the knee was 1.57 rad (90°), starting with the knee flexed at 1.57 (90°) rad and ending in full extension. The range of motion for the elbow was 1.74 rad (100°), starting with the elbow fully extended and ending in flexion. The testing protocol began with a specific warm up (3 contractions at a progressive effort). Following rest, participants performed three maximal voluntary contractions at each velocity. Each set of three contractions was separated by a 3-minute rest period. The order of angular velocities was randomized.

For both isometric and isokinetic strength testing, participants were instructed to contract as fast and as forcefully as possible. The highest torque was

recorded in Nm and normalized to limb lean mass (Nm/kg limb LM). Training load achieved for week 2, 7 and 13 was calculated as the product of the number of sets, repetitions and weight for nine exercises.

#### *2.5.3.1 One Repetition Maximum (1-RM)*

Participant's 1-RM were evaluated at the first McMaster University training session following the pre- and mid-training evaluations. For each resistance exercise, participants were first asked to lift a given load. Following the lift, participants were asked how their body felt while performing the exercise on a scale from 0 to 10 (0=extremely easy, 10=extremely hard) (Robertson et al., 2005). The load was increased by 1-5 kg until a perceived difficulty of 10 was reached, which indicated a participant's 1-RM for a given exercise. The increments were dependent on the effort required for the lift and got progressively smaller as the participant approached the 1-RM (Faigenbaum, Milliken, & Westcott, 2003). 1-RM was achieved within 6-10 repetitions.

### *2.5.4 Assessment of Aerobic Fitness*

To assess aerobic fitness, participants completed the *McMaster All-Out Progressive Continuous Cycling Test* on an electromagnetically-braked cycle ergometer (Corival, Lode, Netherlands). The initial workload (i.e. resistance) and increments were selected according to height and estimated level of habitual physical activity. Workload was increased every 2 min until the participant could no longer pedal at the prescribed cadence (60-70 rpm), despite strong verbal encouragement. Measurements of inspired and expired gases ($O_2$ and $CO_2$) were

made continuously using a calibrated metabolic cart (Vmax29, SensorMedics, Yorba Linda, CA, U.S.A.). Heart rate was measured continuously using a Polar heart rate monitor (Polar Electro OY, Kempele, Findland). The following variables were calculated: peak oxygen uptake ($VO_{2peak}$ in L/min, ml/kg body mass/min and ml/kg LBM/min) defined as the highest 30-sec $VO_2$, peak mechanical power ($W_{peak}$ in Watts, Watts/kg body mass and Watts/kg LBM) defined as the last workload achieved and prorated if the full 2-minute stage was not completed and peak HR ($HR_{peak}$ in beats/min) defined as the highest HR.

### *2.5.6 Assessment of Barriers and Facilitators for Physical Activity*

Participants engaged in one-on-one qualitative interviews at the pre-training evaluation session with the aim of assessing barriers and facilitators for physical activity. This method was chosen as it captures participants' experiences first hand, without any expectations or assumptions, allowing the participant to develop the perspective themselves. A semistructured interview guide was developed by the primary investigator **(Appendix 7)**. Although the interview guide was not formally pilot-tested before the study, it was informed by both relevant literature and the primary investigator's five years of experience working with children with various chronic diseases in a pediatric hospital setting. The questions were based on guides developed by Moola et al. (2011, 2012). Interviews were conducted by the primary investigator in a private room and lasted 5 to 30 minutes in duration. Interviews were audiotaped and supplementary notes were taken during the conversation. Although the interview was semi-

structured, further questions were informed by participants' responses. The researcher did not define physical activity, rather definitions were created with youths' own interpretations. All questions were presented orally and visually on a sheet of paper.

## 2.6 Exercise Training Program

Following the pre-training evaluation session, participants began a 16-week exercise training program. Participants trained three times per week; two sessions were supervised at McMaster University and one session was completed at home.

### *2.6.1 McMaster University Training Sessions*

Each training session consisted of 30-60 min of a combination of aerobic and resistance exercises **(Appendix 8.1)**. Participants began with a 5-min warm up and high-intensity intervals on a stationary bicycle. After a short rest, participants performed a circuit of 5 exercises. Finally, participants completed the session with steady state cycling and a cool down. The intensity of aerobic exercises was based on participant's baseline $W_{peak}$. The intensity of machine-based resistance exercises increased as a percentage of 1-RM, while body weight resistance exercises were a percentage of maximum repetitions completed in 45-sec. As the training program progressed, we increased the stimulus in a step wise fashion by increasing time spent exercising, and alternated between increasing the intensity of exercises and the number of repetitions and sets. Heart rate was monitored continuously throughout the training session. Intensity of aerobic

exercise began at 40% of participant's $W_{peak}$ and strengthening exercises began at 40% of participants' 1-RM. After 8-weeks of training, $W_{peak}$ and 1-RM were reassessed and new values were used to calculate subsequent workout intensities.

### *2.6.2 Home Training Sessions*

Each home training session consisted of 30-60 minutes of a combination of aerobic and muscle strengthening exercises **(Appendix 8.2).** Participants began with a 5-min warm up and high intensity intervals of skipping or another activity of their choice. After a short break they would perform a circuit of 6 body weight or resistance band exercises. Finally, participants completed the session with steady state exercise in an activity of their choice and a cool down. In the first week of training the primary investigator taught the participants each exercise and each participant was given a manual with pictures and descriptions of the various exercises. Similar to the supervised sessions, considerations were made to ensure a continuous progressive increase in the exercise stimulus during the home sessions. To measure compliance to home training participants were given a Polar FT7 heart rate monitor (Polar Electro OY, Kempele, Findland) to be worn during the session. The heart rate monitor recorded data during each training session, which was then uploaded to an online training log by the primary investigator post training. In addition, the primary investigator was in constant contact with the participants and their families to ensure compliance with the home training sessions.

### 2.7 Post-Exercise Nutrition

In light of recent work involving adults (Cermak, Res, de Groot, Saris, & van Loon, 2012) and unpublished findings from our laboratory, we aimed to maximize each training session by providing a nutritional supplement during the recovery period. Immediately following each training session, participants were given a BOOST® high protein beverage to promote muscle anabolism. As there are no guidelines for optimal protein intake post exercise for children, we used the 20 g guideline suggested by Moore et al. (2009) for healthy adults. Participants were given the equivalent amount, converted into g per kg of body mass, which equated to 0.2 g/kg. Two participants were unable to drink BOOST due to dietary allergies and thus were given alternatives matched for protein (GOGO quinoa flakes and Neilson 2% milk).

### 2.8 Compliance

In order to promote compliance to the training program we were in constant contact with participants and their families to provide reminders for both McMaster and home training sessions. Participants were able to attend their McMaster training sessions during the day or evening and during the week or weekends. We scheduled participant's training sessions on the same day and time each week, however if they were unable to attend, we rescheduled at their earliest convenience. Home training sessions included an aerobic activity of the participant's choice. In the winter months, if participants did not have training equipment we provided them with a stationary bicycle. Finally, we provided

various forms of compensation, such as parking vouchers for evaluation and training sessions, volunteer hours and $200 remuneration for study completion.

## 2.9 Statistical analyses

### *2.9.1 Objective 1 – Safety and Feasibility*

Descriptive statistics were used to characterize recruitment, enrolment, retention and adherence rates. Additionally descriptive statistics were used to describe pre- and post-training PCDAI and PUCAI scores.

### *2.9.2 Objective 2 – Efficacy*

Prior to analysis, all variables were analyzed for normality using the Shapiro-Wilk test. Data are presented as mean ± standard deviation (SD) and 95% confidence intervals, unless otherwise noted.

Descriptive statistics were used to assess participant characteristics. Changes in body composition, muscle strength and aerobic fitness over the course of the training program (pre-, mid-, and post-training) were assessed using one-way repeated-measures ANOVAs for normally distributed data and the Friedman's ANOVA for non-normally distributed data. Post hoc analysis was completed using Tukey's honestly significant difference (HSD) for the one-way repeated-measures ANOVA and Wilcoxon signed-rank test with a Bonferroni correction for Friedman's ANOVA.

Cohen's *d* equation was used to calculate effect size for changes in body composition, muscle strength and aerobic fitness variables from pre- to post-

training (Cohen, 1977). Effect size was calculated according to the following equations:

$$d = \frac{\bar{x}_2 - \bar{x}_1}{SD_{pooled}} \qquad SD_{pooled} = \sqrt{\frac{[(N_1-1)SD_1{}^2 + (N_2-1)SD_2{}^2]}{N_1+N_2-2}}$$

Where $x_1$and $x_2$ = means for pre and post training respectively, and $SD_1$ and $SD_2$ = standard deviation for pre and post training, respectively. Given the small sample size, a correction factor was used to mitigate the resulting positive bias of the original equation (Durlak, 2009). The correction factor was calculated according to the following equation:

$$\left(\frac{N-3}{N-2.25}\right) \times \sqrt{\frac{N-2}{N}}$$

An effect size of 0.2 was defined as small, 0.5 as medium and 0.8 as large (Cohen, 1992).

Given that this was a pilot study, sample size was not calculated a priori (Thabane et al., 2010). However, effect sizes from pre to post training for body composition, muscle strength and aerobic fitness variables can be used to design a larger randomized controlled study in the future. ANOVAs were performed using STATISTICA (StatSoft, Tulsa, OK, USA) and all other statistics were performed using SPSS for Windows 18.0 (SSPS Inc, Chicago, IL, USA). Statistical significance was set at $p \leq 0.05$.

### *2.9.3 Objective 3 – Barriers and Facilitators*

The audiotaped interviews were transcribed verbatim and data was subjected to thematic analysis based on the methodologies employed by Saville et al. (2014) and the six-step process described by Braun and Clarke (2006). First, transcripts were read repeatedly by two independent raters to familiarize themselves with the data and extract all relevant meaning units from the transcripts. Meaning units are individual sentences, phrases or paragraphs that contain conceptually relevant information (Braun & Clarke, 2006). Second, raters generated initial codes that identified a feature of the data. There was no frequency threshold employed for including examples of barriers and facilitators because of the small number of participants in this study. Third, each rater sorted meaning units into broad themes and further collated data into subthemes. Fourth, raters met to review and compare the classification of meaning units before generating a thematic map. Cohen's kappa was used to determine interrater reliability (Cohen, 1960; Kvalseth, 1989). The following equation was used:

$$\mathrm{K} = \frac{\Pr(a) - \Pr(e)}{1 - \Pr(e)}$$

Where Pr (*a*) is the relative observed agreement among raters and Pr (*e*) is the hypothetical probability of chance agreement. A kappa value of <0 was considered a poor agreement, 0.1-0.2 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial and 0.81-0.99 almost perfect agreement. Fifth, themes and

subthemes were further refined and defined to adequately express the scope of each. Sixth, the most vivid responses were selected to be included in the report, such that they best represented the essence of each theme.

Following the methodology employed by Galea, Bray & Martin Ginis (2008), a theoretical approach was used to categorize barriers and facilitators for physical activity as determinants of behavior change according to the social cognitive theory (Bandura, 1986; 1997). General barriers and facilitators were separated from those thought to be unique to individuals with IBD (disease-specific). Additionally, all barriers and facilitators were classified according to determinants of behavior change, which included characteristics associated with the person (e.g. physical pain and psychological distress), the activity or target behavior (e.g. enjoyable activity and intensity of activity) and the environment (e.g. social support and facilities).

# CHAPTER 3: RESULTS

## 3.1 Feasibility

This study was conducted from May 2013 to June 2014. Participants were recruited from May 2013 to February 2014. Training began July 2013 and ended June 2014. Of 217 patients screened, 57 (26.3%) were excluded based on pre-defined criteria. 104 patients were approached, 18 demonstrated interest and 11 (10.6%) consented to participate. 10 (90.9%) patients completed the four month exercise training program, while 1 dropped out for medical reasons unrelated to the study. A detailed breakdown of participant flow through each stage of the study is presented in **Figure 1**.

### *3.1.1 Clinical Characteristics*

10 youth with IBD (6 CD, 1 female) completed the exercise training program. The mean age of participants at baseline was 15.4 ± 1.2 years. All participants were in remission at baseline. PCDAI was calculated for 5 participants (mean=6, range=5 to 10) and PUCAI was calculated for 2 participants (mean=5, range=n/a, both 5). Remission status for the remaining 3 participants who had received surgical intervention was confirmed by physician. The mean ± SD (range) for disease duration was 3.2 ± 3.8 (0.4, 12.6) years. Time spent in remission since the last flare-up was 1.1 ± 1.8 (0.1, 5.9) years. 4 participants received surgical interventions for bowel resection and ileostomy, one of which was followed by renastomosis. 8 participants were taking IBD-related medication

over the course of the study. Information on disease location and detailed medical therapy are presented in **Table 2**.

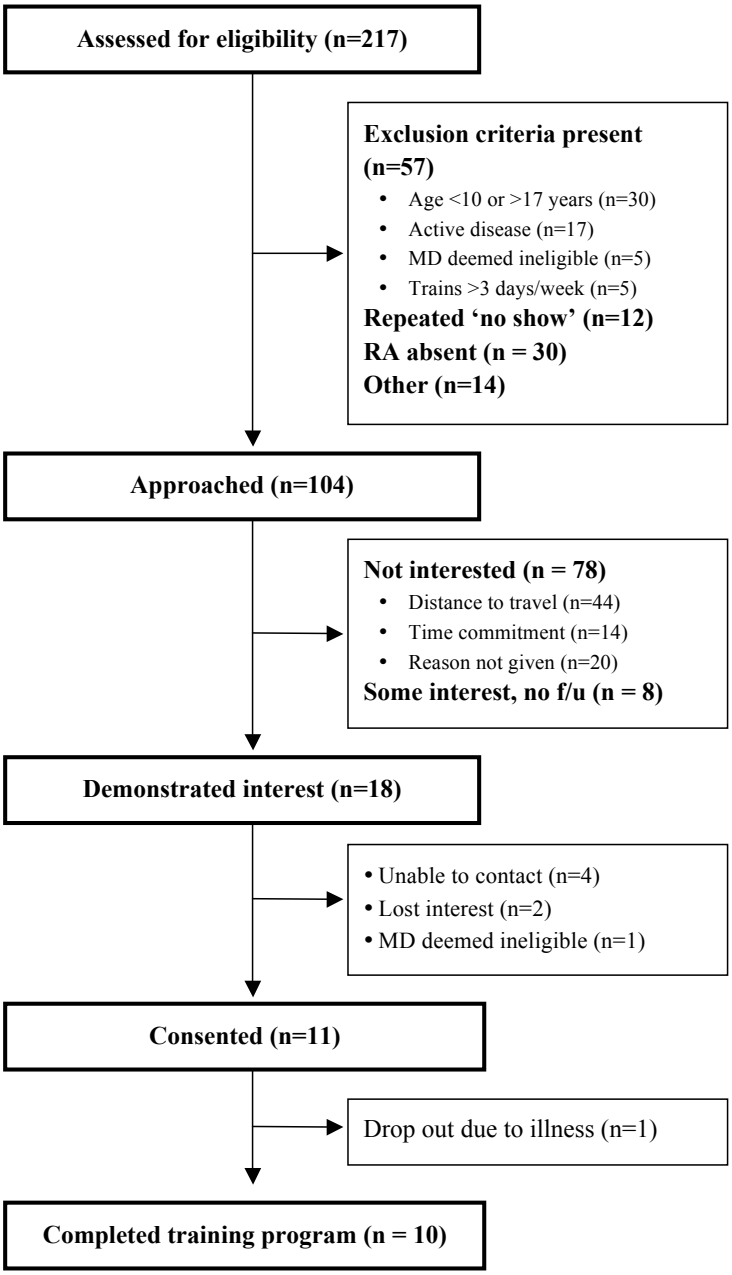


**Figure 1.** Study enrollment flow chart. RA, research assistant; f/u, follow-up.

**Table 2.** Disease characteristics and medical therapy

| ID | Diagnosis | Date of Diagnosis | Disease Location | Surgical Intervention | Medication | | Change in Medication* |
|---|---|---|---|---|---|---|---|
| | | | | | Type | Dose & Frequency | |
| **IBDM01** | UC (pancolitis) | Mar 2012 | Entire colon | None | Prednisone<br>Inflixmab | 25 mg/day<br>Infusion, q-4wk | a. Prednisone tapered 5 mg/wk<br>b. Inflixmab infusions q-8 wk |
| **IBDM02** | CD | Aug 2012 | Ileum Cecum | Ileocecal resection and ileostomy (Aug 2012)<br>Renastomosis (May 2013) | Methotrexate<br>Leucovorin<br>Ondansetron | 25 mg, qwk, subcut<br>5 mg, qwk, p.o.<br>8 mg, a.c. mtx | a. Mtx, 20 mg, qwk, subcut<br>b. Zantac, 150 mg as needed<br>c. Vitamin B12, 1000IU, qwk, subcut |
| **IBDM03** | IBD unclassified (favours CD) | Apr 2012 | Entire colon Query ileum | None | Azathioprine | 100/125 mg, alternate h.s. | Ursodiol, 500 mg, b.i.d. |
| **IBDF04** | UC (pancolitis) | Sept 2011 | Entire colon | None | Inflixmab | 400 mg, q-6wk | None |
| **IBDM05** | CD | Aug 2010 | Entire colon Ileum | Subtotal colectomy and ileostomy (Mar 2012) | Adalimumab<br>FeraMAX<br>Tylenol | 40 mg, qwk, subcut<br>1 tablet daily<br>As needed | None |
| **IBDM06** | UC (pancolitis) | 2001 | Entire colon | Subtotal colectomy and ileostomy | Melatonin<br>Strattera | 6 mg<br>60 mg | None |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **IBDM07** | CD | May 2013 | Stomach, ileum, entire colon | None | Mesalazine<br>Methotrexate<br>Leucovorin<br>Folate | 1.5 g, b.i.d.<br>25 mg, qwk, subcut<br>5 mg, qwk, p.o.<br>5 mg, qwk, p.o. | Mtx 25 mg, p.o. |
| **IBDM08** | CD | Mar 2010 | Ileum | None | Adalimumab | 40 mg, q-2wk | Multivitamin<br>Probiotics |
| **IBDM09** | UC | June 2007 | Entire colon | Subtotal colectomy and ileostomy (May 2013) | Zoloft | 50 mg/day | Salofalk, 500 mg suppository per rectum at bedtime for 3 wks then as needed |
| **IBDM10** | CD | Sept 2013 | Small intestine (jejunum, ileum), upper GI tract | None | Prevacid<br>Folic acid<br>Methotrexate<br>Multivitamin<br>Protein supplement | 15 mg/day<br>1 mg, 5 days/wk<br>20 mg, qwk, subcut | Infliximab, 275 mg<br>Methotrexate, 7.5 mg, qwk |

ac, before; b.i.d., twice daily; CD, Crohn's disease; h.s., at bedtime; mtx, methotrexate; p.o., orally; qwk, every week; subcut, subcutaneously; UC, ulcerative colitis. *Refers to changes in medication while enrolled in the study.

### *3.1.2 Adherence to Exercise Training Program*

Of the 48 exercise training sessions prescribed, participants completed 37 ± 5 sessions (77.7 ± 10.8%). Participants completed 29 ± 2 (89.1 ± 5.2%) of the 32 prescribed McMaster training sessions and 9 ± 4 (55 ± 26.5%) of the 16 prescribed home training sessions. Reasons given for missing McMaster training sessions included: illness, inclement weather, travel and scheduling conflict. Most participants did not indicate why they missed home training sessions, however some reasons provided were illness, fatigue, travel, and time constraints.

### *3.1.3 Satisfaction with the Exercise Training Program*

Participants reported a number of features they liked and disliked about the training program. The most commonly reported positive features were the variety of resistance training machines and the overall structure of the program. The most commonly reported negative feature was the duration of steady state cycling. Additionally, participants provided three main recommendations for future training programs. First they suggested incorporating individual goals into the training program, in addition to the prescribed exercises – for example, performing a chin up by the end of the program. Second, they would like a greater variety of aerobic exercises such as running and elliptical. Finally, they highlighted their desire to workout with other participants in the study during training sessions.

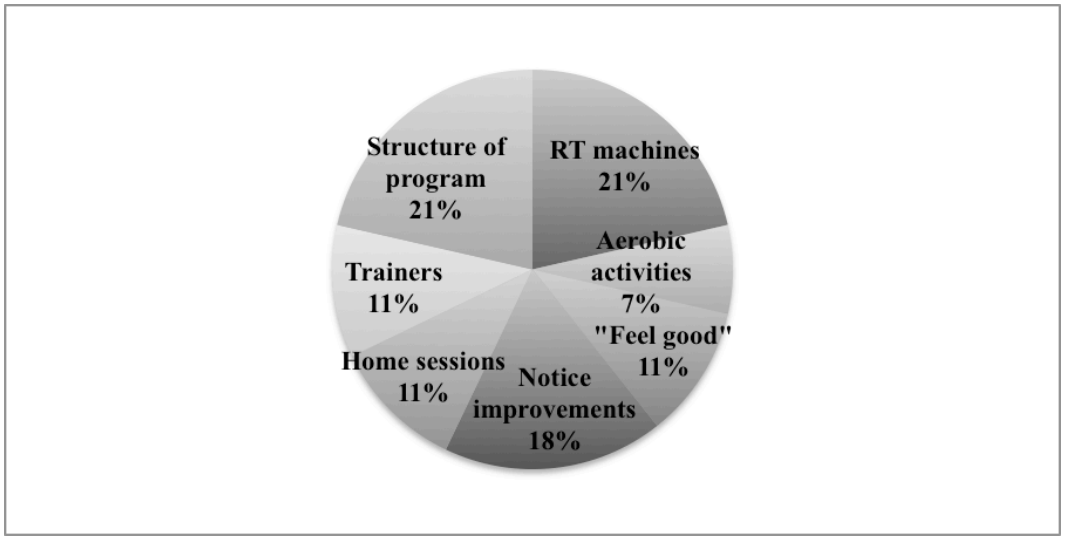


**Figure 2.** Proportion of participants reporting positive features of the exercise training program. RT, resistance training.

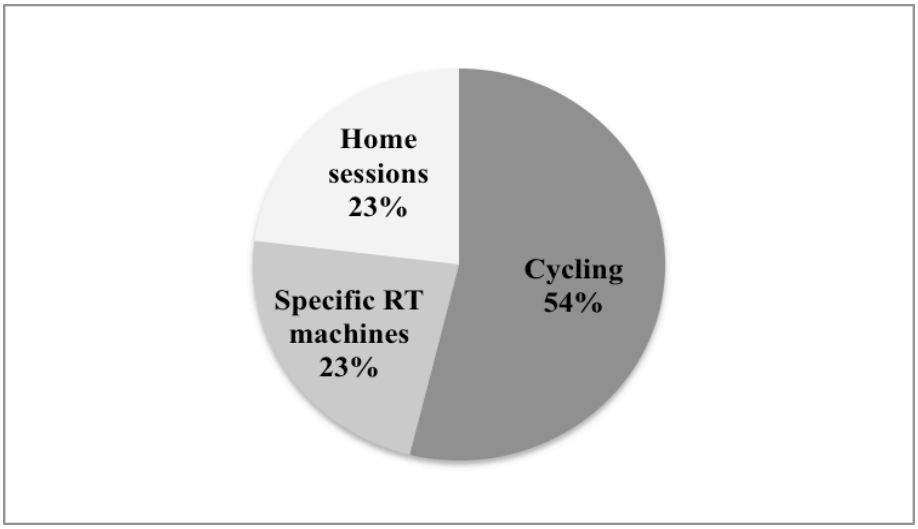


**Figure 3.** Proportion of participants reporting negative features of the exercise training program. RT, resistance training.

### 3.4 Safety

All participants remained in remission post-training (PCDAI; mean=1, range= 0 to 5, PUCAI; mean=5, range=n/a, and confirmation from physician for ostomy patients). Two patients (IBDM03, IBDM04) reported minor disease flare-

ups that resolved without need for medical intervention. Additionally, there were no adverse events associated with exercise training.

Participant-reported changes in disease activity are presented in **Figure 4**. Over the course of training, the majority of patients reported no abdominal pain. Energy/ activity level was predominantly rated as normal or improved, while few participants reported a slight decrease and one instance of activities reduced. The number of stools and stool consistency remained stable except for IBDF04, which corresponded with her reported flare up. IBDM05, IBDM06 and IBDM09 were unable to report number of stools per day due to presence of ostomy pouch. Two participants (IBDM02, IBDM03) reported one instance of trace rectal bleeding each. There were no changes in the presence of extraintestinal manifestations, except for IBDM10 who's oral ulcers were resolved by week 8 of training.

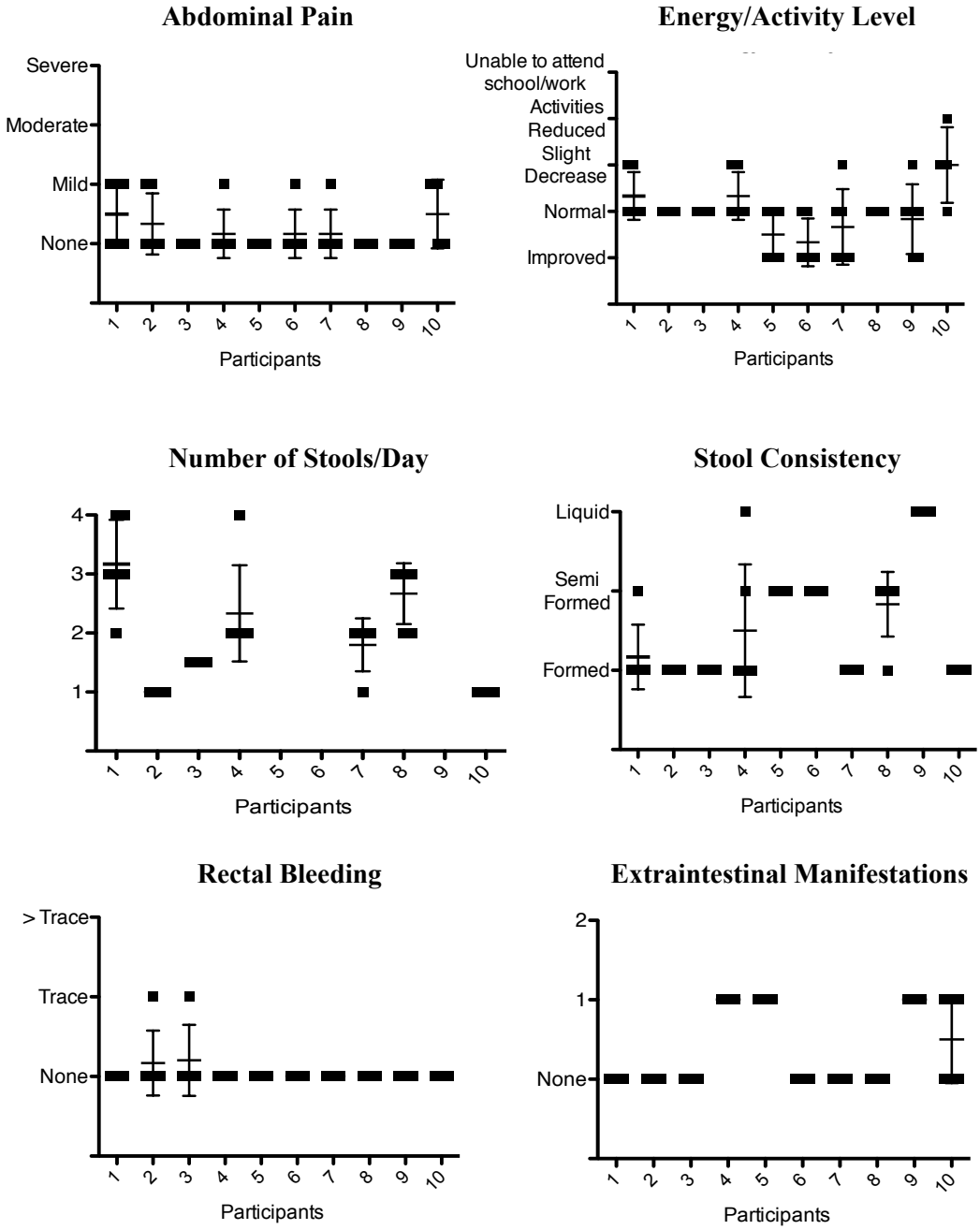


**Figure 4.** Participant-reported levels of disease activity. Data are presented as mean [95% CI]. Variables were measured every two weeks of training, for a total of six time points. Actual scores are shown by the dot plot. The wider the bolded horizontal line, the more data points are represented.

### 3.5 Efficacy of Exercise Training

#### *3.5.1 Participant Characteristics*

Participant characteristics are presented in **Table 3**. Height and weight increased by 1.6 ± 1.4 cm ($p < 0.001$) and 2.7 ± 1.8 kg ($p < 0.001$) respectively, from pre- to post-training. There was a significant increase in BMI from pre- to mid- training and pre- to post-training ($p < 0.05$ and $p < 0.01$ respectively). The number of patients at stages 1-5 of the tanner scale pre-training was 0, 2, 2, 4, and 2 respectively.

**Table 3.** Participant characteristics.

| | PRE | MID | POST |
|---|---|---|---|
| **N (M/F)** | 10 (9/1) | 10 (9/1) | 10 (9/1) |
| **CD/UC** | 6/4 | 6/4 | 6/4 |
| **Age (years)** | 15.4 ± 1.2 [14.6, 16.3] | 15.6 ± 1.2*** [14.7, 16.4] | 15.7 ± 1.2***, §§§ [14.9, 16.6] |
| **Estimated YPHV** | -1.3 ± 1.3 [-2.2, -0.4] | -1.2 ± 1.2 [-2.1, -0.4] | -1.1 ± 1.2**, §§§ [-1.9, -0.2] |
| **APHV** | 16.8 ± 1.6 [15.6, 17.9] | 16.8 ± 1.5 [15.7, 17.9] | 16.8 ± 1.5 [15.7, 17.9] |
| **Height (cm)** | 167.4 ± 7.2 [162.2, 172.5] | 168.2 ± 7.0 [163.3, 173.2] | 169.0 ± 7.0***, § [164.0, 174.1] |
| **Height Percentile** | 40.6 ± 27.4 [21.0, 60.2] | 41.0 ± 27.4 [21.4, 60.6] | 42.0 ± 27.0 [22.7, 61.3] |
| **Weight (kg)** | 54.3 ± 8.3 [48.4, 60.3] | 55.9 ± 9.1** 49.4, 62.3] | 57.0 ± 9.0***, § [50.6, 63.5] |
| **Weight percentile** | 37.7 ± 31.1 [15.5, 59.9] | 39.4 ± 33.0 [15.8, 63.1] | 41.4 ± 32.6 [18.0, 64.7] |
| **BMI (kg/m$^2$)** | 19.4 ± 2.7 [17.5, 21.3] | 19.7 ± 3.0* [17.6, 21.9] | 20.0 ± 2.9** [17.9, 22.1] |
| **BMI percentile** | 39.0 ± 32.7 [15.6, 62.4] | 40.5 ± 34.6 [15.7, 65.3] | 41.0 ± 34.2 [16.6, 65.5] |
| **WC (cm)** | 70.0 ± 7.0 [64.9, 75.0] | 70.4 ± 7.8 [64.8, 76.0] | 70.9 ± 8.3 [65.0, 76.9] |
| **WC percentile** | 37.7 ± 35.6 [12.3, 63.2] | 39.2 ± 41.0 [9.9, 68.5] | 37.2 ± 39.8 [8.7, 65.6] |
| **Tanner** | 3.6 ± 1.1 [2.8, 4.4] | 3.9 ± 1.0 [3.2, 4.6] | 3.9 ± 1.1 [3.1, 4.7] |

Data are presented as mean ± SD [95% CI]. APHV, age at peak height velocity; BMI, body mass index; CD, Crohn's disease; UC, ulcerative colitis; WC, waist circumference; YPHV, years from peak height velocity. Significant differences *$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$ compared to PRE. Significant differences $^{\S}p \leq 0.05$, $^{\S\S\S}p \leq 0.001$ compared to MID.

### *3.5.2 Body Composition*

There was a significant increase in whole body lean mass from pre- to mid-training (40.8 ± 5.2 vs. 42.3 ± 5.3 $p < 0.001$) **(Table 4)**. At the completion of the study, whole body lean mass increased a total of 7.8% (40.8 ± 5.2 vs. 43.2 ± 5.2, $p < 0.001$). The change in lean body mass from pre- to post-training suggested a small effect. There were no changes in whole body fat mass over the course of the training program. Lean body mass (kg) at pre-, mid- and post-training for each participant is presented in **Appendix 9 (Figure A).**

**Table 4.** Body composition at pre-, mid- and post-training.

| | PRE | MID | POST | Δ | Effect Size |
|---|---|---|---|---|---|
| **Fat mass (kg)** | 12.7±5.0 [9.1, 16.3] | 12.4 ± 5.2 [8.7, 16.2] | 12.8 ± 5.6 [8.8, 16.8] | 0.1 ± 1.2 [-0.8, 1.0] | 0.02 |
| **% Body fat** | 22.5 ± 6.5 [17.8, 27.1] | 21.4 ± 6.7 [16.6, 26.1] | 21.5 ± 6.8 [16.6, 26.3] | -1.0 ± 1.2 [-1.9, -0.1] | -0.01 |
| **Lean body mass (kg)** | 40.8 ± 5.2 [37.0, 44.5] | 42.3 ± 5.3** [38.5, 46.1] | 43.2 ± 5.2*** [39.5, 46.9] | 2.4 ± 1.1 [1.6, 3.2] | 0.36 |
| **% Lean body mass** | 74.3 ± 6.3 [69.8, 78.8] | 74.8 ± 6.3 [70.3, 79.3] | 75.3 ± 6.5 [70.7,80.0] | 1.0 ± 1.2 [0.1, 1.9] | 0.14 |

Data are presented as mean ± SD [95% CI]. Δ and effect size describe changes from pre- to post-training. Significant differences **$p$ <0.01, ***$p < 0.001$ compared to PRE values.

### *3.5.3. Muscle Strength*

Muscle strength variables are presented in **Table 5**. Isokinetic knee extension torque at 120°·s$^{-1}$ and 180 °·s$^{-1}$ significantly increased from pre- to post-training with a moderate and small effect respectively (12.8 ± 2.2 vs. 14.2 ± 1.9 and 10.8 ± 4.0 vs. 11.7 ± 2.2 Nm·kg limb LM$^{-1}$, $p < 0.05$ respectively). There were no significant effects of training on isometric knee extensor strength or isometric and isokinetic elbow flexor strength normalized to limb lean mass. The change in isokinetic elbow flexion torque at 120°·s$^{-1}$ and 180 °·s$^{-1}$ suggested a small effect. Training load achieved during McMaster sessions increased over the course of the study for all participants **(Appendix 10)**. Isokinetic knee extension torque at 120°·s$^{-1}$ and 180 °·s$^{-1}$ at pre-, mid- and post-training for each participant is presented in **Appendix 9 (Figures B and C).**

**Table 5.** Muscle strength variables at pre-, mid- and post-training.

| | PRE | MID | POST | Δ | Effect Size |
|---|---|---|---|---|---|
| **Knee Extension** | | | | | |
| **Peak Isometric Torque** | 21.4 ± 3.5 [19.0, 23.9] | 21.4 ± 4.5 [18.2, 24.6] | 21.8 ± 3.5 [19.4, 24.3] | 0.4 ± 2.8 [-1.6, 2.4] | 0.1 |
| **Peak Isokinetic Torque** | | | | | |
| **60°/s** | 15.9 ± 4.5 [12.6, 19.2] | 15.4 ± 3.7 [12.8, 18.0] | 16.5 ± 2.7 [14.5, 18.4] | 0.6 ± 2.4 [-1.1, 2.4] | 0.14 |
| **120°/s** | 12.8 ± 2.2 [11.3, 14.4] | 12.9 ± 2.6 [11.1, 14.8] | 14.2 ± 1.9* [12.8, 15.6] | 1.3 ± 1.2 [0.5, 2.2] | 0.58 |
| **180°/s** | 10.8 ± 4.0 [7.9, 13.6] | 11.1 ± 2.1 [9.6, 12.6] | 11.7 ± 2.2* [10.1, 13.3] | 0.9 ± 2.3 [-0.7, 2.5] | 0.23 |
| **Elbow Flexion** | | | | | |
| **Peak Isometric Torque** | 17.3 ± 3.0 [15.2, 19.5] | 17.0 ± 3.8 [14.3, 19.8] | 17.1 ± 4.2 [14.1, 20.1] | -0.2 ± 2.5 [-2.0, 1.6] | 0.05 |
| **Peak Isokinetic Torque** | | | | | |
| **60°/s** | 11.7 ± 3.0 [9.6, 13.8] | 11.2 ± 2.7 [9.3, 13.1] | 12.3 ± 4.2 [9.3, 15.3] | 0.6 ± 1.9 [-0.8, 2.0] | 0.14 |
| **120°/s** | 10.2 ± 2.5 [8.4, 12.0] | 10.5 ± 3.4 [8.1, 13.0] | 10.9 ± 2.8 [8.9, 12.9] | 0.7 ± 3.0 [-1.4, 2.8] | 0.23 |
| **180°/s** | 9.6 ± 1.8 [8.3, 10.9] | 9.9 ± 2.8 [8.0, 11.9] | 10.3 ± 2.8 [8.3, 12.3] | 0.7 ± 2.5 [-1.1, 2.4] | 0.25 |

Data are presented as mean ± SD [95% CI] and expressed as Nm·kg limb $LM^{-1}$, unless otherwise indicated. Δ and effect size refer to changes from pre- to post-training. *Significant difference compared to PRE, $p < 0.05$.

### *3.5.4 Aerobic Fitness*

Aerobic fitness variables are presented in **Table 6**. $VO_{2peak}$ ($L \cdot min^{-1}$) increased by 0.2 ± 0.2 $L \cdot min^{-1}$ ($p < 0.01$) from pre- to post-training with a moderate effect. The change in $VO_{2peak}$ expressed in $mL \cdot kg^{-1} \cdot min^{-1}$ suggested a moderate effect, while $VO_{2peak}$ expressed in $mL \cdot kg\ LBM^{-1} \cdot min^{-1}$ and % predicted, both suggested a small effect. There was a significant increase in $W_{peak}$ (Watts) from pre- to mid-training, mid- to post-training and pre- to post-training ($p < 0.001$, $p < 0.01$ and $p < 0.001$ respectively). $W_{peak}$ normalized to whole body weight and whole body lean mass increased by 0.4 ± 0.2 $Watts \cdot kg^{-1}$ ($p < 0.001$) and 0.4 ± 0.3 $Watts \cdot kg\ LBM^{-1}$ ($p < 0.001$) respectively from pre- to post-training. There was a significant increase in % predicted $W_{peak}$ from pre- to mid-training, mid- to post-training and pre- to post training ($p < 0.05$, $p < 0.01$ and $p < 0.001$ respectively). $W_{peak}$ expressed in Watts, $Watts \cdot kg^{-1}$, $Watts \cdot kg\ LBM^{-1}$ and % predicted, all suggested a large effect. $VO_{2peak}$ ($mL \cdot kg\ LBM^{-1} \cdot min^{-1}$) and $W_{peak}$ ($Watts \cdot kg\ LBM^{-1}$) at pre-, mid- and post-training for each participant are expressed in **Appendix 9 (Figures D and E)**.

**Table 6.** Aerobic fitness variables at pre-, mid- and post-training.

| | PRE | MID | POST | Δ | Effect Size |
|---|---|---|---|---|---|
| **$VO_{2peak}$** | | | | | |
| **L/min** | 2.0 ± 0.3 [1.8, 2.2] | 2.1 ± 0.3 [1.9, 2.4] | 2.2 ± 0.2** [2.1, 2.4] | 0.2 ± 0.2 [0.1, 0.4] | 0.69 |
| **mL/kg/min** | 37.3 ± 3.6 [34.7, 39.8] | 38.7 ± 4.4 [35.6, 41.8] | 40.57 ± 5.21 [36.8, 44.3] | 3.3 ± 4.4 [0.2, 6.4] | 0.69 |
| **mL/kg LBM/min** | 49.6 ± 5.7 [45.5, 53.7] | 50.8 ± 4.5 [47.6, 54.0] | 52.4 ± 4.8 [48.9, 55.9] | 2.8 ± 5.7 [-1.3, 6.9] | 0.45 |
| **% Predicted** | 73 ± 14 [64, 83] | 76 ± 11 [68, 84] | 79 ± 15 [69, 90] | 6 ± 9 [-1, 12] | 0.34 |
| **$W_{peak}$** | | | | | |
| **Watts** | 134.9 ± 19.1 [121.2, 148.5] | 149.0 ± 24.3*** [131.6, 166.4] | 160.7 ± 15.6***, §§ [149.6, 171.8] | 25.8 ± 6.4 [21.3, 30.4] | 1.24 |
| **Watts/kg** | 2.5 ± 0.2 [2.3, 2.7] | 2.7 ± 0.3* [2.4, 2.9] | 2.9 ± 0.4*** [2.6, 3.1] | 0.4 ± 0.2 [0.2, 0.5] | 1.11 |
| **Watts/kg LBM** | 3.3 ± 0.2 [3.1, 3.5] | 3.5 ± 0.3 [3.3, 3.7] | 3.7 ± 0.3*** [3.5, 4.0] | 0.4 ± 0.3 [0.3, 0.6] | 1.19 |
| **% Predicted** | 61 ± 8 [56, 67] | 66 ± 7* [61, 71] | 72 ± 9***, §§ [65, 78] | 10.1 ± 3.6 [8, 13] | 1.45 |

Data are presented as mean ± SD [95% CI]. Δ and effect size refer to changes from pre- to post-training. Significant differences *$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$ compared to PRE. Significant differences $^{\S}p \leq 0.05$, $^{\S\S}p \leq 0.01$ compared to MID.

### 3.6 Barriers and Facilitators for Physical Activity

Overall, 189 meaning units were analyzed independently by two raters. Among these, 95 were identified as representing barriers to regular physical activity and 91 as facilitators. 3 meaning units could not be categorized according to the SCT. Cohen's kappa indicated a substantial level of agreement (K = 0.79) between the two raters. Discrepancies were thoroughly discussed until agreement was reached. A summary of general and disease-related barriers and facilitators for each category are presented in **Table 7**.

#### *3.6.1 General Barriers for Physical Activity*

***Barriers related to the person.*** Participants described both physical and psychological barriers towards physical activity. Physical barriers included lack of strength and endurance to engage in physical activities. Psychological barriers included a lack of self-motivation, which manifested itself in frequent laziness, lack of inspiration and the perceived effort to be physically active. Finally, participants lacked confidence in their physical abilities, which acted as a personal barrier. One participant was uncomfortable working out in a gym with others as he felt as though he did not fit in. When asked why he felt this way, he explained: "I don't feel [as] physically active as I should be."

**Table 7.** Categories and definitions or examples of barriers and facilitators.

| Variable Type | Category | Definition/Example | Frequency |
|---|---|---|---|
| **General Barrier** | Personal | *Physical:* lack of strength and stamina | 14 (43.8) |
| | | *Psychological:* laziness, lack of self-motivation, lack of confidence in physical abilities | |
| | Activity-related | *Psychological:* sport-related pressure, lack of enjoyment of specific activities | 8 (25.0) |
| | Environment | *Physical:* lack of equipment and/or facilities | 10 (31.3) |
| | | *Social:* peer influence | |
| | | Screen-based sedentary behaviour | |
| **Disease-Specific Barrier** | Personal | *Burden of disease*<br>a. *Physical:* pain, lack of energy, ileostomy pouch, urgencies and bathroom use, negative effect of hospitalization<br>b. *Psychological:* depression and stress, worry about bathroom use | 54 (85.7) |
| | Activity-related | Exercise-induced pain | 4 (6.3) |
| | Environment | *Social:* less active compared to peers, missed opportunity to be active in childhood vs. friends | 5 (7.9) |

| | | | |
|---|---|---|---|
| **General Facilitator** | Personal | *Physical:* avoid negative effects of inactivity<br>*Psychological:* perceived importance for future health, self-motivation | 12 (21.8) |
| | Activity-related | Alternative to sitting, nature of activity, renewed energy post-exercise | 13 (23.6) |
| | Environment | *Physical:* access to facilities and equipment<br>*Social:* social support including companionship and parental encouragement, physically active role model | 30 (54.5) |
| **Disease-Specific Facilitator** | Personal | *Physical:* state of remission, disease management<br>*Psychological:* self-motivation, negative association with deconditioned state | 23 (63.9) |
| | Activity-related | Individualized exercise program tailored to disease status, disease-related benefits due to physical activity | 4 (11.1) |
| | Environment | *Physical:* disease-friendly environment<br>*Social:* social support including creating opportunities to be active and disease awareness | 9 (25.0) |

Frequency is presented as number (percentage) within each variable type.

***Barriers related to the environment.*** Physical barriers, such as lack of access to exercise equipment or facilities for activity were commonly expressed among participants. Additionally, participants revealed how peers can act as barriers towards physical activity. One participant described that he doesn't engage in physical activity unless there are other people around to talk to. Whereas another participant implied that his friends' lack of interest in a particular activity negatively impacted his participation such an activity:

> "I used to longboard a lot. Like even after I was diagnosed I started getting into it a lot, just cause my friends were getting into it. But then, I don't know, it sort of …died down I guess. Uh, just, they stopped doing it, so…[I stopped doing it]."

Finally, screen-based sedentary behaviors, such as playing video games and watching television were reported as barriers for physical activity.

### *3.6.2 Disease-Specific Barriers for Physical Activity*

***Barriers related to the person.*** The burden of disease was the most common barrier for physical activity described by participants. The burden of disease manifested itself physically and psychologically. Physically, symptoms such as abdominal pain and lack of energy, in addition to the ostomy pouch getting in the way of certain activities, posed serious difficulties. Urgencies and the number of times a participant needed to use the bathroom greatly impacted their desire to engage in physical activity. Diet restrictions made it difficult to maintain optimal physique as one participant describes: "when you have IBD then that sort of affects how you eat and you get skinnier, and you're a little less active. Yeah, you're not going to be that active." Many participants described their negative

experience upon the first presentation of disease symptoms and subsequent hospitalization for diagnosis and stabilization. Time in the hospital restricted activity leading to a deconditioned state that was very difficult to reverse post-discharge. One participant confirms, "I think once I was in the hospital and my energy dropped so much that I wasn't really…I wasn't really…physically active for a long time."

In addition to physical limitations, participants experienced numerous psychological barriers towards physical activity, the most common of which was the constant worry about their disease. Given the nature of IBD, participants worried about symptom exacerbation, urgencies, lack of access to bathrooms and risk of accidents. Additionally, participants reported feeling stressed about their disease and felt that it was a lot to handle for someone their age.

One participant described that he did not engage in physical activity before his ostomy surgery due to both physical and psychological barriers. He described his physical barrier:

> "If I had to go to the bathroom my stomach would always hurt, right, so…all day I would be already in pain pretty much [which prevented me from being physically active]."

Psychological challenges:

> "Well because I had to use the bathroom I'd be mentally like: 'oh no, where's the nearest bathroom?' and then there would be…a video going through your head like, 'you're gonna have an accident, you're gonna have an accident, haha you're gonna have an accident'."

***Barriers related to physical activity.*** Knee pain experienced during running and biking acted as a barrier. Individuals with IBD can develop extraintestinal

manifestations, such as arthralgia, which can act as a challenge for engaging in physical activity and exercise. When participants were asked if there were any activities they avoided and why, one participant answered:

> "Running because my knees will hurt after that. And it hurts when I run cause [of]…the pressing, yeah."

***Barriers related to the environment.*** Participants described their involvement in physical activity compared to that of their friends. They believed they were less active than their friends due to their disease, which acted as a barrier for future participation. One participant attributed his inactivity to missed opportunities to be active in childhood with friends, resulting in subsequent lack of development of physical activity habits. When asked the difference between him and his friends in terms of engaging in physically activity and exercise, he described:

> "Uh, I think they [friends] got into sports and…running and stuff like that when they were really young. Because I never got to do any of that stuff because I was…really sick. So probably if I didn't get sick I'd probably be a lot more active than I am now…as active as my friends."

### *3.6.3 General Facilitators for Physical Activity*

***Facilitators related to the person.*** Participants correlated inactivity with negative health outcomes and personality traits, which encouraged them to be physically active. For example, one participant described his motivation to be active as: "if you're not that physically active, there's not much you can do in life…not hard work." (10) Additionally, participants wanted to be active, as they believed it would be important for health in the future, such as avoiding arthritis and heart problems. Finally, participants described self-motivation as a facilitator for

physical activity. They employed memories of success in the past and positive self-talk in order to motivate them to be active in the future. For example one participant explained: "I think that if I push myself I can do it [be as active as I want to be]."

***Facilitators related to physical activity.*** Participants wanted to engage in physical activity as an alternative to sitting. They no longer wanted to sit or lay down constantly, rather they wanted to get up and move. One participant described an experience while watching her brother's hockey team train: "but we're like we might as well do something because a lot of the parents just sit there in like chairs and its just…why are you doing this?" Additionally, activities that were fun in nature and not competitive facilitated participation for some participants. Many participants described a renewed energy post-exercise that allowed them to accomplish more in a day compared to lying on the couch all day. One participant described what encourages her to be physically active:

> "I feel like if I do workout I accomplish more…I like to keep going because I'm already up and doing stuff. You also have a renewed energy, which is different from your just really sluggish on the couch all day. I don't actually need to take a nap."

***Facilitators related to the environment.*** Physical and social factors facilitated participation in physical activity. Access to a workout room and equipment at school and an opportunity to take part in an exercise training program for individuals with IBD both enabled participants to be physically active.

Companionship during physical activity greatly increased the likelihood of engagement. Participants wanted to participate in activities their friends were

doing. As well, they felt greater enjoyment and ease being physically active with peers as they were motivating and encouraging each other over the duration of activity. Several participants described individuals in their life who were physically active that made them want to engage in physical activity and improve their sport skills. Finally, parental support and encouragement acted as a facilitator towards physical activity. One participant described the value of growing up in a family that is physically active in terms of facilitating a physically active lifestyle:

> "Yeah, I think…when you're raised up in a family who's…always exercising and always at a hockey practice or a baseball practice, then…it just kind of seems like this is what I should follow and you end up liking that stuff, which I really like because like I love sports. So…I'm happy that I have that support there because we all…go to each others games and we all support each other."

### *3.6.4 Disease-Specific Facilitators for Physical Activity*

***Facilitators related to the person.*** Disease quiescence was the main facilitator for participation in physical activity and exercise. Quiescence was defined as an absence of pain and urgencies and regained energy. In addition, participants who received surgery and live with an ostomy pouch describe the positive impact it has had on their ability to be active. They described the comfort they feel knowing they won't have an accident:

> "It's [disease] not impacting [my ability to be active] at all. I guess it would be impacting that I can, I can [be physically active]. Now I feel like I'm not going to go…I'm not going to have an accident. Now its [sense of urgency] gone, now I can do gym and I can run and just yeah I can do all kinds of stuff."

Participants described self-motivation as a personal facilitator for activity. They treat their disease symptoms and difficulties engaging in physical activity and exercise as a challenge to conquer. They contrasted this to others who accept the struggles of IBD and allow them to prevent participation in activity. Upon diagnosis, many participants experienced the negative effects of a deconditioned state where activities of daily living were a struggle to accomplish. Now they use this negative memory as a facilitator to engage in physical activity and avoid re-entry into the detrimental cycle of deconditioning. When asked what encourages participants to be physically active, one adolescent reported:

> "Its just my own personal thing. Considering I used to get…really tired just walking up my first flight of stairs, before I got surgery and a little bit after, I want to get to the point where anything that's like remotely tiring is…extremely active and stuff."

***Facilitators related to physical activity.*** Given the variable nature of disease symptoms and exacerbations, participants highlighted the importance of programs tailored to daily disease status. They suggested designing programs that allow individuals to exercise at their own pace and include alternatives to planned activities, to accommodate for participants who are experiencing symptom exacerbation. In addition, participants discussed experiencing disease-related health benefits while engaging in physical activity. For example, one participant described the relationship between abdominal pains and activity:

> "I feel like [if] I'm always laying down then my cramps start to randomly come back. But if I just…move around, walk around, it just stays away."

***Facilitators related to the environment.*** Physical and social environments were introduced as facilitators for physical activity. Participants highlighted the importance of participating in physical activity and exercise in a disease-friendly environment that supports the needs of individuals with IBD. This includes physical factors such as close proximity to a bathroom and the feeling of ease being around individuals who were aware of the disease and understood the symptoms associated with it, for example having to take breaks to use the bathroom. One participant describes wanting to exercise in an environment with the following conditions:

> "If I'm with people who sort of know my disease and understand it and they are okay with it."

Parents, teachers and peers play an important role in facilitating physical activity by finding enjoyable activities that fit within the restrictions imposed by IBD. One participant described the supportive role his peers played following colectomy surgery. Although the participant experienced limitations in mobility and energy, his friends were able to create a role for him that met his abilities. He described: "My friends said I could referee and stuff. They tried to include me as much as they could."

# CHAPTER 4: DISCUSSION

Our data demonstrate that 16-weeks of exercise training in youth in remission from IBD has the capacity to attenuate deficits in lean mass, muscle weakness and aerobic deconditioning. Importantly, these physiological benefits were observed without change in remission status. Taken together, these results provide direct evidence that exercise is both safe and effective for youth in remission from IBD. In addition to reporting barriers and facilitators for physical activity and exercise similar to those of the general public, this group of patients also described factors that were unique to individuals with IBD such as the physical and psychological burden of disease. To our knowledge, this is the first study to assess the safety, feasibility and efficacy of an exercise training program in a cohort of young IBD patients. In addition, this was the first study to qualitatively examine perceptions towards physical activity, specifically barriers and facilitators, in this population.

## 4.1 Feasibility

### *4.1.1 Recruitment*

A total of 217 patients were assessed for eligibility in this study over a period of nine months. Of these, 26.3% were deemed ineligible to participate or we were unable to contact them due to participant's repeatedly missing appointments and/or the investigator being absent from clinic. Of 104 patients approached for participation in this study, 10.6% consented to participate. The primary reason for the low recruitment rate in our study was the long distance to

travel twice a week to McMaster University for training sessions, as reported by patients. Patients seen at McMaster Children's Hospital may have travelled up to 2 hours to attend IBD clinic, making it unfeasible to drive this distance twice a week for four months.

Our pool of potential participants was approximately half of that in a 3-d/week, 12 week exercise training study in children with juvenile idiopathic arthritis (JIA) (Singh-Grewal et al., 2007). This is expected as JIA affects ~1 in 1000 children worldwide and higher than that of IBD (Manners & Bower, 2002). Once participants were excluded based on ineligibility and inability to contact, our recruitment rate was lower than a 35% rate reported by Singh-Grewal et al. (2007). Recruitment rates may have differed due to the fact that JIA study patients were offered six locations for supervised training along with 2 unsupervised sessions per week compared to our one. Nonetheless, 10 out of 11 participants completed our exercise training study (90.9%), which was comparable to the 88.8% retention rate in their study.

### *4.1.2 Adherence*

The adherence rate to McMaster training sessions was high; however, participants demonstrated low adherence to home training. This is in accordance with previous pediatric exercise training studies that have compared adherence to supervised and unsupervised training programs (van Brussel et al., 2011). Our overall adherence rate was higher than that of Singh-Grewal et al. (2007), who reported 56% completion of training sessions, which may have been attributed to

a greater proportion of unsupervised training sessions per week. Additionally, participants in our study achieved a higher adherence rate compared to a 65% in a partially supervised 6-month exercise training study in youth with CF. Similar to the study by Singh-Grewal et al. (2007), supervision was only provided for one of three training sessions per week, which may have negatively influenced adherence. Our supervised adherence rate was similar to a study by Omori et al. (2012) in children with JIA, who demonstrated an 89±9% adherence rate for a 12 month exercise study, training twice a week in supervised conditions.

Adherence to training in this study was influenced by parental support and/or self-motivation. In pediatric exercise training studies, participants are reliant on parents for transportation to training sessions. With regards to home training, participants may have varied according to parental involvement, in that participant's parents may have given them reminders and/or performed the training with them had higher adherence rates. As such, motivational strategies must be individualized to participants depending on the level of parental support. In the absence of parental support, participants exhibited different levels of self-motivation, which influenced home training adherence rates. Taken together, the poor adherence during home training speaks to the need for greater motivational strategies and/or an alternative location of training that would facilitate adherence for future studies.

### *4.1.3 Satisfaction*

As part of the post-training interview, participants shared aspects of the training program they enjoyed, disliked and would recommend changing for future studies. Participants enjoyed the variety of resistance training machines as opposed to the single mode of aerobic exercise (stationary bicycle). They were all satisfied with the structure of the program, including duration, number of training sessions and location of training. Some participants appreciated the home training sessions as they were an opportunity to learn how to incorporate exercise into their daily lives, potentially increasing the likelihood of long-term behavior changes. These participants found that the home session was more convenient than coming to McMaster for a third weekly session, which aligned with our rationale for adding a home training session.

Participants strongly disliked steady state cycling, due to the long duration and feeling of boredom. They preferred the high intensity intervals, which is in accordance with physical activity patterns observed in children, which are characterized by short bursts of high intensity activity interspersed with varying intervals of low or moderate intensity activity (Baquet et al., 2007). Additionally they reported difficulties completing the home training sessions as they often forgot and lacked motivation to complete the exercises. This is supported by low adherence rates often seen in unsupervised or home-based exercise training programs (van Brussel et al., 2011).

Qualitative information on the preferred mode of aerobic activity and optimal setting for training, gained from the interviews, will serve as important data to inform the design of future exercise programs to optimize adherence and enjoyment. Specifically, programs should be designed with a variety of modes of aerobic activity of varying intensities. Additionally, participants would have a greater likelihood of adhering and enjoying exercise sessions in a supervised environment where they are exercising with their peers.

**4.2 Safety**

All participants remained in remission at the post-training evaluation, based on PCDAI and PUCAI scores and physician confirmation. Given the nature of IBD, patients often experience sporadic exacerbation of disease symptoms that will occur regardless of the activities they perform. Over the course of the training study there were few deviations in disease characteristics from the normal level to which participants experience these symptoms on a regular basis. Two participants reported minor flares that quickly resolved themselves and allowed them to continue in the training program. Our results were consistent with exercise training studies in adults with IBD where no disease exacerbations were reported (Elsenbruch et al., 2005; Gupta et al., 2006; Loudon et al., 1999; Ng, Millard, Lebrun, & Howard, 2007; Robinson et al., 1998).

Results from this study are similar to those in children with CF and JIA (van Brussel et al., 2011; van Doorn, 2010). A systematic review by van Brussel et al. (2011) concluded that exercise therapy studies in children with JIA were

completed without short-term detrimental effects, specifically flares in arthritis. Additionally, a systematic review of exercise training studies in patients with CF concluded that there have been no detrimental effects of exercise training (van Doorn, 2010). For the first time, we have data to suggest that, similar to adults with IBD and children with other chronic diseases, it is safe for youth with IBD to engage in prolonged exercise training programs without change in remission status. These results provide scientific evidence for the safe prescription of exercise training in this population.

## 4.3 Efficacy

### *4.3.1 Lean body mass*

There was a significant increase in lean body mass from pre-to mid-training and pre- to post- training. Due to the fact that this study lacked a control group, it is difficult to ascertain whether these changes were due to the training program per se or to normal growth and development. Thus, we compared changes in lean body mass during the training program to changes in lean body mass one would see in healthy children over a similar period of time. Over a four month period, healthy children of the same chronological age would typically increase lean mass by 1.3 ± 0.4 kg (Sala, Webber, Morrison, Beaumont, & Barr, 2007). The increase in lean body mass seen in our sample is significantly higher than what is seen in a healthy population for the same period of time ($p = 0.01$), suggesting that exercise training was capable of reducing the deficits of lean body typically seen in youth with IBD.

In a study by Selvadurai et al. (2002), participants with CF who performed 18 days of RT, 5 days/week increased lean body mass (as measured by skinfold thickness) to a similar extent to which was seen in our study. Lean body mass increased by 7.4%, suggesting a small effect size ($d$ = 0.36) (Selvadurai et al., 2002). Similarly, in a home-based resistance training program in 8-18 year olds with JIA, muscle thickness of the vastus lateralis increased from pre- to post-training ($p$ = 0.017) in response to six weeks of circuit style body weight and resistance training (40 min/session) (Van Oort, Tupper, Rosenberg, Farthing, & Baxter-Jones, 2013). Taken together, youth with IBD are capable of increasing lean body mass in response to exercise training, similar to children with other chronic inflammatory diseases.

Gains in lean body mass may have been due, in part, to the synergistic effects of protein supplementation and resistance training of our training program. Amino acid and/or protein-containing meals after resistance exercise stimulates muscle protein synthesis rates, which results in net muscle protein accretion and muscle fiber hypertrophy (Breen & Phillips, 2012; Phillips, 2014). In a meta-analysis by Cermak et al. (2013), protein supplementation in healthy adults resulted in ~1 kg greater gains in fat free mass after 12 ± 1 weeks of resistance-type exercise training when compared to training without additional protein supplementation. This is further supported by unpublished findings from our laboratory indicating that protein post-exercise induces greater whole body protein balance (WBPB) in the 24h period post-exercise compared to a no protein

and a carbohydrate beverage (Volterman & Timmons, *unpublished*). Similarly, a resistance training study in obese youth found that chocolate milk provided post-exercise increased WBPB after 7 days of training, compared with a carbohydrate beverage (Gillis & Timmons, *unpublished*). Although we did not have an exercise group that did not receive protein supplementation, results from our study suggest that the benefits of protein provided post-exercise in healthy children and adults may also be seen in youth with IBD. Future work should confirm the role of protein intake post-exercise in this population in order to optimize lean body mass accrual.

There was no change in whole body fat mass, or fat mass as a percent of total body mass, which was not surprising given that these participants were quite lean to begin with. Weight loss is dependent on an energy imbalance, wherein energy expenditure exceeds energy intake. A lack of significant changes in FM (kg) was most likely due to participant's maintenance of their habitual diet throughout the training program, although we did not assess dietary intakes. It is also important to note that, when individuals exercise they tend to overcompensate and increase their dietary intake, reducing the potential to reach the maximal effects of exercise on body composition (King et al., 2012). Furthermore, there was no difference in the change in fat mass over the course of training compared to what would be expected over the same time in healthy children (Sala et al., 2007).

### *4.3.2 Muscle strength*

There was a significant increase in isokinetic knee extensor strength at 120°·s$^{-1}$ and 180 °·s$^{-1}$ from pre- to post-training. However, we did not observe significant changes in isometric knee extensor strength or isometric or isokinetic elbow extensor strength over the course of the training program. A lack of change in upper body strength may be associated with a lack of specificity in our training program in that our resistance exercises did not directly target the elbow flexors. Bicep curls were prescribed for home training sessions using a resistance band, however, participants demonstrated low adherence to the home-based sessions, thereby diminishing the imposed stimulus for elbow flexors. The gain in lower limb strength in our study could have been reinforced by the aerobic component of our study on a stationary bicycle. This falls in line with the findings in an exercise training study in children with CF where lower body strength improved the most in the aerobic training group compared with the resistance training group (Orenstein et al., 2004).

Results of this study are consistent with a recent meta-analysis that concluded that strength training is generally effective in childhood and youth (ES of 1.12, $p < 0.001$). Regardless of maturational age, healthy children seem to be capable of increasing muscular strength. Furthermore, with protein supplementation post-exercise, adults can experience an increase in muscle fiber CSA accompanied by a 20% greater increase in 1-RM leg press strength following training (Cermak et al., 2012). It is possible that the protein

supplementation provided to participants post-exercise contributed to the concomitant gains in muscle strength and lean body mass.

Few studies have included resistance training as part of an exercise intervention in youth with chronic diseases. Van Ooort et al. (2014) assessed the effects of six weeks of body weight and resistance exercise on isokinetic strength ($60°\cdot s^{-1}$) of the elbow flexor and knee extensor. Much like our findings, the authors reported no significant increase in muscle strength (Van Oort et al., 2013). Although this study did not demonstrate significant changes in elbow flexor strength, change in strength effect sizes were similar to those seen in our study. An in-hospital exercise training program was created for children with CF, in which patients were randomized into aerobic or resistance training groups. Patients in the resistance training group experienced an increase in lower limb strength by 18.32±7.2% (Selvadurai et al., 2002). It is unclear whether or not lower limb strength was measured isometrically or isokinetically. Regardless, this reported change was higher than changes observed after our training program. This is likely due to the in-hospital, supervised nature of the program, which facilitated high adherence, and included 5 training sessions per week. These findings speak to the importance of supervision and greater frequency of training in order to optimize muscle strength gains with resistance training. This is further supported by work by Behringer et al. (2010) who confirmed an association between a greater frequency of training sessions per week and higher strength gains. They also concluded that long term interventions are more beneficial than

short ones. Therefore, a balance between frequency of training sessions per week and duration of training program is important.

### *4.3.3 Aerobic Fitness*

We observed an increase in absolute $VO_{2peak}$ from pre- to post-training, but not when normalized to total body mass or lean body mass. There were significant increases in absolute $W_{peak}$ and when normalized to total body mass and lean mass over the course of the training program.

These results are similar to a 12-week exercise training study in children with JIA where participants did not experience a significant improvement in $VO_{2max}$ over the course of the study (Singh-Grewal et al., 2007). The authors reasoned that this was due to low adherence and an insufficient training stimulus. In healthy children, studies suggest that prepubertal children show only modest improvements in $VO_{2peak}$ after training, whereas pubertal children are capable of achieving 20-25% increases with training, which is similar to adults (Singh-Grewal et al., 2007). In order for healthy prepubescent children to improve $VO_{2max}$, training intensities must be up to 90% of maximal heart rate for 40-60 minutes, which is significantly higher than heart rates corresponding to peak power levels prescribed in our study (Armstrong & Barker, 2011). Furthermore, given that we had varying proportions of pre-, mid- and post-pubertal participants, the differential training effect may have influenced the magnitude and significance of change in $VO_{2peak}$. Studies with larger sample sizes are necessary to assess this idea.

The increase in peak power, but not maximal aerobic capacity may be explained by an increase in mechanical efficiency. This suggests that the oxygen cost of exercising at given submaximal load may have decreased, resulting in an increased ability to sustain work and achieve a higher maximal power output. Alternatively, it is plausible that an in increase in peak power and not maximal oxygen uptake is related to the specificity of our training program. Cycling was used as both an assessment tool (McMaster All-Out Progressive Cycling test) and as a part of training to increase aerobic fitness (interval and steady state cycling). It is possible that participants may have increased tolerance to cycling, which may lead to improvements in peak power, but not maximal oxygen uptake.

Considering $SV_{max}$ is the main factor associated with increased $VO_{2peak}$ with training in children in adolescents (Armstrong & Barker, 2011), it may be that youth with IBD have a limited capacity to train maximal stroke volume. Patients with IBD may also experience deficits at the level of the muscle, leading to inadequate oxygen uptake at maximal workloads. Further studies should assess SV and muscle oxygenation in these patients in order to determine if it is limited with training.

The increased inflammatory mediators that are characteristic of patients with IBD may also play a role in reducing exercise capacity. Although we did not measure inflammation in our patients, resting levels of proinflammatory cytokines in patients in remission have been found to be elevated (Nguyen et al., 2012). It is therefore plausible that muscle atrophy secondary to chronically elevated

cytokines levels, like TNF-α, may lead to impairments in aerobic capacity independent of inflammatory disease (Roubenoff, 2003).

Although $VO_{2peak}$ did not increase significantly with training, participants did increase their endurance through peak mechanical workload. Future studies should investigate the effect of varying workload intensities during the training period on maximal oxygen uptake, and assess whether patients with IBD display any limitations with regards to training $SV_{max}$ and/or oxygen uptake deficiencies at the level of the muscle at maximal intensities.

**4.4 Barriers and Facilitators for Physical Activity**

In this study we sought to understand the barriers and facilitators for physical activity in youth in remission from IBD. Via qualitative methodology and guided by the social cognitive theory, participants shared their perspectives and experiences with physical activity, for the first time in this pediatric patient population. Youth with IBD experience a number of barriers and facilitators similar to the general public (Bauman et al., 2012; Brockman, Jago, & Fox, 2011; Sallis, Prochaska, & Taylor, 2000); however, prominent in their accounts was the notion of the personal burden of disease as a significant barrier for physical activity. Thus, youth with IBD face unique barriers and facilitators that represent important considerations when designing and delivering physical activity and exercise opportunities. It is important for those involved in this process, such as parents, teachers, and clinicians, to understand the general and disease specific factors that hinder and promote participation in these behaviours.

The most commonly reported barrier for physical activity was the daily burden of disease. Youth with IBD described this burden as manifesting itself both physically and psychologically. *Physically*, youth describe the detrimental impact of abdominal pain and lack of energy when engaging in physical activity and exercise. Additionally, feelings of urgency and the number of times these patients may need to use the bathroom were shared as barriers. Both youth and adults with IBD have discussed these disease-specific barriers towards activity previously. In a qualitative study by Nicholas et al. (2007), which assessed the lived experience of children and adolescents with IBD, patients discussed their concerns relating to IBD symptoms. Specifically, they described how episodic pain often disrupted their daily activities and often resulted in mobility limitations (Nicholas et al., 2007). Similarly, results of a UK survey completed by adults with IBD described barriers to exercise such as fatigue and pain (Robbins et al., 2013). In this same study, 80% of respondents reported that their IBD had forced them to stop exercising either temporarily or permanently due to fatigue, disease flare up, an increased need for the toilet, and pain (Robbins et al., 2013). Youth with CF have described the detrimental impact of their disease on physical activity participation (Moola et al., 2012; Wilkes et al., 2009). Specifically the unpleasant physical symptoms associated with CF, such as breathlessness and exhaustion, often interfere with activity (Moola et al., 2012). Youth with CF sometimes find it too difficult to do activities of daily living, let alone engage in physical activity (Moola et al., 2012). Given the recurrent presence of physical symptoms, such as

pain and fatigue, it is critical to develop coping strategies to facilitate and support the maintenance of a physically active lifestyle. Perhaps equally important, health professionals must design programs to gradually increase fitness, while minimizing physical discomfort and including bathroom breaks, ultimately remaining sensitive to the physical burden of disease (Moola et al., 2012).

Many participants described a negative experience in the hospital upon diagnosis and disease stabilization. During this time they shared that they were unable to be active so they became weak and their fitness declined. When discharged from the hospital, although their disease was stabilized, their physical functioning had significantly declined and participants described the immense difficulty of regaining their strength and the barrier it posed towards engagement in physical activity and exercise. Several participants believed they still experienced weakness from hospitalizations that occurred up to a year before beginning this study. These reports are consistent with the commonly described cycle of deconditioning in special populations. Compared to healthy children, those with a chronic disease are often restricted in their participation in physical activity and exercise (van Brussel et al., 2011). The condition and associated symptoms often causes hypoactivity, which spirals into a cycle of deconditioning and detraining. Deconditioning leading to the reduction of muscle strength may lead to further disability and decrease future recreational physical activity options (Bar-Or & Rowland, 2004). Deconditioning is also common in patients with critical illness as they often bed-ridden and subsequently immobile for prolonged

periods of time (Abdulsatar, Walker, Timmons, & Choong, 2013). Deconditioning experienced during hospitalization and the difficulty in returning to activity that is perceived as "too difficult" or "too tiring" among chronically ill youth highlights the importance of a gradual progression in training. These all-too-common struggles further reinforce the need to incorporate physical activity, when appropriate, during periods of hospitalization, to attenuate the cycle of deconditioning as soon as possible and help patients recover their physical activity habits as soon as possible.

Due to the cyclical nature of IBD, participants described a constant worry about symptom exacerbation and flare up. Furthermore, specific worries regarding having to use the bathroom and having an accident were described as significant barriers towards engagement in physical activity and exercise. Other youth with IBD perceive limited control over their lives due to the nature of IBD. Specifically, they live with the possibility that their disease could flare up at any point (Nicholas et al., 2007). In a systematic review of youth with disabilities, barriers towards physical activity included fear of incontinence and being out of control (Shields, Synnot, & Barr, 2012).

The social environment plays an important role in determining physical activity levels. Participants in our study described general facilitators to physical activity and exercise such as companionship, parental encouragement and a physically active role model. In a study by Brockman et al., (2011) one of the primary motivators was the sense of enjoyment experienced through social

aspects of play. Additionally, in healthy youth, there is strong relationship between parental support and PA engagement suggesting that parents still play an important role in their teenager's lives (Sallis et al., 2000).

Children with cystic fibrosis have also described the effect of parental support on participation in physical activity. Specifically, they reported that growing up around sport and physical activity subsequently influenced physical activity perceptions and behaviours (Moola et al., 2012). These results were mimicked in our study. One participant described how growing up in a household that was physically active had a positive impact on her participation in sport. She appreciated how her family supported one another during each exercise endeavor, which greatly facilitated her engagement in constant physical activity.

Disease specific facilitators related to the environment include social support that creates opportunities to be physically active. Due to the cyclical nature of disease, youth may feel fatigued or in pain on a sporadic basis. Peers and parents act as important facilitators for physical activity and exercise providing support and modifying activities to fit within their disease limitations. These findings are similar to youth with CF who have described positive perceptions toward physical activity due to parental support. Specifically, they described that their parents problem-solved to seek out activities their children could successfully participate in and provided encouragement throughout (Moola et al., 2012).

These findings have important implications for exercise prescription for youth with IBD. Physical activity and exercise programs must account for the chronic, cyclical nature of IBD and the physical and psychological burden it exerts over patients. It is important for physical activity and exercise programs to provide adequate social support from peers and parents to facilitate participation. Physical activity in youth is a complex behavior determined by many variables, such as personal, activity-related and environmental factors. Interventions must target changes in variables from all categories of the social cognitive theory to achieve substantial behavior change (Sallis et al., 2000).

**4.5 Limitations**

Firstly, we were limited by the small sample size for this study. We had difficulties recruiting patients with IBD to commit to an exercise training program given the far distance they often travelled to see their physician and the perceived time commitment. Nonetheless, data from our study do provide effect sizes for future sample size calculations as well as important qualitative information about the barriers and facilitators to physical activity and exercises, satisfaction with the current training program, and recommendations to optimize enjoyment in the future.

Given the pilot nature of this study we did not include a control group. Without a control group it is difficult to ascertain whether the changes in physiological outcomes were due to the exercise training itself or due to normal growth and development or factors related to disease progression. Nevertheless,

we did normalize our results to body composition variables and in some cases compared changes during training to those that would occur over the same period of time in healthy children without exercise training.

Nine out of ten participants were males, which limits the generalizability of our results to the female IBD population. There is no indication of a higher proportion of males presenting with IBD in the general population, as such we approached an even number of males and females during the recruitment period (57 M and 47 F). This is in alignment with the trend towards a greater reduction in physical activity and exercise with increasing age in female adolescents. Additionally, self-selection plays a role in recruitment; individuals who are typically more active and more comfortable engaging in exercise may be more likely to enroll in such studies.

Given that previous work had shown youth with IBD to have deficits in fitness even in remission, we chose to target this population. That being said, our results are limited to patients in remission from IBD. The safety, feasibility and response to exercise may be different for patients with active disease. In addition, they may experience heightened barriers with regards to participation in physical activity and exercise and unique facilitators.

We did not provide participants with any dietary instructions, nor did we measure diet. As such, changes in lean mass could have been due to additional protein intake outside of our supplemental beverage. Moreover, the extent to which participants may have overcompensated with their caloric intake post-

exercise is unknown. Finally, inherent in qualitative research is the potential for investigator bias. In order to account for this we assessed the reliability of the classification of barriers and facilitators using a kappa statistic and two independent raters. Additionally, qualitative findings from this study are preliminary in nature. Given that very little is know about physical activity for youth with IBD, our data serve to form the basis of what we know and future studies with larger sample sizes are needed to increase our understanding and generalizability of our findings.

**4.6 Future Directions**

Results from this pilot study will serve to inform the design of a larger, multi-center, randomized control study. By *increasing sample size*, important comparisons can be conducted, such as the response to exercise training in youth with Crohn's disease compared with ulcerative colitis. A larger sample size may also allow eligibility criteria to be based on type and dose of medication consumed. In order to improve recruitment rate, *collaboration* with other IBD centers across Ontario is imperative. Given that the highest rate of IBD has been reported in Ontario, including a multi-center component to this study will likely be beneficial. Additionally, future studies should include a *cohort of control* IBD patients in order to differentiate the effects of training from normal growth, development and progression of disease.

Given that home adherence was low in this study, future studies should be designed in order to improve adherence to home training sessions. This can

include assessments of stages of change and motivational interviewing to promote adherence. Since participants in this study described the importance of peer support, assessing the impact of group-based training, with other youth with IBD is important. Further, incorporating program enhancements as described by participants may serve to improve home adherence. Alterations include developing specific goals at the outset of the program to progressively work towards accomplishing and providing a greater variety of exercises. Finally, the design of community-based programs may be beneficial to improve adherence, especially in hospitals that attract patients from far distances.

Participants in this study exhibited gains in peak mechanical power but not maximal oxygen uptake over the course of the training program. To investigate this more thoroughly, a future trial in this population could include measures of muscle oxygenation (near infrared spectroscopy to investigate utilization; magnetic resonance spectroscopy to measure muscle metabolism). As well, a measure of cardiac output could help to further clarify the adaptation to exercise, with respect to the contributions of oxygen delivery versus oxygen utilization. Furthermore, future studies are needed to assess how youth with IBD respond to varying levels of training intensity in order to achieve improvements in $VO_{2peak}$, given that this level of training didn't exacerbate symptoms.

Given that exercise is safe, feasible and effective for patients in remission from IBD, is it important to assess the feasibility of exercise for patients with active disease. Qualitative analyses including patients with active disease will be

important to illuminate barriers and facilitators to physical activity in order to optimize accessibility. Future qualitative analyses should assess the influence of disease type and duration on barriers and facilitators for physical activity and exercise. These considerations will ultimately allow for results that may be generalized to the entire IBD population, as opposed to only those in remission from disease.

**Conclusion**

This study has taken the first steps toward understanding the effects of exercise training on body composition, health-related fitness and disease activity in youth with IBD. Further, this study was the first to incorporate qualitative interviews providing youth with IBD a platform to share the unique, disease-related barriers and facilitators they experience with regards to participation in physical activity. Our results fill a significant gap in IBD research in Canada, and worldwide, by providing novel information regarding the role of exercise in disease management for children and youth suffering with this condition and their families. Finally, the major findings of this study represent the building blocks for designing safe and effective exercise guidelines to promote a healthy, active living in youth with IBD.

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## APPENDIX 1: Studies Examining Physical Fitness in Pediatric IBD Patients

**Table 1.** Overview of studies examining physical fitness in pediatric IBD patients.

| Study | Number of patients | Fitness measurements | Healthy reference population | Results |
|---|---|---|---|---|
| **Bechtold *et al.* (2010)** | 45 UC<br>98 CD | Grip strength[1] | 296 healthy German children and adolescents[2] | Patient grip strength was significantly lower than healthy reference population (mean *z*-score ± SD: -0.63 ± 1.3, $p <$ 0.05). |
| **Nguyen *et al.* (2013)[3]** | 7 CD in remission<br>7 healthy controls | $VO_{2peak}$ | Gender and biological age-matched healthy controls from local community | Patient $VO_{2peak}$ was significantly lower than healthy controls (mean ± SD: 53.5 ± 4.6 vs. 43.1 ± 6.5 ml/kg/min respectively, $p = 0.01$). |
| **Ploeger *et al.* (2011)** | 10 UC<br>9 CD in remission or mild disease activity | PP<br>MP<br>$W_{peak}$<br>$VO_{2peak}$ | PP, MP and $W_{peak}$: Age- and sex-matched healthy controls from Bar-Or and Rowland (2004); $VO_{2peak}$: Age- and sex-matched healthy controls from local community | Patient PP, MP, $W_{peak}$ and $VO_{2peak}$ were significantly lower than healthy controls (~90, 89, 91 and 75% of predicted, respectively). |
| **Ploeger *et al.* (2012)** | 15 CD in remission<br>15 healthy controls | $W_{peak}$<br>$VO_{2peak}$ | Gender and biological age-matched healthy controls from local community | Patient $W_{peak}$ was similar to healthy controls (3.6 ± 0.7 vs. 3.9 ± 0.6 W/kg respectively); $VO_{2peak}$ was significantly lower than healthy controls (mean ± SD: 43.9 ± 9.9 vs. 53.6 ± 7.9 ml/kg/min respectively, $p < 0.05$). |
| **Werkstetter** | 20 UC | Grip strength[1] | 296 healthy German | Grip strength was lower in newly |

| | | | | |
|---|---|---|---|---|
| ***et al.* (2011)** | 82 CD | | children and adolescents[2] | diagnosed patients at baseline with higher catch up over time compared to patients with longstanding disease. |
| **Werkstetter *et al.* (2012)** | 12 UC<br>27 CD in remission or mild disease activity<br>39 healthy controls | Grip strength[1]<br>Physical activity[4] | 296 healthy German children and adolescents | Patient grip strength was significantly lower than healthy reference population (Pair-matched difference [Mean, 95% CI]: -1.02 [-1.58;-0.47], $p \leq 0.015$));<br>Patients trended towards less steps per day and shorter duration of physical activity ($p = 0.064$ and $p = 0.051$ respectively). |

[1]Maximal isometric grip force of the nondominant hand, measured by standard adjustable-handle Jamar Dynamometer (Preston, Jackson, MI); [2](Neu, Manz, Rauch, Merkel, & Schoenau, 2001a; Neu, Rauch, Manz, & Schoenau, 2001b); [3]Participants in this study were the same as those included in the study by Ploeger et al. (2012). [4]Number of steps and total duration of physical activity was assessed with SenseWear $Pro_2$ armbands (Bodymedia Inc., Pittsburgh, Pennsylvania, USA) over three consecutive days. CD: Crohn's disease; MP: mean power; PP: peak power; UC: ulcerative colitis; $VO_{2max}$: peak oxygen uptake; $W_{peak}$: peak aerobic mechanical power.

## APPENDIX 2: Exercise Studies in Adults with IBD

**Table 2.** Overview of exercise studies in adults with IBD.

| Study | Number of patients | Exercise intervention (FITT) | Adherence | Results |
|---|---|---|---|---|
| **Robinson *et al.* (1998)** | 117 CD patients:<br>60 Exercise<br>57 Controls | **F** At least 10 sessions/mo for 1 yr<br>**I** Progressively increased by increasing number of reps, advancing body positions and using resistance tubes or weights<br>**T** Home- based, low-impact exercises focused on hip and lumbar regions<br>**T** 5 min warm up, 12 exercises, 5 min cool down | 62% at 3 mo<br>52% at 12 mo<br>23% full compliance | • Bone mineral density improved at the hip and lumbar spine in the compliant patients<br>• No adverse effects of exercise on disease activity |
| **Loudon *et al.* (1999)** | 12 CD patients in remission or with mild disease activity | **F** 3 sessions/wk for12 wks<br>**I** Progressively increased distance and duration<br>**T** Aerobic – group walking program<br>**T** 20-35 min/session | Avg of 2.9 sessions/wk | • Significant improvements in fitness and quality of life, reduction in stress<br>• No disease flares |
| **Candow *et al.* (2002)** | 12 CD patients | **F** 3 sessions/wk for 12 wks<br>**I** 60-70% 1-RM<br>**T** Resistance training<br>**T** 3 sets, 8-10 reps, 12 exercises | *Unknown* | • Increase in muscle strength ($p < 0.05$)<br>• No change in disease activity |
| **Elsenbruch *et al.* (2005)** | 30 UC patients<br>30 UC controls | **F** 1 session/wk for 10 wks<br>**I** Moderate | *Unknown* | • Greater improvements in quality of life in intervention |

| | | | | | |
|---|---|---|---|---|---|
| | All in remission or with mild disease activity | **T**<br><br><br><br>**T** | Stress management training, exercise, mediterranean diet, behavioural techniques and self care strategies<br>6 hrs/session | | group<br>• No effects on clinical or physiological parameters<br>• No change in disease activity |
| **Gupta *et al.* (2006)** | 175 patients (18 with GI issues, including CD)<br>50 controls | **F**<br>**I**<br>**T**<br><br><br>**T** | 8 sessions over 10 days<br>Low<br>Yoga, meditation, stress management, nutrition, group therapy<br>3-4 hrs/ session | *Unknown* | • Significantly lower anxiety in intervention group, non significant decrease for GI subjects<br>• No change in disease activity |
| **Ng *et al.* (2007)** | 16 CD patients<br>16 CD controls<br>All in remission or with mildly active disease | **F**<br>**I**<br>**T**<br>**T** | 3 sessions/wk for 3 mo<br>60% $HR_{max}$ (=40% of $VO_{2max}$)<br>Aerobic – *independent walking*<br>30 min/session | 100% | • Statistically significant improvements quality of life<br>• No detrimental effects in disease activity |
| **D'Inca *et al.* (1999)** | 6 CD patients in remission<br>6 controls | **F**<br>**I**<br>**T**<br>**T** | Singe session<br>60% $VO_{2max}$<br>Aerobic – cycling<br>60 min | *N/A* | • No significant effects on intestinal permeability or lipoperoxidation<br>• No change in disease activity immediately or after 6 mo |

CD, Crohn's disease; F, frequency; I, intensity; T, type; T, time; UC, ulcerative colitis.

## APPENDIX 3: Pediatric Crohn's Disease Index (PCDAI)

**HISTORY (Recall, 1 week)**

Abdominal pain: None ____(0)
Mild - Brief, does not interfere with activities ____(5)
Mod/severe-daily, longer lasting, affects activities, nocturnal ____(10)

Stools: (per day)
0-1 liquid stools, no blood ____(0)
Up to 2 semi-formed with small blood, or 2-5 liquid ____(5)
Gross bleeding, or ≥ 6 liquid, or nocturnal diarrhea ____(10)

Patient Functioning, General Well-Being (Recall, 1 week)

No limitation of activities, well ____(0)
Occasional difficulty in maintaining age appropriate activities, below par ____(5)
Frequent limitation of activity, very poor ____(10)

**LABORATORY**

| | | | | | | |
|---|---|---|---|---|---|---|
| HCT (%) | <u>≤10 yrs:</u> | >33 | ___(0) | <u>11-14M:</u> | ≥35 | ___(0) |
| | | 28-32 | ___(2.5) | | 30-34 | ___(2.5) |
| | | <28 | ___(5) | | <30 | ___(5) |
| | <u>11-19F:</u> | ≥34 | ___(0) | <u>15-19M:</u> | ≥37 | ___(0) |
| | | 29-33 | ___(2.5) | | 32-36 | ___(2.5) |
| | | <29 | ___(5) | | <32 | ___(5) |
| ESR (mm/hr) | | <20 | ____(0) | | | |
| | | 20-50 | ____(2.5) | | | |
| | | >50 | ____(5) | | | |
| Albumin (g/dL) | | ≥3.5 | ____(0) | | | |
| | | 3.1-3.4 | ____(5) | | | |
| | | ≤3.0 | ____(10) | | | |

**EXAMINATION**

Weight

Weight gain or voluntary weight stable/loss ____(0)
Involuntary weight stable, weight loss 1-9% ____(5)
Weight loss ≥ 10% ____(10)

Height

At Diagnosis:
<1 channel decrease ____(0)
≥1, <2 channel decrease ____(5)
>2 channel decrease ____(10)
or

Follow-up:*
Height velocity ≥-1SD ____(0)
Height velocity <-1SD, >-2SD ____(5)
Height velocity ≤-2SD ____(10)

Abdomen
No tenderness, no mass ____(0)
Tenderness, or mass without tenderness ____(5)
Tenderness, involuntary guarding, definite mass ____(10)

Perirectal disease
None, asymptomatic tags ____(0)
1-2 indolent fistula, scant drainage, no tenderness ____(5)
Active fistula, drainage, tenderness, or abscess ____(10)

Extra-intestinal Manifestations
(Fever ≥38.5 for 3 days over past week, definite arthritis, uveitis, E.nodosum, P. gangrenosum)
None ____(0)
One ____(5)
≥ Two ____(10)

**TOTAL SCORE** _____

**FIG. 1.** Pediatric Crohn's disease activity index. From ref. (12).

## APPENDIX 4: Pediatric Ulcerative Colitis Activity Index (PUCAI)

| Item | Points |
|---|---|
| 1. Abdominal pain | |
| No pain | 0 |
| Pain can be ignored | 5 |
| Pain cannot be ignored | 10 |
| 2. Rectal bleeding | |
| None | 0 |
| Small amount only, in less than 50% of stools | 10 |
| Small amount with most stools | 20 |
| Large amount (>50% of the stool content) | 30 |
| 3. Stool consistency of most stools | |
| Formed | 0 |
| Partially formed | 5 |
| Completely unformed | 10 |
| 4. Number of stools per 24 hours | |
| 0−2 | 0 |
| 3−5 | 5 |
| 6−8 | 10 |
| >8 | 15 |
| 5. Nocturnal stools (any episode causing wakening) | |
| No | 0 |
| Yes | 10 |
| 6. Activity level | |
| No limitation of activity | 0 |
| Occasional limitation of activity | 5 |
| Severe restricted activity | 10 |
| Sum of PUCAI (0−85) | |

## APPENDIX 5: Overall Well-Being Questionnaire

Date: _____ ID: _____

**EXERCISE TRAINING IN YOUTH WITH IBD**

**STATUS:** (refer to previous week)

| **General well being**: | | **Abdominal Pain:** | | **Pain Scale:** |
|---|---|---|---|---|
| | | | | 0 ——— 10 |
| Well | ☐ | None 0 | ☐ | no pain worst pain |
| Slightly below par | ☐ | Mild 1-3 | ☐ | |
| Poor | ☐ | Moderate 4-7 | ☐ | |
| Very Poor | ☐ | Severe 8-10 | ☐ | |
| Terrible | ☐ | Location: _____ | | |

---

**Energy/Activity Level:**

Normal ☐ Slightly Decreased ☐ Unable to attend school/work ☐

Improved ☐ Activities Reduced ☐ Number infirm days: _____

---

**Stools:**

Average number per day _____ / week _____

| **Consistency:** | | **Blood:** | | **Mucus:** | |
|---|---|---|---|---|---|
| Formed | ☐ | None | ☐ | None | ☐ |
| Semi formed | ☐ | Trace | ☐ | Trace | ☐ |
| Liquid | ☐ | Greater than Trace | ☐ | Greater than Trace | ☐ |

Perianal discomfort N ☐ Y ☐

Nausea ☐

Vomiting ☐

Nocturnal Stools: _____

---

**Other Manifestations:**

None ☐

Oral Ulcers ☐

Iritis/Uveitis ☐

☐

1

Date: _____ ID: _____

Fever greater than 38.5 x 3 day

Pyoderma ☐

Erythema nodusum ☐

Arthralgia ☐ Location: _____

Arthritis ☐ _____

Cutaneous vasculitis ☐

Incurrent illness (describe): _____

_____

_____

---

**Nutrition:**

Good ☐

Some wasting ☐

Emanciated ☐

**Appetite:**

Normal ☐

Improved ☐

Decreased ☐

**Supplements:** N ☐ Y ☐

If yes, please describe: _____

_____

**Enteral Feeds** N ☐ Y ☐

If yes, please describe: _____

_____

**Psycho-Social**: _____

**Parental Concerns:** _____

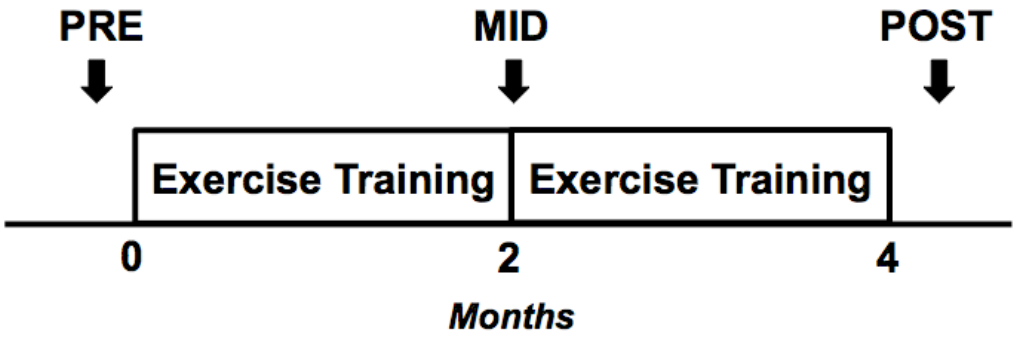
---

**Menstrual Cycle:**

Regular ☐ None ☐

Irregular ☐ N/A ☐

**APPENDIX 6: Study Timeline**



**APPENDIX 7: Interview Guide**

## *I. INTRODUCTION AND INSTRUCTIONS*

Thank you for agreeing to participate in this interview. Just to remind you, I am trying to understand your thoughts, feelings and attitudes toward physical activity and exercise. In addition, I would like to know if there are any barriers that exist, (due to your disease or other factors) which make participation in physical activity and exercise difficult.

**Use of Tape Recorder**

- As you will recall, this interview will be recorded to increase accuracy and to reduce the chance of misinterpreting what you say.
- All tapes and transcripts will be kept under lock and key by the researcher.
- Names will be removed from transcripts. Participants will have coded numbers attached to their name, which only I will know.
- Only my supervisor and I will have access to transcripts (with personal names removed) of this focus group.
- I'll also ask that when using abbreviations or acronyms, you say the full name at least once to aid transcription.

## *II. INTERVIEW*

1. When you think of physical activity, what comes to mind?
2. Which forms of physical activity do you currently participate in?
3. **Are there any forms of physical activity that you avoid?**
    - **If so, what about them makes you avoid them?**
4. Do you enjoy being physical active?
5. Is physical activity important to you?
6. Would you currently describe yourself as physically active?
7. Are you as active as your siblings?
8. Are you as active as your peers?
9. **Are there any things that make it difficult for you to do physical activity?**
10. **Are there any things that make it easier for you to do physical activity?**
11. **Who and/ or what encourages you to be physically active?**

12. **Have you ever been told not to be physically active?**
13. **Has your relationship with physical activity changed since you were diagnosed with IBD?**
14. **Can you explain whether your disease (IBD) impacts how active you want to be?**
15. What do other people think about the physical abilities of youth with IBD?
16. Are there things that people should know/you would like to tell other people about the physical abilities of kids with IBD/ what its like to do PA with IBD that they do not already know?
17. We are trying to help kids with IBD maintain physical activity levels or become more active. Do you have any final advice for us?

***Only responses provided to highlighted questions were analyzed in this thesis.***

## APPENDIX 8: Exercise Training Protocol

### 8.1 McMaster University Training Sessions

| DAY 1 | | DAY 2 | |
|---|---|---|---|
| **5 min** | **WARM UP** – cycle | **5 min** | **WARM UP** – cycle |
| **7-11 min** | **AEROBIC**<br>Cycle – *Intervals*<br>Start: 3 min @ 50% $W_{peak}$<br>Intervals: 1-5 x 30s @ 80-100% $W_{peak}$, each followed by 30s @ 50% $W_{peak}$<br>End: 3 min @ 50% $W_{peak}$ | **7-11 min** | **AEROBIC**<br>Cycle – *Intervals*<br>Start: 3 min @ 50% $W_{peak}$<br>Intervals: 1-5 x 30s @ 80-100% $W_{peak}$, each followed by 30s @ 50% $W_{peak}$<br>End: 3 min @ 50% $W_{peak}$ |
| **10-20 min** | **RT**<br>Leg Press<br>Chest Press<br>Lat Pull Down<br>Low Back Extension<br>Bicycle<br>*1-3 sets, 12-15 reps, 40-70% 1-RM or max reps in 45s* | **10-20 min** | **RT**<br>Leg Extension<br>Leg Curl<br>Pec Fly<br>Seated Row<br>Abdominal Crunches<br>*1-3 sets, 12-15 reps, 40-70% 1-RM or max reps in 45s* |
| **10-20 min** | **AEROBIC**<br>Cycle – *Steady State*<br>40-70% $W_{peak}$ | **10-20 min** | **AEROBIC**<br>Cycle – *Steady State*<br>40-70% $W_{peak}$ |
| **5 min** | **COOL DOWN** – *dynamic and static stretching* | **5 min** | **COOL DOWN** – *dynamic and static stretching* |

RT, resistance training. Ranges in time, intensities and number of sets and repetitions reflect increases in the training stimulus over the course of the 16-week exercise training program.

**8.2 Home Training Sessions**

| Time | Activity |
|---|---|
| **5 min** | **WARM UP** – *skipping or activity of choice* |
| **10-15 min** | **AEROBIC**<br>Skipping or activity of choice – *Intervals*<br>*1-5 x 30s @ 80-100%* $HR_{peak}$ |
| **10-20 min** | **RT**<br>Push Ups<br>Wall Squats<br>Band Rows<br>Band Bicep Curls<br>Band Tricep Extensions<br>Plank<br>*1-3 sets, 40-70% of max reps in 45s* |
| **5-15 min** | **AEROBIC**<br>Activity of choice – *Steady State*<br>40-70% $HR_{peak}$ |
| **5 min** | **COOL DOWN** – *dynamic and static stretching* |

RT, resistance training. Ranges in time, intensities and number of sets and repetitions reflect increases in the training stimulus over the course of the 16-week exercise training program.

**APPENDIX 9: Individual Changes in Physiological Outcomes**

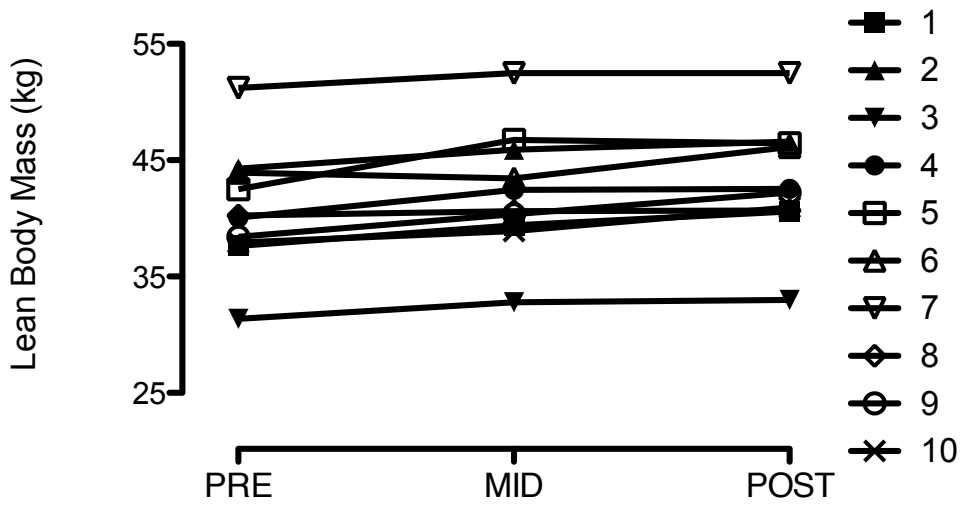



**Figure A.** Lean body mass (kg) mass at pre-, mid- and post-training.

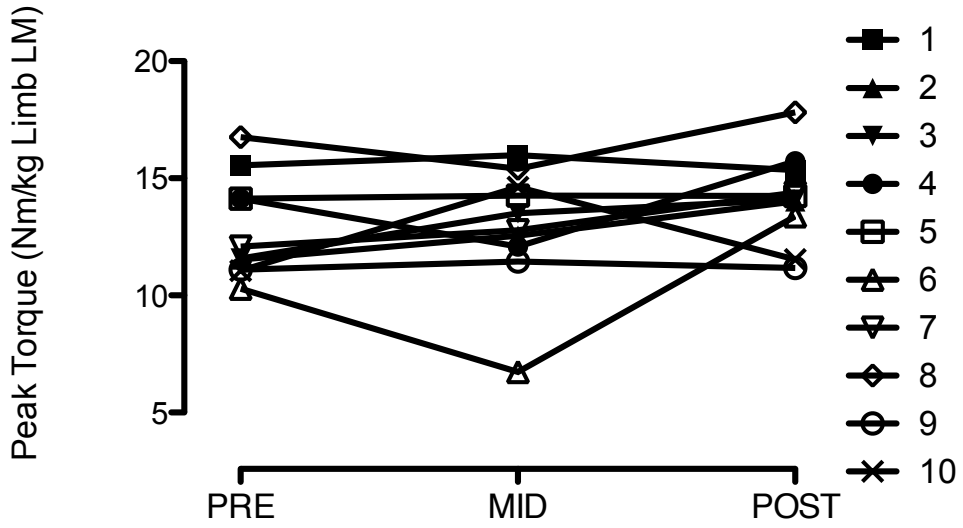



**Figure B.** Isokinetic knee extensor strength (Nm·kg Limb $LM^{-1}$) at 120°·$s^{-1}$ at pre-, mid- and post-training.

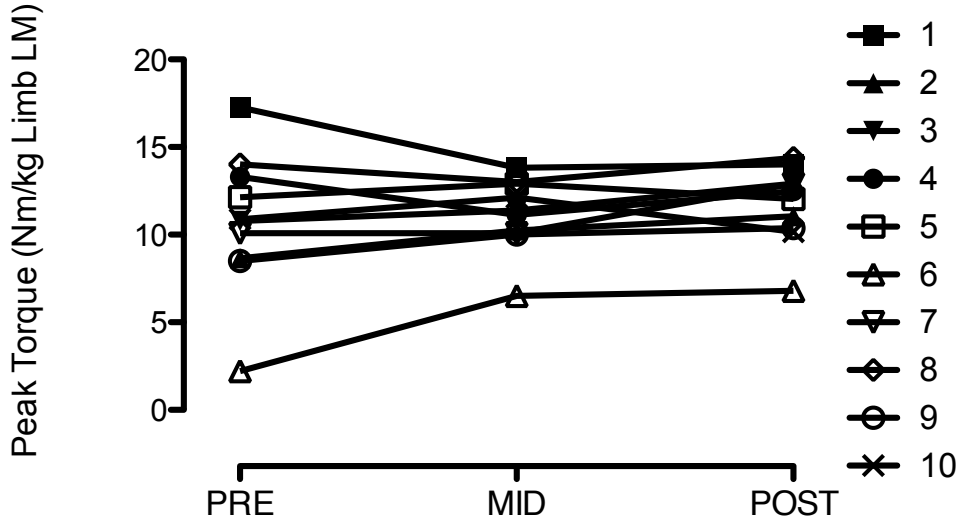



**Figure C.** Isokinetic knee extensor strength (Nm·kg Limb $LM^{-1}$) at 180 °·$s^{-1}$. at pre-, mid- and post-training.

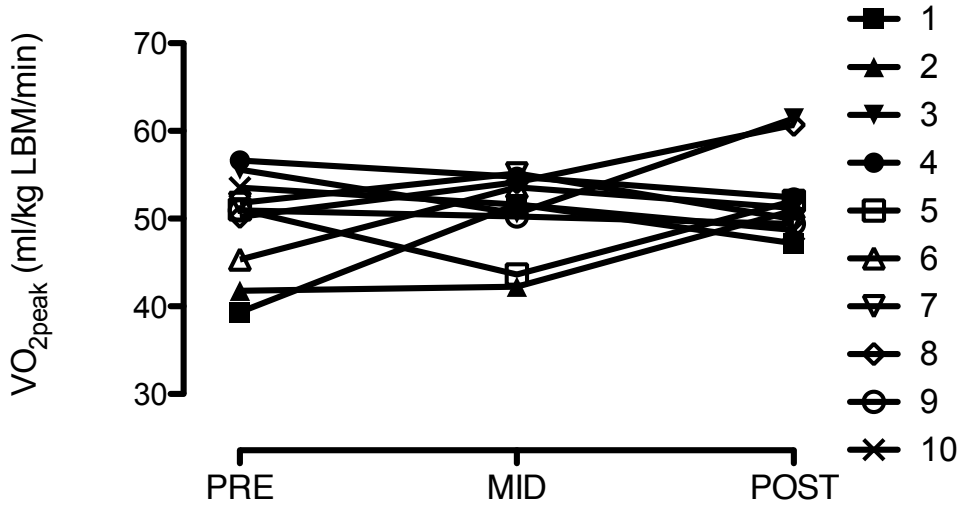



**Figure D.** Maximal aerobic capacity (ml·kg $LBM^{-1}$·$min^{-1}$) at pre-, mid- and post-training.

.

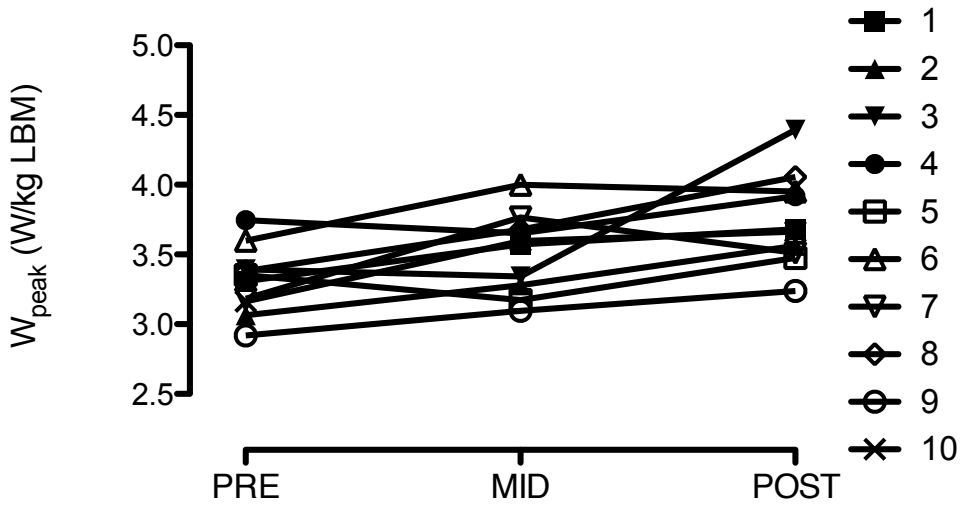



**Figure E.** Peak mechanical power (W·kg $LBM^{-1}$) at pre-, mid- and post-training.

**APPENDIX 10: Training Load**

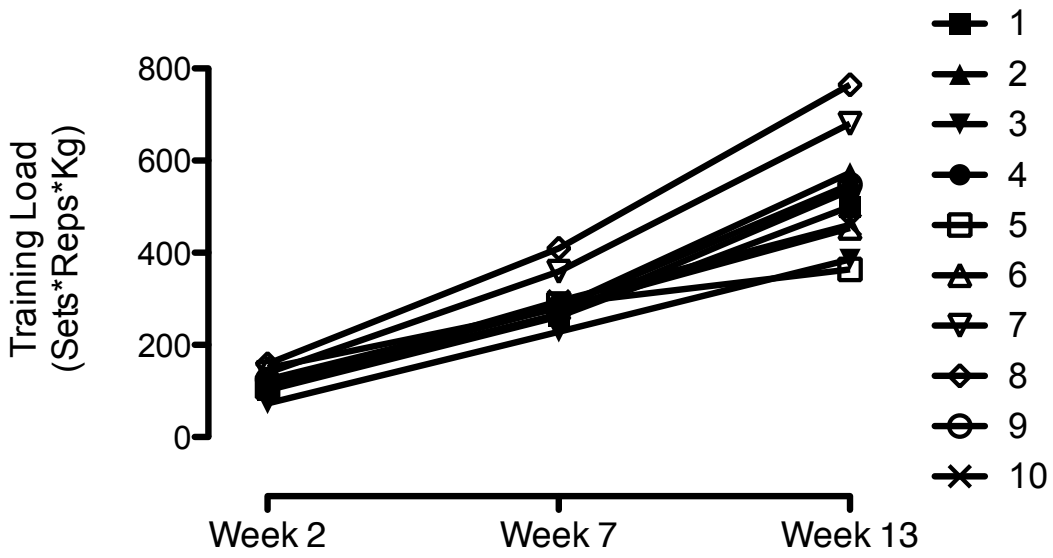



**Figure A.** Change in training load over the course of the training program.

## APPENDIX 11: Parent/Guardian Consent Form

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**Parent Information and Consent Form**

| | |
|---|---|
| **Title of Study:** | The effects of exercise training on fitness, function and quality of life in youth with inflammatory bowel disease: A pilot study |
| **Principal Investigator:** | *Rachel Walker (BSc Kin), Department of Kinesiology, McMaster University* |
| **Local Principal Investigator:** | *Brian W. Timmons (PhD), Department of Pediatrics, McMaster University* |
| **Co-Investigators:** | *Robert M. Issenman (MD, FRCP), Department of Pediatrics and Pediatric Gastroenterology and Nutrition, McMaster University* |

**INTRODUCTION**

Your child is being invited to participate in a research study under the supervision of Dr. Brian Timmons because they are between 10 and 17 years of age and have been diagnosed with inflammatory bowel disease. In order to decide whether or not you want to be a part of this research study, you should understand what is involved and the potential risks and benefits. This form gives detailed information about the research study, which will be discussed with you. Once you understand the study, you will be asked to sign this form if you wish to provide consent for your child to participate. Feel free to discuss it with your friends and family and take your time while making your decision.

**WHY IS THIS RESEARCH BEING DONE?**

Strategies to manage the life- long implications of inflammatory bowel disease (IBD) are essential. Exercise is a non- pharmacological, non- invasive intervention that can reduce the physical and psycho- social health deficits experienced by children with chronic disease. For adults with IBD, exercise has been shown to improve fitness, bone health and quality of life. However, we do not yet know how exercise and physical activity affect disease activity or secondary complications in children with IBD. Once we understand its influence, we can take the first steps towards recommending safe and effective exercise for children with IBD.

**WHAT IS THE PURPOSE OF THIS STUDY?**

The purpose of this study is to assess the effects of a 16-week exercise training program on body composition, fitness, muscle strength, quality of life and biomarkers of inflammation in youth with IBD.

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**WHAT WILL MY RESPONSIBILITIES BE IF I TAKE PART IN THE STUDY?**

If you volunteer to participate in this study we will ask you to bring your child to the Department of Kinesiology in the Ivor Wynne Center at McMaster University *2 times* a week for a 16-week period for exercise training sessions. We will also ask you to supervise them while they complete *one training session per week* at home. Additionally we will ask you to bring them to our lab at McMaster Children's Hospital *3 times* for evaluation sessions; once before the training begins ("baseline"), halfway through the training program ("mid- training") and following completion of the training program ("post- training"). We will schedule the weekly training sessions and three evaluation sessions according to you and your child's availability.

The table below provides a summary of what to expect and the amount of time required for each visit:

| Visit | What to Expect | Approximate Time Required |
|---|---|---|
| Baseline, mid & post-training evaluations | *** We will ask your child to arrive at our laboratory after an overnight fast.**<br>• Your child's height, weight and waist circumference will be measured.<br>• A blood sample will be drawn from a vein in their arm using a small needle.<br>• They will receive a DXA scan. A DXA scan tells us how much bone, fat, and muscle your child has.<br>• Your child will have a maximal exercise test conducted on a special bicycle. This exercise test (called a "$VO_{2max}$ test") lasts 8 to 12 minutes and is used to determine aerobic fitness by breathing through a mouthpiece.<br>• After the exercise test your child will rest for half an hour. During this time they will be asked to fill out two questionnaires regarding their medical history and physical activity habits respectively.<br>• Following rest we will measure their arm and leg strength using a Biodex dynamometer. This device requires your child to bend and straighten one arm and one leg repeatedly against a resistance.<br>• Before leaving we will give them a physical activity monitor to wear for 7 days and return at their next training session.<br>* At the first evaluation session, we will take your child to | **9 hours**<br>(3 hours/ visit) |

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| | | |
|---|---|---|
| | the Department of Kinesiology in the Ivor Wynne Center to receive familiarization with the exercise equipment that they will use during each MAC training session. | |
| MAC Training | • 30-60 minutes of circuit style training consisting of combinations of cycling and strength training.<br>• Each week we will progressively increase the intensity of the exercises.<br>• There will be several other kids participating in the study at each training session.<br>• During each training session your child can watch movies and/ or listen to music.<br><br>*At the first and last training sessions your child will be asked to participate in a qualitative interview (~30 min). At this time I will ask them how important exercise is to them and about any barriers they may experience with regards to exercise participation.<br><br>*At the first training session post "baseline" and mid-training" evaluations, we will have your child perform one repetition maximum (1-RM) testing (~30 min). This will tell us the greatest amount of weight your child can lift, once, for each exercise.<br><br>*As a result the first training session post "baseline" and "mid-training" evaluations and the last training session will be **1.5 hours** in duration.* | **32 hours** (1 hour/ session; 2 sessions/ week) |
| HOME Training | We will provide your child with a resource package containing a "menu" of exercises that they will be able to perform easily at home. The Master's student will demonstrate these exercises to your child before the first at home training session. We will ask your child to spend 30-60 minutes (including rest time) performing exercises from the resource package. We will provide them with a booklet to record which exercises they perform each session. Each week we will progressively increase the intensity of the exercises.<br><br>**We would ask that you encourage and supervise your child as he/she is performing their exercises.* | **16 hours** (1 hour/ week) |
| | **TOTAL** | **57 hours over** |

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| | |
|---|---|
| | **~18 weeks** |

**WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?**

*i) DXA – Dual Energy X-ray Absorptiometry:* The DXA machine is like an x-ray that measures bone mineral content and muscle mass. But this test delivers only 1/100th of the amount of radiation that is delivered from a chest x-ray. This is less than the amount of radiation your child is exposed to on a daily basis from sources of natural background radiation, i.e., just walking around outside. This test only takes a few minutes to complete and doesn't hurt. Your child will need to lie still during the test.

*ii) Exercise Testing:* The $VO_{2max}$ test requires your child to give a maximal effort. This means that they will feel quite tired after they are done the test, but this feeling will not last long.

*iii) Biodex Dynamometry:* The muscle strength test requires your child to give maximal effort to show how strong they are. This means that their arms and legs may feel quite tired after they are done the test. It is possible that 24 to 48 hours after this test, the arm and leg muscles will be sore and this is the body's normal way of getting stronger.

*iv) Fasting Blood Samples:* Your child may be afraid of the needles used for the necessary blood samples. The pain can be minimized by using a topical anesthetic cream. We can provide this if you wish.

*v) Exercise Training:* The types and duration of exercises we ask your child to do may not be what they are used to. As a result they may feel tired during and/ or after the training sessions. As the program progresses and they become more comfortable with the exercises and stronger, it will not be as tiring. If the fatigue is significant and persists, we encourage you or your child to let us know and we can adjust their training program accordingly.

**HOW MANY PEOPLE WILL BE IN THIS STUDY?**

We plan to test 10 children with ulcerative colitis and 10 children with Crohn's disease between the ages of 10 and 16 years. Your participation is voluntary. If you chose not to participate or to stop participation even after you have started, this decision will in no way affect your normal care at the McMaster Children's Hospital.

**WHAT ARE THE POSSIBLE BENEFITS FOR ME AND/OR FOR SOCIETY?**

By participating in this study, you will learn about your child's body composition, fitness level, and muscle strength. All of these measures have the potential to improve over the course of the 16 week exercise training program. We will make each exercise session fun and enjoyable for your child and allow them to meet other children with IBD. Ultimately results from this study will be used to design a larger, more definitive study and contribute to developing safe and effective exercise

programs for youth with IBD.

**WHAT INFORMATION WILL BE KEPT PRIVATE?**

All of your information will be stored in locked filing cabinets under the supervision of Dr. Brian Timmons for 10 years. We will supervise access to your child's information by other people in our group, only if necessary. Your child will be assigned a subject number, and this number will be used to identify them. Records identifying your child will be kept confidential and in a secure place. If the results of the study are published, their identity will remain confidential.

**CAN PARTICIPATION IN THE STUDY END EARLY?**

If your child volunteers to be in this study, you and your child have the right to withdraw at any time. You have the option of removing your data from the study. The investigator may withdraw your child from this research if circumstances arise which warrant doing so. In no way, will early withdrawal affect the clinical care your child receives from the McMaster Children's Hospital.

**WILL THERE BE ANY COSTS?**

Your child's participation in this research project will require you to make multiple visits to the McMaster University Medical Centre. Any parking costs for participating in the study will be reimbursed. We cannot provide you with mileage reimbursement. For their participation, we will give your son/daughter $100 as a token of our appreciation for his/her commitment to the project. We will also provide them with a snack at each of the evaluation sessions. If they complete more than 80% of the training sessions their name will also be entered into a draw for a $100 gift card to FutureShop.

**IF I HAVE ANY QUESTIONS OR PROBLEMS, WHOM CAN I CALL?**

If you have any questions about the research now or later, or if you think you have a research-related injury please contact Rachel (the student investigator) at 905-334-6890. You may also contact Dr. Timmons at 905-521-2100, ext 77218 during the day or at 289-237-8613 during the evening and on weekends.

If you have any questions regarding your rights as a research participant, you may contact the Office of the Hamilton Integrated Research Ethics Board at 905-521-2100, ext. 42013.

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**CONSENT STATEMENT**

I have read the preceding information thoroughly. I have had the opportunity to ask questions, and all of my questions have been answered to my satisfaction. I agree to allow my child to participate in this study entitled: *"The effects of exercise on fitness, function and quality of life in youth with inflammatory bowel disease"*. I understand that I will receive a signed copy of this form.

**Please check the small box below if you agree to have Dr. Timmons contact you in the future to participate in a research study other than the one described in this information form. Any future studies would be approved by the Research Ethics Board and would require you to sign a new consent form.

☐

Name of Participant (Child's Name)

Name of Legally Authorized Representative

Signature of Legally Authorized Representative Date

**Consent form administered and explained in person by:**

Name and title

Signature Date

**SIGNATURE OF INVESTIGATOR:**
In my judgement, the participant is voluntarily and knowingly giving informed consent and possesses the legal capacity to give informed consent to participate in this research study.

Name and title

Signature of Investigator Date

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**FUTURE RESEARCH**

At the end of the study, we may wish to store leftover blood samples for use in a future study. We will not store your child's sample longer than 10 years. All records identifying your child will remain confidential. Information about your child will not be released. If the results of the study are published, your child's identity will remain confidential.

**CONSENT STATEMENT FOR STORAGE OF BLOOD SAMPLES**

I have read the preceding information thoroughly. I have had the opportunity to ask questions, and all of my questions have been answered to my satisfaction. I agree to have my child's blood stored so it can be used in future research studies, approved by the Research Ethics Board, other than the one described in this information form.

_____
Name of Participant (child's name)

_____
Name of Legally Authorized Representative

_____ _____
Signature of Legally Authorized Representative Date

**Consent form administered and explained in person by:**

_____
Name and title

_____ _____
Signature Date

**SIGNATURE OF INVESTIGATOR:**
In my judgement, the participant is voluntarily and knowingly giving informed consent and possesses the legal capacity to give informed consent to have their child's blood and urine stored so it can be used in future research studies approved by the Research Ethics Board other than the one described in this information form.

_____
Name and title

Hamilton Integrated Research Ethics Board JUN 12 2013

_____ _____
Signature of Investigator Date

## APPENDIX 12: Child Assent Form

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**Child Information and Assent Form**

| | |
|---|---|
| **Title of Study:** | The effects of exercise training on fitness, function and quality of life in youth with inflammatory bowel disease: A pilot study |
| **Principal Investigator:** | *Rachel G. Walker (BSc Kin), Department of Kinesiology, McMaster University* |
| **Local Principal Investigator:** | *Brian W. Timmons (PhD), Department of Pediatrics, McMaster University* |
| **Co-Investigators:** | *Robert M. Issenman (MD, FRCP), Department of Pediatrics and Pediatric Gastroenterology and Nutrition, McMaster University* |

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**Why are we doing this study?**
A research study is a way to learn about people. We are doing this study to see if exercise training is safe for you and if it can improve your fitness. Some kids with inflammatory bowel disease might have problems exercising or they may not like it. We also want to learn more about what you think of the exercise we ask you to do and if you feel comfortable doing it. Doing this study will help doctors figure out which exercises are safe and improve fitness in kids with inflammatory bowel disease. This information will probably help these kids live healthier so they can do the things they want to do.

**Why am I being asked to be in the study?**
You are being asked because you are 10- 17 years of age and are in remission from inflammatory bowel disease (ulcerative colitis or Crohn's disease).

**If I am in the study what will happen to me?**
If you decide that you want to be part of this study, we will ask you to visit us twice a week for 4 months for exercise training sessions. We will also ask you to do exercises at home once a week. Finally we will ask you to visit us three times for evaluations, once before you

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start the training program ("baseline"), halfway through the training program ("mid"), and after the training program is finished ("post").
This is what you can expect from each visit:

**Baseline, mid & post-training sessions:** You will have your height, weight and waist circumference measured. You will get a DXA scan. A DXA scan tells us how much bone, fat, and muscle you have. For this, you will have to lie still on a bed for a few minutes while a machine scans you. We will take a small blood sample from you. You will be asked to ride a special bicycle to see how fit you are. After this you will be allowed to rest for half an hour. During this time we will ask you to fill out two short questionnaires. One will ask you if you were ever sick in the past and the other will ask how much exercise you do. The questions are simple and there are no right or wrong answers. Following rest, we will test how strong your arms and legs are. Finally we will take you to another building so you can practice using the exercise equipment that you will use during each MAC training session. Before you leave we will give you a special activity monitor to wear for a week. This activity monitor is attached to a belt worn around your waist. Your parents will help you remember when to put it on and when to take it off.

**MAC training**: We will ask you to visit our lab twice a week. During these visits you will get to ride a bike, run on a treadmill and lift weights. You will be able to watch movies and/ or listen to music during these visits. There will be a few other kids with IBD exercising with you at each visit. Each week we will make the exercises a bit harder. At the first and last MAC training session we will ask you to participate in an interview. At this time I will ask you about what you think about exercise and if it is important to you. I will also ask you if anything in your life makes it hard for you to participate in physical activity and sports.

**HOME training:** We will give you a book with pictures and descriptions of different exercises for you to do at home once a week. The research student (Rachel) will show you how to do each exercise before your first in-home training session. We will give you a booklet to write down which exercises you do each week. Rachel and your parents will remind you to do these exercises each week.

**Will I be hurt if I am in the study?**
There are some things about this study you should know.

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*DXA:* The DXA machine is like an x-ray that measures your bones and muscles, but it is not as strong as a real x-ray machine. This test only takes a few minutes to complete and doesn't hurt. You will need to lie still during the test.

*Exercise Test:* The cycling test, which will tell us how fit you are, might make you feel a little tired. But it will be like when you play sports and the feeling won't last long.

*Muscle Strength Test:* This test might make your arm and leg muscles feel a little tired. A couple of days after the test your arm and leg may feel sore but this is your body's way of getting stronger. The sore feeling won't last too long.

*Fasting Blood samples:* A single small needle will be used to take some of your blood. A small bruise might appear where the needle goes through your skin. If you do not want to feel the small needle go into your arm, we can give you a special cream for your skin. This blood sample will be taken in the morning before you have breakfast.

*Exercise Training:* The exercise that we ask you to do each week may be different than what you normally do. At first you might feel tired during and/or after each session, but as you get stronger each week you will not feel as tired.

*If you think something's wrong at any time then you should let us know or tell your mom or dad to let us know. You are always able to talk to your nurse or doctor about anything that is bothering you.*

**Will the study help me?**

This study will help you learn how to fit exercise into your daily routine. The study will also tell you and your parents how fit you are at the beginning of the training program and how much more fit and stronger you become over the 16 weeks. This study might also give us some clues if exercise can affect inflammation. This will let us give better information to help other kids with IBD.

**Do I have to be in this study?**

You do not have to be in this study if you do not want to be. If you decide that you do not want to be in the study after we begin, that's OK too. Nobody will be angry or upset. We are discussing the study with your parents and you should talk to them about it too.

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**What if I have questions?**
You can ask questions at anytime if you do not understand any part of the study. If you have questions now or later, you can contact me (Rachel) or ask your parents to contact me at 905-334-6890. You may also contact Dr. Timmons at 905-521-2100, ext. 77218 during the day or at 289-237-8613 during the evening and on weekends.

**What happens after the study?**
When we are finished this study we will write a report about what was learned. The report will not include your name. We will also share the news with you.

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**Assent:**

If you decide you want to be in this study, please print/write your name. If you decide that you do not want to be in the study, even if you have already started in the study, all you have to do is tell Rachel or Brian.

_____ (Print your name) would like to be in this research study.

_____ (Date of assent)

_____ (Name of person who obtained assent)

_____ (Signature of person who obtained assent and Date)

_____ (Local Principal Investigator name)

_____ (LPI signature and Date)