Associations among Sitting, Physical Activity, Resilience, and Quality of Life in People with Inflammatory Bowel Disease Compared to Healthy Controls

A Dissertation

Presented in Partial Fulfillment of the Requirements for the

Degree of Doctorate of Philosophy

with a

Major in Education

in the

College of Graduate Studies

University of Idaho

by

Katrina Taylor

Major Professor: Chantal A. Vella, Ph.D.

Committee Members: Philip W. Scruggs, Ph.D.; Michelle M. Wiest, Ph.D.;

Onesmo B. Balemba, Ph.D.

Department Administrator: Philip W. Scruggs, Ph.D.

August 2016

Authorization to Submit Dissertation

This dissertation of Katrina Taylor, submitted for the degree of Doctorate of Philosophy with a Major in Education and titled "Associations among Sitting, Physical Activity, Resilience, and Quality of Life in People with Inflammatory Bowel Disease Compared to Healthy Controls," has been reviewed in final form. Permissions, as indicated by the signatures and dates below, is now granted to submit final copies to the College of Graduate Studies for approval.

Major Professor: _____ Date: _____
Chantal A. Vella, Ph.D.

Committee Members: _____ Date: _____
Philip W. Scruggs, Ph.D.

_____ Date: _____
Michelle M. Wiest, Ph.D.

_____ Date: _____
Onesmo B. Balemba, Ph.D.

Department Administrator: _____ Date: _____
Philip W. Scruggs, Ph.D.

Abstract

PURPOSE: The aims of the study were to (i) determine whether the 10-item or 25-item Connor-Davidson Resilience Scale (CD-RISC) was a valid measure of resilience in people with inflammatory bowel disease (IBD); (ii) understand the differences in health-related quality of life (HRQOL), physical activity, sitting, and resilience levels among IBD disease states (i.e., disease remission versus disease flare) and healthy controls; and (iii) explore the associations among differing intensities of physical activity, resilience, and HRQOL in people with IBD. METHODS: IBD participants (n = 242) and healthy controls (n = 265) completed an online survey measuring physical activity, sitting, resilience, and HRQOL levels using previously validated surveys. Confirmatory factor analysis, analysis of covariance, and multiple regression were used to address the aims of the study. RESULTS: The 10-item CD-RISC was found to be a more valid measure of resilience in people with IBD than the 25-item instrument. HRQOL was lower in both IBD groups compared to healthy controls with IBD-flare participants exhibiting the lowest levels of HRQOL. Physical activity levels were higher in healthy controls than people with IBD, with no differences between disease states. There were no differences in time spent sitting across groups. Moderate-to-vigorous physical activity (MVPA) and walking were independently associated with physical but not mental HRQOL. Participants with higher levels of activity reported higher levels of physical HRQOL. CONCLUSIONS: People with IBD have lower HRQOL, physical activity, and resilience levels compared to healthy controls but with no differences in time spent sitting. Furthermore, HRQOL was negatively impacted by a disease flare but disease state did not affect physical activity or resilience levels. Walking and MVPA were independently associated with physical but not mental HRQOL and participants with higher levels of activity

reported higher levels of physical HRQOL. Future research is warranted to investigate these findings using objective measures of physical activity and sitting.

Acknowledgements

Over the past four years I have received support and encouragement from a great number of individuals. Dr. Chantal Vella has been a mentor, colleague, and friend. Her unwavering guidance has made this a thoughtful and rewarding experience. Dr. Vella's patience, knowledge, and ability to have faith in me when my own faith was lacking has brought me to where I am now. I would like to thank my dissertation committee of Philip Scruggs, Michelle Wiest, and Onesmo Balemba for their support over the last two years as I transitioned from a collection of ideas to a completed study. The time and knowledge provided by my committee have been valuable to producing this final product.

Outside of my committee, there have been many people who have listened to my troubles and delights throughout this process and I am grateful to all those who have supported my endeavors. In particular, Dr. David Paul has been a valuable help and an excellent 'teaching assistant' as I have juggled teaching and completing my dissertation over the last twelve months. Lynda Taylor, my mother, has been an integral part of my support system throughout my education and has always taught me that with determination, anything is possible.

Gatorade Sports Science Institute are recognized for their financial support of this dissertation. The receipt of a grant allowed us to conduct this research study in the manner I had hoped. Lastly, to all of the people who took 15 minutes out of their day to complete the survey, you helped provide an insight to improving quality of life in people who live with inflammatory bowel disease.

Dedication

To the inspirational women who stood next to me every step of the way.

Lynda Taylor and Dr. Chantal Vella, without either of you this would never have been possible.

Table of Contents

List of Figures

List of Tables

Chapter One: Introduction

Inflammatory bowel disease (IBD) is a debilitating autoimmune disease, affecting the gastrointestinal tract that collectively refers to Crohn's disease and ulcerative colitis. IBD provides challenges to the patient, physician, gastroenterologist, and researchers alike, in that there is not a definitive cause or cure for the disease; however, it is known to affect more than 3.6 million people in Europe and the United States (Loftus, 2004; Molodecky et al., 2012). It is believed that a combination of genetic and environmental factors contributes to the onset of IBD. El Sayed (2013) suggested that IBD occurs in response to environmental triggers, such as infections, medications, or other agents, in individuals who are genetically susceptible to immunological disease.

IBD is commonly recognized by symptoms such as weight loss, gastrointestinal bleeding, bloody diarrhea, abdominal pain, and intestinal obstructions. Although commonly referred to as the collective term IBD, ulcerative colitis and Crohn's disease have distinctly different disease mechanisms while exhibiting similar symptoms (Podolsky, 2002). In ulcerative colitis, the inflammation is limited to the colon whereas in Crohn's disease it can occur at any position along the gastrointestinal tract from the mouth to the anus (El Sayed, 2013; Mulder, Noble, Justinich, & Duffin, 2014). Onset of IBD usually occurs between the ages of 15 and 30 years (Bernstein, Rawsthorne, Cheang, & Blanchard, 2006). With no current cure for IBD, many patients will live with a decreased quality of life from a young age.

Previous research suggests that patients with IBD have a decreased health-related quality of life (HRQOL) because of the severe and debilitating nature of the disease (Moradkhani, Beckman, & Tabibian, 2013). Ghosh & Mitchell (2007) found that more than

half of patients have flare-ups of their disease at least every few months. Further, more than 75% of patients report that their leisure activities are affected, particularly during flare-ups. Understandably, HRQOL is influenced by clinical symptoms, disease severity, surgical interventions, and extraintestinal manifestations in IBD patients (Hjortswang et al., 2003). In terms of managing treatment of IBD, maintenance and improvement in HRQOL is becoming an increasingly important goal for patients and health-care professionals.

One of the most influential and cost-effective coping strategies to improve HRQOL in chronic disease patients is physical activity (Frazier, 2000; Westerhuis, Zijlmans, Fischer, van Andel, & Leijten, 2011). However, the knowledge about the beneficial effects of physical activity on IBD disease severity, management, and HRQOL is limited. Many physicians do not recommend physical activity to patients with IBD for the fear of symptom exacerbation (Ng, Millard, Lebrun, & Howard, 2007); yet a small number of studies suggest low to moderate physical activity is safe for patients with this disease (Packer, Hoffman-Goetz, & Ward, 2010). Furthermore, studies suggest that IBD patients may benefit from exercise particularly in relation to extraintestinal manifestations of the disease such as osteoporosis, fatigue, and anemia (Narula & Fedorak, 2008), though the research is limited. Research suggests that physical activity may offer an avenue to improve HRQOL in IBD patients, particularly the psychological factors, without causing disease exacerbation. However, there is no established mechanism underlying the physiological benefits of physical activity as well as a lack of knowledge of the ability to tolerate higher intensities of physical activity in IBD patients (Bi & Triadafilopoulos, 2003).

Another factor for consideration in terms of improving HRQOL in IBD patients is the psychological construct, resilience. Resilience has recently received attention from

researchers investigating the levels of resilience experienced by patients with chronic diseases such as type 2 diabetes, human immunodeficiency virus (HIV), and cancer (Carver, 2005; Farber, Schwartz, Schaper, Moonen, & McDaniel, 2000; Yi, Vitaliano, Smith, Yi, & Weinger, 2008). It is believed that patients who score higher on a resilience scale are more likely to perceive change and stress in a positive manner, particularly in terms of personal growth, whereas those who are rated lower on resilience scales tend to perceive similar situations as a threat (Carver, 1998). Additionally, studies have previously reported that patients with higher levels of resilience also have improved physiological symptoms of their diseases and HRQOL (Richardson, 2002; Steinhardt, Mamerow, Brown, & Jolly, 2009).

No research has yet been conducted with resilience in IBD patients, though research on irritable bowel syndrome, a functional disorder of the large intestine that is less destructive than IBD, has shown that patients with the illness score higher in neuroticism and thus lower in resilience (Zarpour & Besharat, 2011). Interestingly, previous research has shown that irritable bowel syndrome patients tend to catastrophize more than IBD patients, suggesting that we cannot make any assumptions that the two groups of patients would score similarly on a resilience scale. This highlights the need for research to be developed in IBD patients in terms of disease and HRQOL management and improvement.

Need for the Study

With the growing prevalence of IBD in countries that are adopting a Western lifestyle, as well as the lack of a known cure for these debilitating diseases, interventions are needed to improve the HRQOL of these patients. The individual patient costs of IBD are staggering with an annual cost of $19,000 for Crohn’s disease and $15,000 for ulcerative colitis, neither of

which include any costs for surgical interventions, which typically cost upwards of $40,000 each time (Crohn's and Colitis Foundation of America, 2014). However, even following expensive surgery and medical therapies, the HRQOL of IBD patients typically does not improve, and thus there is a need for different HRQOL management techniques.

Over the last decade there has been a focus within the exercise science field on the concept of 'exercise is medicine'. Research has found exercise to be beneficial for management of disease severity and HRQOL in cardiovascular disease and type 2 diabetes (Warburton, Nicol, & Bredin, 2006). Although much research supports the link between exercise and HRQOL in metabolic and cardiovascular diseases, findings are equivocal in terms of the benefits of exercise on HRQOL in IBD patients. In addition, the psychological concept of resilience is receiving increased attention in the health literature as a mechanism for improved HRQOL and disease management in cancer (Carver, 2005), cardiovascular disease (Kubzansky, Sparrow, Vokonas, & Kawachi, 2001), diabetes (Steinhardt et al., 2009), and HIV (Farber et al., 2000). However, research has not studied the relationships between resilience and HRQOL in IBD patients.

Therefore the significance of the current research is to provide meaningful conclusions about the relationships between physical activity and resilience on HRQOL in patients with IBD. This study should provide IBD patients with insight as to the benefits of physical activity and higher levels of resilience on HRQOL. In addition it will provide a solid foundation for further research to be conducted upon, particularly in terms of physical activity interventions and resilience training in IBD patients.

Objective and Purpose Statement

The objective of this cross-sectional, internet-based survey research study was to explore the relationships among physical activity, resilience, and HRQOL in a worldwide cohort of IBD patients.

There were three purposes of this study:

1. To validate the CD-RISC survey in a cohort of participants with IBD.
2. To investigate differences in HRQOL, resilience, and physical activity between participants with IBD and healthy controls.
3. To characterize the relationships among HRQOL, physical activity, and resilience in participants with IBD.

Research questions.

1. Is the 10-item or 25-item CD-RISC survey a more valid representation of resilience in participants with IBD?
2. Are there differences in total, physical, and mental HRQOL between IBD and healthy control participants?
3. Are levels of resilience different between IBD and healthy control participants?
4. Are physical activity levels (energy expenditure, time in sedentary behavior, and time in moderate-vigorous physical activity) different between IBD and healthy control participants?
5. Are physical activity levels related to HRQOL in IBD participants?
6. Are levels of resilience related to HRQOL in IBD participants?
7. Do resilience and physical activity have more of an effect on one aspect of HRQOL, (i.e. psychological functioning), than the other aspects in IBD participants?

8. Do resilience mediate the relationship between physical activity and HRQOL in IBD participants?

Hypotheses.

1. Both the 10-item and 25-item CD-RISC survey will be a valid representation of resilience in IBD participants
2. IBD participants will report lower overall scores of HRQOL on the Short Form-36 when compared to healthy control participants.
3. IBD participants will report different levels of resilience on the CD-RISC when compared to healthy control participants.
4. IBD participants will report similar levels of physical activity on the short-form International Physical Activity Questionnaire when compared to healthy control participants.
5. Physical activity levels will be correlated with levels of HRQOL in IBD participants.
6. Resilience levels will be correlated with levels of HRQOL in IBD participants.
7. Resilience levels will be correlated with mental functioning for HRQOL, whereas physical activity levels will be correlated with levels of physical functioning for HRQOL in IBD participants.
8. Physical activity levels will be correlated with levels of HRQOL, and resilience levels will mediate this relationship.

Independent and dependent variables.

The independent variables will include the two groups of participants, (i.e. IBD and healthy control participants).

The dependent variables will include:

- Overall HRQOL
- Physical health component of HRQOL
- Mental health component of HRQOL
- Total physical activity
- Time in sedentary behavior
- Time in moderate-vigorous physical activity
- Resilience

Delimitations and Limitations

Delimitations of the current study include the geographical location of participants, (i.e. the United States, United Kingdom, and Canada), as well as being limited to English-speaking patients with IBD or healthy controls. Data collection is also limited to online survey responses.

A major limitation within the present study were the measures being collected. Physical activity was being measured through the short-form International Physical Activity Questionnaire, a validated instrument, but as with all survey instruments is known to overestimate physical activity in comparison to objective measures such as pedometers or accelerometers. Similarly, resilience and HRQOL are both latent constructs and thus we are measuring them through instruments rather than direct measures.

Definitions

Cytokine – A cytokine is a protein that is released by cells and has a specific effect on the communication, interaction, or behavior of cells. Cytokines include interleukin-6 and tumor necrosis factor-alpha which trigger an inflammatory response in cells.

Extraintestinal Manifestations – Extraintestinal manifestations are symptoms and diseases associated with IBD that occur outside of the gastrointestinal tract and can include but are not limited to osteoporosis, anemia, ankylosing spondylitis, psoriasis, arthritis, and chronic fatigue syndrome.

Fistulas – A fistula is an abnormal connection between an organ, vessel, or other structure. Usually fistulas occur in the wall of hollow/tubular organs. In particular in IBD, fistulas occur in intestinal wall connecting one loop of the intestine to another or to the surface or skin.

Host Immune Response – The host immune response is the response of the immune system of the individual in reaction to a foreign substance, (i.e., antigen).

Monozygotic Twin Concordance Rates – Monozygotic twins are twins that are derived from one zygote and developed into two independent growing cells and thus two individuals of the same sex and genetic construction. Concordance refers to the probability of a certain characteristic being present in a pair of individuals, given that one of the pair has the characteristic. Therefore, monozygotic twin concordance rates are the probability of IBD occurring in a monozygotic twin if the other twin already has the disease.

Skip Lesions – A skip lesion is inflammation of the intestines that is patchy and misses areas that are left unharmed.

Strictures – A stricture of the intestine, also known as a stenosis, is a narrowing of the intestine or any part of the gastrointestinal tract. Severe strictures can cause a blockage of the intestines and often lead to scarring of the tissue.

Transmural Inflammation – Transmural inflammation means that the inflammation occurs along the entire thickness of the intestinal wall, leading to thickening of the wall. Transmural inflammation is common in Crohn's disease, whereas in ulcerative colitis the inflammation is only present in the mucosal layer of the intestine.

Chapter Two: Literature Review

Inflammatory bowel disease (IBD) is a term used to describe a group of diseases that occur in the gastrointestinal tract, including Crohn's disease and ulcerative colitis. Prevalence estimates of IBD include approximately 1.4 million people in the United States (Molodecky et al., 2012) and 2.2 million people in Europe (Loftus, 2004), with more than 600,000 people in the United Kingdom (Crohn's and Colitis UK, 2014). Canada has the highest prevalence of IBD with 1 in every 150 people currently living with the disease (Crohn's and Colitis Foundation of Canada, 2012), with no real understanding of the underlying cause of these diseases. The occurrence of IBD has increased in Europe and the United States in the latter part of the 20th century with it becoming more common in the rest of the world as other countries begin to adopt a more Western lifestyle (Loftus, 2004).

Ulcerative colitis and Crohn's disease are both relapsing and remitting disorders characterized by chronic inflammation of the gastrointestinal tract, in particular the distal ileum and/or the colon (Podolsky, 2002; Shanahan, 2012). Although both ulcerative colitis and Crohn's disease are collectively referred to as IBD, the two diseases have been shown to be distinct and histopathologically different from one another but share many of the same signs and symptoms (Lennard-Jones, 1989; Podolsky, 2002). Ulcerative colitis was the initial sub-classification of IBD to be considered as a distinct entity. It was first termed as ulcerative colitis in 1859 by Sir Samuel Wilks and was further accepted as a disease by the Royal Society of Medicine in London in 1909 (Mulder et al., 2014).

Ulcerative colitis is a disease of mucosal inflammation that is limited to the colon with symptoms such as bloody diarrhea, rectal tenesmus, and abdominal discomfort (Kornbluth & Sachar, 2010). Over the last half of the century there have been more than a thousand articles

published that have studied the immunology and biology of ulcerative colitis. The most predominant theory of the cause of ulcerative colitis is an autoimmune reaction following a immunological response to unknown bacteria in the colon (Hanauer, 2004). Furthermore, it has been found that the cytokine tumor necrosis factor alpha (TNF-alpha) plays a major role in the ulcerative colitis inflammatory process (Mulder et al., 2014).

In 1932, Crohn's disease was recognized as separate disease to ulcerative colitis (Crohn, Ginzburg, & Oppenheimer, 1932). Crohn's disease is described as a disease of transmural inflammation with skip lesions involving any part of the gastrointestinal tract from 'gum-to-bum' (Mulder et al., 2014). Crohn's disease often results in the formation of fistulas and strictures within the bowel or bladder (Bernstein et al., 2006; Bilski, Mazur-Bialy, Wierdak, & Brzozowski, 2013; Carter, Lobo, & Travis, 2004). Recent research has suggested that pro-inflammatory cytokines interleukin-6 (IL-6) and TNF-alpha are related to the intestinal inflammation that is inherent to Crohn's disease (Lee, Radford-Smith, & Taaffe, 2005). This relationship is less understood than with ulcerative colitis possibly due to the transmural nature of the inflammation in Crohn's disease.

It is commonly accepted in the IBD literature that a combination of environmental factors and a genetic predisposition lead to the development of Crohn's disease or ulcerative colitis (El Sayed, 2013; Narula & Fedorak, 2008). It is believed that the immunological response that occurs in the gastrointestinal tract results from an excessive host immune response towards the gut microbiota in genetically susceptible individuals (Leone, Chang, & Devkota, 2013). Recent studies have discovered an increase in IBD prevalence in different ethnicities, (i.e. Asian populations), that are adopting a Western lifestyle (Zhou, Ren, Irvine, & Yang, 2009). A parallel 33% decrease in the percentage of identical twins both being

diagnosed with IBD (monozygotic twins concordance rates) (Cosnes, Gower-Rousseau, Seksik, & Cortot, 2011), suggests that environmental factors play an increasing role in the pathogenesis of the disease, rather than a reliance of genetic predisposition.

Disease onset can occur at any age and is known to typically peak between the ages of 15 and 30 years. Another peak in disease onset occurs later in life at 50 – 70 years of age (Andres & Friedman, 1999; Bernstein et al., 2006; Hanauer, 2006). With the lack of a known cure the onset of this disease at such a young age can cause lifelong illness (Carter et al., 2004). The disease can be further complicated by resultant weight loss, surgical interventions, medical therapies, and the diagnosis of extraintestinal manifestations (Otto et al., 2012). Extraintestinal manifestations are symptoms or problems that occur outside of the intestines such as osteoporosis, ankylosing spondylitis, and anemia (Bi & Triadafilopoulos, 2003). The major symptoms of IBD are diarrhea, abdominal pain and cramping, gastrointestinal bleeding, reduced appetite and malnutrition, weight loss, and fatigue all of which can significantly impact the life of patients with this disease (Casati & Toner, 2000; Husain & Triadafilopoulos, 2004; Sewitch et al., 2001).

de Rooy et al. (2001) surveyed IBD patients and found that concerns about loss of bowel control, production of unpleasant odors, feeling dirty or smelly, and issues with sexual relationships were ranked as the highest concerns for both ulcerative colitis and Crohn's disease. Furthermore, a high number of symptoms have been reported in IBD with 69% of patients reporting symptoms flare-ups at least every few months, while 75.6% of patients have reported that symptoms affect their ability to enjoy leisure activities (Ghosh & Mitchell, 2007). Due to the cyclical nature of the disease, IBD is characterized by a series of exacerbations followed by periods of remission, with 25 – 50% of patients relapsing within 12

months (Husain & Triadafilopoulos, 2004; Sewitch et al., 2001). In order to reduce the symptom impact of IBD, many patients participate in complex medical therapies, including steroids, immunosuppressants, and anti-inflammatory medications (Otto et al., 2012). Surgical interventions are also common in both ulcerative colitis (20 – 30% of patients) and Crohn's disease (70 – 80%) (Carter et al., 2004).

With the high prevalence of IBD in Western countries such as the United States, United Kingdom, and Canada, and no currently known cure for this debilitating disease, the primary therapeutic goal is to induce long-term remission. Furthermore, it has been recognized that even in long-term remission, patients may not be asymptomatic or enjoy a high health-related quality of life (HRQOL). In fact, it is suggested that HRQOL is reduced in symptomatic patients and those who are in remission (Martin, Leone, Fries, & Naccarato, 1995; Naliboff et al., 2012).

Health-related Quality of Life and Inflammatory Bowel Diseases

Injury to the gut wall and subsequent symptoms of distress significantly impact on the HRQOL of IBD patients (Casati & Toner, 2000; Husain & Triadafilopoulos, 2004; Sewitch et al., 2001). The cyclical nature of IBD, partnered with the long-term complications of the disease, as well as the emotional and social burdens can have a negative impact for patients on a number of different levels (Casellas, Lopez-Vivancos, Casado, & Malagelada, 2002). One of the most commonly recognized levels is HRQOL (Moradkhani et al., 2013).

HRQOL has been defined as a multidimensional concept, which incorporates the physical, emotional, and social features of health perception and functioning (Irvine, 1997; van der Eijk, Stockbrugger, & Russel, 2000). In IBD patients there are a number of factors

that negatively affect HRQOL including abdominal discomfort, rectal bleeding, diarrhea, fecal urgency, impaired appetite, need for long-term medication use, and hospitalization or surgery (van der Eijk et al., 2000). Therefore it is not surprising that patients with IBD have been reported to experience poor HRQOL in comparison to healthy controls (Verma, Tsai, & Giaffer, 2001).

Moradkhani et al. (2013) found that individuals with IBD who reported high perceived stress, low perceived social support, and a high number of previous relapses, and who were female reported low HRQOL scores. Previous research has also found that clinical symptoms, severity of disease, surgical intervention, disease recurrences per year, and extraintestinal manifestations are consistently associated with HRQOL in IBD (Casellas, Lopez-Vivancos, Badia, Vilaseca, & Malagelada, 2000; Casellas, Lopez-Vivancos, Vergara, & Malagelada, 1999; Hjortswang et al., 2003). Furthermore, HRQOL can be influenced by socio-demographic, clinical, psychological, and treatment-related factors (Cohen, 2002; Sainsbury & Heatley, 2005).

Cohen (2002) found that HRQOL was impaired in Crohn's disease patients with clinically active disease. Furthermore, disease activity and surgical interventions were negatively correlated with HRQOL (Cohen, 2002). In addition, others have consistently shown that the HRQOL of patients with clinically active IBD was significantly lower in comparison to the HRQOL of those IBD patients in remission (Andersson, Olaison, Bendsten, Myrelid, & Sjodahl, 2003; Bernklev et al., 2005, 2006; Casellas, Lopez-Vivancos, Badia, Vilaseca, & Malagelada, 2001; Casellas et al., 2002; Guthrie et al., 2002; Zhou et al., 2009).

With the knowledge that HRQOL is diminished in patients with IBD, the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) was established in 1995.

The EFCCA has the goal to improve the well-being of patients with IBD and their partners and families. One of the most important aspects of the mission of the EFCCA is the promotion of improving HRQOL for IBD patients. It has been discussed that a patient's coping strategy and response to the stressors of IBD may be an important determinant of HRQOL as well as psychiatric comorbidity and disability (McCombie, Mulder, & Gearry, 2013), suggesting that the work of EFCCA and current research in this field is of utmost importance to improving the lives of people with IBD.

The research into the predictors of HRQOL in IBD and the solutions to the impaired HRQOL is somewhat sparse (Moradkhani et al., 2013). However, throughout all chronic diseases, the management of HRQOL is becoming increasingly important as a treatment goal. Research by van der Have et al. (2014) found that HRQOL was consistently impaired in Crohn's disease patients by work disability, increased disease activity, number of relapses, and hospitalization rates; however medical therapies were significantly associated with an improved HRQOL. In a cohort of Crohn's disease patients, 57.5% of patients had undergone surgical treatment with 87% of these patients reporting that their HRQOL improved following surgery (Ghosh & Mitchell, 2007). However, it is interesting to note that 69.3% experienced a recurrence of symptoms and more than a quarter of patients experienced serious complications which negatively impacted HRQOL (Ghosh & Mitchell, 2007). These findings suggest that HRQOL is not a fixed concept but instead changes depending on the status of the patient. In another study, patients with ulcerative colitis were reported to have a median postoperative bowel frequency of six stools per 24-hour period (Daperno et al., 2004). Also at least 10% of patients need one or more additional surgeries for treatment and complications

(Daperno et al., 2004), suggesting that surgical interventions may not be the most effective therapy to enhance an IBD patient's HRQOL.

It seems that following a diagnosis of IBD, there is a general level of acceptance by patients and physicians that the diagnosis will have a negative impact upon patients' lives (Ghosh & Mitchell, 2007). This often has a significant impact on the mental health of patients with IBD, particularly in terms of diagnoses of depression and anxiety (Bitton et al., 2003; Levenstein et al., 2000). There is also research suggesting that long-term perceived stress and symptoms of depression increase with disease-activity and risk of relapse (Bitton et al., 2003; Levenstein et al., 1993, 2000; Mittermaier et al., 2004), associated with the cyclical nature of the disease. The measurement of HRQOL in IBD patients allows researchers and/or physicians to reflect on the patient's perception of their health and quantify the broader impact of the disease and/or therapy upon patients' lives, as well as providing guidance for the management of the disease (Zahn, Hinz, Karner, Ehehalt, & Stremmel, 2006).

The ability to address perceived psychological factors associated with mental health in IBD is important for two main reasons: (1) to decrease the impact of the illness on HRQOL—and (2) to decrease the effects of the illness on treatment compliance and health care utilization (Kennedy et al., 2004; Waters, Jensen, & Fedorak, 2005). This highlights the importance of finding an approach to improve HRQOL in patients with IBD. A number of studies have evaluated non-pharmacological treatment approaches to improve mental well-being and HRQOL in patients with IBD (Keller et al., 2004; Kennedy et al., 2004; Larsson et al., 2003; Maunder & Esplen, 2001; Waters et al., 2005), including physical activity (Ng et al., 2007). Physical activity may be an effective coping strategy for patients with IBD to improve their HRQOL, particularly when considering the relationship in terms of the

Common Sense Model of Illness (McCombie et al., 2013). The Common Sense Model of Illness proposes that a sick person's psychological outcomes (i.e. HRQOL, anxiety, depression), will be predicted by several factors, such as disease severity, illness perceptions, and coping styles (McCombie et al., 2013). Coping in the Common Sense Model of Illness aims to diminish the physical, emotional, and psychological burden linked to chronic illness (Snyder, 1999), and can help to reduce or even eliminate the distress caused by the preceding factors in the model, (i.e. disease activity and illness perceptions) (Knowles, Wilson, Connell, & Kamm, 2011; McCombie et al., 2013). It is possible that physical activity may be able to act as a suitable coping strategy for patients with IBD in order to diminish the illness perceptions or even the disease severity; however there is a paucity of research in this area.

Physical Activity and Inflammatory Bowel Diseases

The current exercise guidelines for patients with IBD are lacking due to the barriers to exercise that these patients face. Additionally, there is a paucity of data on the type and amount of physical activity that is beneficial for IBD patients. Ball (1998) produced guidelines for IBD patients, suggesting 20 to 60 minutes of aerobic activity for two to five days per week, and resistance training at least twice per week; however these guidelines were based on the benefits of exercise for the general population. The British Society of Gastroenterology developed general guidelines for IBD patients to address complications such as osteoporosis. The guidelines advise patients to participate in at least some physical activity and engage in active sports, such as soccer, fencing, and even football, to provide additional benefits (Scott, Gaywood, & Scott, 2000). However, it is difficult to make more detailed recommendations due to the unpredictable, changing nature of the disease, the

symptoms associated with the disease, (i.e. pain, fatigue, and fecal incontinence) (Martin, 2011), and the minimal amount of research in this area. It has been suggested that low to moderate physical activity is safe (Martin, 2011; Packer et al., 2010) and beneficial in IBD patients (Narula & Fedorak, 2008). It is thought that exercise may also help prevent IBD comorbidities such as colon cancer (Sellar & Courneya, 2011), with recent research estimating that 5.3% of all colon cases in the UK were due to physical inactivity (Parkin, 2011).

There is some data to support that physicians do not recommend exercise to IBD patients due to the fear of symptom exacerbation (Ng et al., 2007); however there is no evidence to support exacerbation of symptoms with light to moderate exercise in IBD patients (Nathan, Norton, Czuber-Dochan, & Forbes, 2013). This belief stems from healthy people engaging in endurance exercise, such as marathon running, as there can be a number of gastrointestinal issues, including nausea, gastric bleeding and ischemia, and 'runners trots', which would all be detrimental to people with IBD (Sullivan & Wong, 1992). On the contrary, there is some anecdotal evidence showing that IBD patients are able to participate in high-intensity, competitive sport, such as American football, rowing, soccer, and rugby. This suggests that there is the possibility for people with IBD to participate in physical activity without exacerbating symptoms, and patients may even be able to participate safely in high-intensity exercise; however, the research has not thoroughly investigated the safety and benefits of exercise in this population.

In the last decade, the potential benefits of physical activity on disease severity and HRQOL in IBD patients have been investigated; however, there is still very little data. Mack, Wilson, Gilmore, & Gunnell (2011) found that only one in four IBD patients engage in

recommended physical activity levels to achieve health benefits. The most commonly reported activities in this cohort were walking and gardening with smaller proportions of both Crohn's disease and ulcerative colitis patients engaging in recommended physical activity levels (17.9% and 21% respectively), than healthy controls (24.1%) (Mack et al., 2011). This lack of physical activity is unsurprising with the notion that IBD patients have a reduced capacity for exercise. Exercise capacity is reduced in pediatric IBD patients (Ploeger et al., 2011), and research has shown similar findings in adult patients with Crohn's disease (Otto et al., 2012). With a reduced exercise capacity and lack of physical activity, there has been no evidence to suggest that sedentary behavior is advised (Nathan et al., 2013).

Research suggests that acute exercise does not cause symptom exacerbation in IBD patients. D'Inca et al. (1999) investigated the effects of a bout of physical activity on symptom exacerbation and disease status in IBD patients. IBD patients and healthy controls participated in a single 60-minute cycling session. The researchers found that there was no change in intestinal permeability in either group, and no exacerbation of disease status was observed in the IBD patients (D'Inca et al., 1999). Likewise, Ng et al. (2007) found that acute aerobic activity performed between 40 and 60% of maximal oxygen consumption does not have a significant effect on intestinal permeability. Research has also suggested that patients with Crohn's disease can walk an average distance of 3.5 km without experiencing any exacerbation of symptoms (Loudon, Corroll, Butcher, Rawsthorne, & Bernstein, 1999). Recently, a study by Ploeger et al. (2012) has provided promising research into the tolerance of acute physical activity in pediatric patients with Crohn's disease. It was concluded that neither moderate exercise or high-intensity interval training caused significant increases in immune markers or cytokine responses, and did not lead to any symptom exacerbation

suggesting that both moderate and high-intensity interval training may be safe exercise in patients with Crohn's disease (Ploeger et al., 2012).

Much of the research in the field of chronic physical activity and IBD has focused on the effects of physical activity on HRQOL and extraintestinal manifestations. Loudon et al. (1999) found that pre- and post- measures of HRQOL and stress levels were significantly improved in IBD patients following a 3-month walking program. Loudon et al. (1999) found significant improvements in HRQOL in patients with mild-activity or in-remission Crohn's disease following a 3-month walking program (three times per week at 60% of maximal heart rate), in comparison to a non-exercising control group. Elsenbruch et al. (2005) conducted a mind-body intervention, which included an exercise component, in a cohort of patients with ulcerative colitis. Findings indicated significant improvements in HRQOL, particularly mental health and psychological functioning, in comparison to the control group. A randomized, controlled study examined the effects of a 12-month, low-impact exercise program on bone mineral density in a cohort of patients with Crohn's disease. Exercise significantly increased bone mineral density in the hip and spine of patients with Crohn's disease in comparison to the control group (Robinson et al., 1998).

Regular physical activity is known to provide important health benefits to all of those who engage in the recommended guidelines. These health benefits are largely due to the reduction in risk of cardiovascular diseases, development of healthy bones and muscles, and the positive effects on anxiety and depression. Yet the benefits of exercise on the gastrointestinal system are still unclear. Exercise is believed to improve chronic constipation and has also been shown to be protective against colorectal cancer; however, it may cause nausea, diarrhea, abdominal cramps, and gastrointestinal bleeding (Sullivan & Wong, 1992).

Research into the benefits of physical activity for IBD patients shows positive attributes, with the ability to improve HRQOL, and reduce the negative impact of extraintestinal manifestations, such as osteoporosis and anxiety/depression. The research has also shown that physical activity does not exacerbate the severity of the disease or its symptoms, though there is still a paucity of data in this area. In summary, light to moderate physical activity can improve fitness in IBD patients as well as improving HRQOL, particularly the psychological aspects, without exacerbating the disease itself. However there are still many unanswered questions with regards to the ability of IBD patients to tolerate higher intensities of exercise and the potential benefits this may have on HRQOL (Bi & Triadafilopoulos, 2003).

Resilience and Inflammatory Bowel Diseases

It is accepted that individuals with IBD have a diminished HRQOL and one of the main treatment goals for these patients is to increase HRQOL. A developing psychological construct in the literature is resilience and the effect it can have on chronic illness and disease. Resilience is the ability to 'bounce-back' from adversity, overcome challenges, and is associated with positive growth (Earvolino-Ramirez, 2007). Resilience refers to an individual's capacity to maintain psychological and physical well-being in the face of adversity (Yi et al., 2008). Current research details resilience as a multi-dimensional construct including variables such as temperament and personality (Campbell-Sills, Cohan, & Stein, 2006). Connor & Davidson (2003) also personalized the concept of resilience by describing it as the individual qualities that enable one to thrive in the face of adversity and a measure of coping ability. Resilience has begun to receive interest from policy and practice in relation to

its potential influence on health, well-being and HRQOL (Yazdi-Ravandi et al., 2013), as well as being an important factor for the prevention of and ability to live with chronic pain (Smith et al., 2009).

Individuals who are considered to be more resilient are more likely to perceive change and stressful situations in a positive manner and as an opportunity for personal growth, whereas individuals who lack resilience are more likely to perceive stressful situations as a threat (Carver, 1998). Previous research has suggested that higher ratings of resilience have a positive effect on perceived stress and are related to positive self-ratings of physical health and symptoms in the general population (Soderstrom, Dolbier, Leiferman, & Steinhardt, 2000). Resilience has shown to be inversely related to depression and anxiety in a population of university students (Beasley, Thompson, & Davidson, 2003).

Resilience was originally investigated as a psychological construct in childhood development, particularly in the face of adversities such as child trauma and neglect (Rutter, 1985; Werner & Smith, 1992). However, more recently research has focused on the associations between resilience and mental and physical illnesses, including physical symptoms and HRQOL (Richardson, 2002). Resilience has been associated with decreased disease susceptibility, improved disease outcomes, and better treatment management in a myriad of chronic diseases, including cancer (Carver, 2005), HIV (Farber et al., 2000), cardiac disease (Kubzansky et al., 2001), and diabetes (Yi et al., 2008). Findings from a longitudinal study with cardiovascular disease patients indicated a positive correlation between indicators of resilience (e.g., positive life orientation) and recovery from the disease (Agarwal, Dalal, Agarwal, & Agarwal, 1995). In another study, self-care self-efficacy, a closely linked trait to resilience, was investigated and found to be significantly and positively

correlated with HRQOL as well as being negatively correlated with depression in stroke patients (Robinson-Smith, Johnston, & Allen, 2000). A cross-sectional study of 200 patients with HIV/AIDS found that higher resilience was related to lower distress, higher perceived HRQOL in physical and mental functioning, and more positive personal beliefs (Farber et al., 2000).

Interestingly, research has been conducted on the effects of resilience in patients with type 2 diabetes showing that those with greater resilience had significantly better diabetes self-management, hemoglobin-A1C levels, total cholesterol, and blood pressure measurements (Steinhardt et al., 2009). Furthermore, Navuluri (2000) found that physical activity was correlated with health-related resilience in men and attitudes toward treatment compliance in women with diabetes in a cross-sectional study of 155 patients. Robottom et al. (2012) also found that resilience in Parkinson's disease was significantly associated with less disability, improved HRQOL, and reduced non-motor symptoms but not disease severity in this cohort.

This research suggests that resilience and its associated factors may be a positive adaptation for patients with chronic diseases in terms of physical and mental health, as well as their disease management. Currently, there is no research into the levels of resilience exhibited by IBD patients, nor is there any research into the disease severity of those patients with higher or lower levels of resilience. Research suggests that patients with irritable bowel syndrome, a functional disorder of the colon that is known to be less damaging than IBD, scored low on the resilience scale, (i.e. higher in neuroticism (Zarpour & Besharat, 2011), anger and fear (Elsenbruch, 2011; Zoccali et al., 2006)). Assumptions cannot be made that IBD patients would exhibit similar levels of resilience as previous research has shown that

irritable bowel syndrome patients are more prone to catastrophize their symptoms and HRQOL in comparison to IBD patients (Seres et al., 2008). Therefore, understanding resilience and the role it may play in HRQOL in IBD is of growing importance.

In summary, with an increased prevalence of IBD throughout the Western countries, (i.e. United States, United Kingdom, and Canada), and no known cure for this gastrointestinal disease, focus should be driven towards treatment management with the goal to achieve long-term remission and an increased HRQOL for patients. Previous research suggests that patients with IBD have a decreased HRQOL in comparison to healthy populations and surgical interventions often do not improve HRQOL in the long-term, but medical therapies can have some positive influence. One possible method to improve HRQOL in IBD patients may be to have patients engage in physical activity or increase physical activity levels in those who are already active. However, there is a lack of data in this field and the few previous studies in IBD patients have limited their investigations to low to moderate physical activity. Partnered with small sample sizes and a lack of physical activity interventions, there is a need for research to determine the prevalence of physical activity in the IBD population as well as the ability to tolerate higher intensities of physical activity. Another factor thought to have potential to improve HRQOL in chronic disease patients is the psychological construct of resilience. Previous research has suggested resilience is correlated with improved HRQOL in patients with cardiovascular disease, HIV/AIDS, Parkinson's disease, and type 2 diabetes and related physical symptoms. Yet no research has investigated the relationship between resilience and IBD. Therefore, the aim of this study is to investigate the effects of physical activity and resilience on HRQOL in participants with IBD.

Chapter Three: Methodology

Study 1: Validation of the Connor-Davidson Resilience Scale (CD-RISC) in participants with IBD

Participants

Four hundred participants with a self-reported, confirmed diagnosis of IBD (ulcerative colitis or Crohn's disease) will be recruited for the current study. Participants will be between 18 and 65 years of age. All participants will be recruited through online social networking sites that have specific groups for participants with IBD, such as Crohn's and Colitis Foundation of America, Crohn's and Colitis UK, and Crohn's and Colitis Foundation of Canada. The United States, United Kingdom, and Canada will be the three geographical target areas for recruitment purposes. The University of Idaho's Institutional Review Board has certified this study as exempt and all participants will provide informed consent before participation. Participants will be asked to complete the Connor-Davidson Resilience Scale (CD-RISC), which is part of a larger survey using the online Qualtrics survey software, with the survey taking approximately 15-20 minutes to complete.

Instrumentation

The Connor-Davidson Resilience Scale (CD-RISC) is a 25-item instrument developed to measure resilience, initially in relevance to treatment outcomes for anxiety, depression, and stress reactions. It includes 25 items that represent a myriad of different resilient characteristics, (i.e. goal-setting, faith, humor, tolerance of negative affect, and patience). Participants score the survey on a 5-point Likert scale, based on their feelings over the past month, ranging from not true at all (0), rarely true (1), sometimes true (2), often true (3), and

true nearly all of the time (4). Total scores for the CD-RISC survey range from 0-100, with higher scores meaning the participants have greater resilience. Recently, Campbell-Sills & Stein (2007) have suggested that a 10-item version of the CD-RISC is a more valid instrument with an improved factor structure in comparison to the 25-item instrument. This study will determine whether the 25-item or 10-item survey is valid for participants with IBD.

The 25-item scale has been shown to have adequate internal consistency, test-retest reliability, and convergent and divergent validity in the general population and patient cohorts (Connor & Davidson, 2003). Furthermore it has been shown that the original CD-RISC instrument has adequate internal reliability (alpha=0.89) with the mean score of 80.4 and standard deviation of 12.8 in the general population (Connor & Davidson, 2003). However, since the original development of the CD-RISC, a 10-item and 2-item version have been used and established (Vaishnavi, Connor, & Davidson, 2007). More recently, Campbell-Sills & Stein (2007) have reported a reliable 10-item version of the CD-RISC that measures resilience on a unidimensional resilience scale.

Sample Size Estimates

A-priori sample size calculations were conducted to estimate an appropriate sample size for the confirmatory factor analysis of the CD-RISC using the n:q rule, (i.e. the number of observations in relation to the number of items), which should be at least 5:1 (Kline, 2010). The CD-RISC has 25 observations and therefore 125 observations from the IBD participant cohort is required for adequate power.

Statistical Analyses

Data will initially be screened for multicollinearity and multivariate outliers. Confirmatory factor analyses will be used to determine whether a 25-item or 10-item CD-RISC scale is a better representation of resilience in IBD participants. The confirmatory factor analysis component of structural equation modeling (SEM) produces the strongest combination of individual variables, (i.e. items), in each category to form a latent variable such as resilience.

Goodness of fit will be evaluated using the root mean square error of approximation (RMSEA) and the associated 90% confidence interval. C-Fit, the p-value for test of close fit that estimates the probability that RMSEA<0.05, and comparative fit index (CFI) will also be used to identify goodness of fit in the analyses. The chi-square test will be used in addition to other measures of fit. Each of these fit indices provides different information in regards to model fit with the combination providing a reliable and conservative evaluation of model fit (Jaccard & Wan, 1995). For confirmatory factor analysis, the final acceptance or rejection of the two models will be based on: (1) conventional criteria for good model fit (RMSEA < 0.08, C-Fit, 90% confidence interval <0.08; CFI >0.90); (2) the strength of the parameter estimates, (i.e. factor loadings >0.40 and absence of prominent cross-loadings); and (3) the ability to interpret the solution on a conceptual level.

All confirmatory factor analyses will be conducted with the sample variance-covariance matrices being analyzed using the latent variable software program, AMOS 20.0. All data will be prepared and screened using the statistical software package, SPSS 24.0.

Study 2: Resilience and physical activity as predictors of HRQOL in participants with IBD

Participants

Four hundred participants with a self-reported, confirmed diagnosis of IBD (ulcerative colitis or Crohn's disease) will be recruited for the current study. Participants will be between 18 and 65 years of age. All participants will be recruited through online social networking sites that have specific groups for participants with IBD, such as Crohn's and Colitis Foundation of America, Crohn's and Colitis UK, and Crohn's and Colitis Foundation of Canada. The United States, Great Britain, and Canada will be the three geographical target areas for recruitment purposes.

Two hundred and fifty healthy control participants will also be recruited. All participants will be between 18 and 65 years of age and will be free from any cardiovascular, metabolic, renal, or pulmonary disease. Participants will be recruited through academic institutions in the United States, Great Britain, and Canada via an email and link to the survey.

The University of Idaho's Institutional Review Board has certified this study as exempt and all participants will provide informed consent before participation. Once provided with the necessary instructions, each participant will be asked to complete the online survey that includes the Short Form-36 (SF-36), the International Physical Activity Questionnaire-Short Form (s-IPAQ), and the Connor-Davidson Resilience Scale (CD-RISC), as well as demographic information. The survey will be developed using the online Qualtrics survey software and will take approximately 15-20 minutes to complete. Following the survey, the first one hundred participants will be provided with a $5 Amazon gift card.

Instrumentation

Demographics.

Demographic survey questions will include age, sex, and health insurance availability. These basic demographic variables are in addition to IBD-specific questions such as diagnosis, history of diagnosis, and previous and current medical treatment information, (i.e. previous surgical intervention and current drug therapies). These variables will be used as covariates in the analyses.

HRQOL.

HRQOL will be measured by the SF-36 which was designed to assess functional status, well-being, and general perception of health and is a widely accepted generic, multidimensional, instrument. The instrument consists of 36 questions that represent eight subscales: physical functioning, bodily pain, vitality or energy level, social functioning, mental health, general health perceptions, role limitation because of physical problems, and role limitation because of personal or emotional problems. Scores will be calculated for overall HRQOL, physical health, and mental health.

SF-36 individual scales are scored on a range from 0-100, where 0 indicates the lowest rating of HRQOL and 100 indicating the highest HRQOL. Reliability of the SF-36 has been shown to exceed the recommended 0.70 standard (Tsai, Bayliss, & Ware, 1997), with reliability estimates for physical and mental summary scores often exceeding 0.90 in the general population (Ware, Gandek, & IQOLA Project Group, 1994). Furthermore, the SF-36 has been successfully validated in participants in the US and other countries, as well to diseased populations (McHorney, Ware, Rogers, Raczek, & Lu, 1992; Ware, Snow, Kosinski, & Gandek, 1993).

Internal consistency, measured with Cronbach's alpha, for the SF-36 in IBD patients has been found to range from 0.72 to 0.90 in patients with Crohn's disease and from 0.74 to 0.91 in patients with ulcerative colitis (Bernklev et al., 2005). Intraclass correlations ranged from 0.56 to 0.89 in Crohn's disease patients with no significant difference between test and retest (Bernklev et al., 2005). The SF-36 with ulcerative colitis patients showed an intraclass correlation of 0.63 to 0.92 with statistically significant differences through repeat testing for bodily pain and physical functioning but none of the other dimensions (Bernklev et al., 2005). Scores for overall HRQOL, physical health, and mental health will be used as dependent variables in the analyses.

IBD questionnaire.

The IBD-Questionnaire (IBDQ) will be utilized with the IBD participants to assess disease-specific quality of life. The IBDQ is formed by 32 items with four domains: bowel symptoms, systemic symptoms, social, and emotional aspects. All questions are presented on a Likert scale with 1 being the lowest rating of quality of life and 7 being the highest rating of quality of life. The total score ranges from 32 to 224 with higher scores representing better quality of life (Guyatt, Deyo, Charlson, Levine, & Mitchell, 1989; Mitchell et al., 1988). Intraclass correlations conducted on the English adaptation of the IBDQ ranged from 0.73 to 0.93 in a cohort of patients with IBD over a 4-week period (Han, McColl, Steen, Barton, & Welfare, 1998). Furthermore, the IBDQ dimensions showed high internal validity with Cronbach's alpha values ranging from 0.72 to 0.89 with the internal validity being similar whether the instrument was interviewer- or self-administered (Han et al., 1998). Total score and subscale scores (bowel, systemic, social, and emotional) will be used as moderator variables in the analyses.

Physical activity.

The IPAQ was developed in 1998 to facilitate the surveillance of physical activity and has become the most widely used physical activity questionnaire (van Poppel, Chinapaw, Mokkink, van Mechelen, & Terwee, 2010). The s-IPAQ contains 7 items in which participants record their activity at various intensity levels: 1) vigorous-intensity activity, 2) moderate-intensity activity, 3) walking, and 4) sitting. Energy expenditure (MET-minutes/week), time spent in sedentary activity, and time spent in moderate-vigorous physical activity will be calculated and reported. These variables will be used as dependent variables in the analyses.

The s-IPAQ has been used in several countries to assess the population prevalence of physical activity in participants aged between 18 and 65 years (Craig et al., 2003). Previous research has reported that typical s-IPAQ correlations are ~0.80 for reliability and 0.30 for criterion validity (when compared to accelerometer data) (Craig et al., 2003). These results for reliability and validity are at least as good as other established self-report physical activity instruments (Kaleth, Ang, Chakr, & Tong, 2010; Mannerkorpi, 2005).

Resilience.

The CD-RISC factor structure that will be used for the purpose of the analysis of this portion of the study will depend on the results from the confirmatory factor analyses (study 1).

The CD-RISC is a 25-item instrument developed to measure resilience, initially in relevance to treatment outcomes for anxiety, depression, and stress reactions. It includes 25 items that represent a myriad of different resilient characteristics, (i.e. goal setting, faith, humor, tolerance of negative affect, and patience). Participants score the survey on a 5-point

Likert scale, based on their feelings over the past month, ranging from not true at all (0), rarely true (1), sometimes true (2), often true (3), and true nearly all of the time (4). Total scores for the CD-RISC survey range from 0-100, with higher scores meaning greater resilience.

The 25-item scale has been shown to have adequate internal consistency, test-retest reliability, and convergent and divergent validity in the general population and patient cohorts (Connor & Davidson, 2003). Furthermore it has been shown that the original CD-RISC instrument has adequate internal reliability (alpha=0.89) with the mean score in the general population is 80.4 with a standard deviation of 12.8 (Connor & Davidson, 2003). The 10-item CD-RISC has been found to highly correlated with the original 25-item instrument (r=0.92), as well as indicating high internal consistency with a Cronbach's alpha of 0.85 (Campbell-Sills & Stein, 2007).

Sample Size Estimates

A priori sample size calculations were performed and based on the n:q rule, (i.e. the number of observations in relation to the number of items), should be at least 5:1 (Kline, 2010). The current survey has a maximum of 68 items that will be used in the model, depending on the choice of the CD-RISC. The use of 68 items suggests that a minimum of 340 participants with IBD would be required to produce adequate power to allow for model estimation and statistical inference (Kline, 2010). A general rule of thumb has also stated that no less than 400 observations should be recorded if the data are not normally distributed (Kline, 2010), and therefore a minimum of 400 observations will be collected from participants with IBD.

Statistical Analyses

All data will initially be screened for missing data, normality, and outliers, and will be dealt with accordingly. Independent sample t-tests will be used to compare IBD and healthy control participants on demographic characteristics including age, sex, health insurance availability, BMI, resilience, physical activity, and HRQOL. Pearson-product moment correlations will then be conducted to evaluate whether there are relationships between physical activity levels (total energy expenditure, time in sedentary behavior, and time in moderate-vigorous physical activity) and HRQOL (total, mental, and physical HRQOL), and resilience levels and HRQOL (total, mental, and physical HRQOL) in IBD participants. Correlations will also be conducted between physical activity levels and resilience levels in IBD participants. All preliminary data analysis and cleaning will be conducted in SPSS 24.0 with an alpha level set at 0.05.

SEM, employing AMOS 20.0, will be used as the primary method for examining the relationships among physical activity, resilience, and HRQOL in the IBD participants. Applying the methods recommended by Kline (1998), the analysis will be conducted in a two-stage model. Confirmatory factor analysis of the scales will be conducted to determine how well the individual items of each latent variable combine to represent physical activity, resilience, and HRQOL. The second part of the analysis will be SEM, which will examine the relationships between these variables in the IBD cohort.

Once the underlying structure of each measurement model is established with confirmatory factor analysis using maximum likelihood estimation, a structural equation modeling approach will be used to test the hypothesized mediation relationships. The path analysis model that will be tested is that both physical activity and resilience are hypothesized

to have a direct effect on HRQOL. Further, physical activity is also hypothesized to have an indirect effect on HRQOL with resilience mediating this relationship. This exploratory model will be evaluated in IBD participants.

Further exploratory analyses will be conducted using the subscales of the HRQOL measurement; particularly it will be of interest whether resilience has more of an impact on the psychological components, such as mental health, emotional well-being or social functioning of HRQOL. While physical activity may have more of an impact on the physiological components of HRQOL, such as bodily pain, physical functioning, and general health. In the path analysis it will also be interesting to include the different aspects of physical activity, (i.e. time in sedentary behavior), in an exploratory fashion to try and understand whether the lack of physical activity has a negative effect of HRQOL in IBD participants.

All models will be estimated using the Maximum Likelihood method. As quality of fit of SEM models are known to be highly influenced by sample size, multiple model fit indices will be utilized including chi-square, the ratio of chi-square to the degrees of freedom (CMIN/DF), the CFI, and RMSEA. For the CMIN/DF index, a value of <4.0, RMSEA <.08 and CFI >0.90 are generally considered to represent a reasonable model fit to the data.

Work Plan/Timeline

My current timeline is that I shall propose my dissertation in the middle of May, 2015. Once my dissertation has successfully passed the proposal stage, I plan to submit my IRB for revision by the end of May, 2015 with the determination to begin data collection in early June, 2015. Data collection should be complete by the middle of September, 2015. Data

cleaning and analyses will be conducted through the end of September and October, 2015 with the hope to start the writing process in November, 2015. I aim to defend my dissertation in March, 2016 of the spring semester and graduate with my Ph.D. at commencement in May 2016.

References

Agarwal, M., Dalal, A. K., Agarwal, D. K., & Agarwal, R. K. (1995). Positive life orientation and recovery from myocardial infarction. *Social Science and Medicine*, *40*(1), 125–130.

Andersson, P., Olaison, G., Bendsten, P., Myrelid, P., & Sjodahl, R. (2003). Health-related quality of life in Crohn's proctocolitis does not differ from a general population when in remission. *Colorectal Disease*, *5*(1), 56–62.

Andres, P. G., & Friedman, L. S. (1999). Epidemiology and natural course of inflammatory bowel disease. *Gastroenterology Clinics of North America*, *28*(2), 255–281.

Ball, E. (1998). Exercise guidelines for patients with inflammatory bowel disease. *Gastroenterology Nursing*, *21*(3), 108–111.

Beasley, M., Thompson, T., & Davidson, J. (2003). Resilience in response to life stress: The effects of coping style and cognitive hardiness. *Personality and Individual Differences*, *34*(1), 77–95.

Bernklev, T., Jahnsen, J., Henriksen, M., Lygren, I., Aadland, E., Sauar, J., … Moum, B. (2006). Relationship between sick leave, unemployment, disability, and health-related quality of life in patients with inflammatory bowel disease. *Inflammatory Bowel Diseases*, *12*(5), 402–412.

Bernklev, T., Jahnsen, J., Lygren, I., Henriksen, M., Vatn, M., & Moum, B. (2005). Health-related quality of life in patients with inflammatory bowel disease measured with the short form-36: Psychometric assessments and a comparison with general population norms. *Inflammatory Bowel Diseases, 11*(10), 909–918.

Bernstein, C. N., Rawsthorne, P., Cheang, M., & Blanchard, J. F. (2006). A population-based case control study of potential risk factors for IBD. *American Journal of Gastroenterology, 101*(5), 993–1002.

Bilski, J., Mazur-Bialy, A. I., Wierdak, M., & Brzozowski, T. (2013). The impact of physical activity and nutrition on inflammatory bowel disease: The potential role of cross-talk between tissue and skeletal muscle. *Journal of Physiology and Pharmacology, 64*(2), 143–155.

Bi, L., & Triadafilopoulos, G. (2003). Exercise and gastrointestinal function and disease: An evidence-based review of risks and benefits. *Clinical Gastroenterology and Hepatology, 1*(5), 345–355.

Bitton, A., Sewitch, M. J., Peppercorn, M. A., deB Edwardes, M. D., Shah, S., Ransil, B., & Locke, S. E. (2003). Psychosocial determinants of relapse in ulcerative colitis: A longitudinal study. *American Journal of Gastroenterology*, *98*(10), 2203–2208.

Campbell-Sills, L., Cohan, S. L., & Stein, M. B. (2006). Relationship of resilience to personality, coping, and psychiatric symptoms in young adults. *Behaviour Research and Therapy*, *44*(4), 585–599.

Campbell-Sills, L., & Stein, M. B. (2007). Psychometric analysis and refinement of the Connor-Davidson Resilience Scale (CD-RISC): Validation of a 10 item measure of resilience. *Journal of Trauma Stress*, *20*(6), 1019–1028.

Carter, M. J., Lobo, A. J., & Travis, S. P. L. (2004). Guidelines for the management of inflammatory bowel disease. *Gut, 53*(Suppl 5), 1–16.

Carver, C. S. (1998). Resilence and thriving: Issues, models, and linkages. *Journal of Social Issues*, *54*(2), 245–266.

Carver, C. S. (2005). Enhancing adaptation during treatment and the role of individual differences. *Cancer, 104*(Suppl 11), 2602–2607.

Casati, J., & Toner, B. B. (2000). Psychosocial aspects of inflammatory bowel disease. *Biomedical Pharmacotherapy*, *54*(7), 388–393.

Casellas, F., Lopez-Vivancos, J., Badia, X., Vilaseca, J., & Malagelada, J. R. (2000). Impact of surgery for Crohn's disease on health-related quality of life. *American Journal of Gastroenterology, 95*(1), 177–182.

Casellas, F., Lopez-Vivancos, J., Badia, X., Vilaseca, J., & Malagelada, J. R. (2001). Influence of inflammatory bowel disease on different dimensions of quality of life. *European Journal of Gastroenterology and Hepatology*, *13*(5), 567–572.

Casellas, F., Lopez-Vivancos, J., Casado, A., & Malagelada, J. R. (2002). Factors affecting health-related quality of life in patients with IBD. *Quality of Life Research, 11*(8), 775–781.

Casellas, F., Lopez-Vivancos, J., Vergara, M., & Malagelada, J. R. (1999). Impact of inflammatory bowel disease on health-related quality of life. *Digestive Diseases*, *17*(4), 208–218.

Cohen, R. (2002). The quality of life in patients with Crohn's disease. *Alimentary Pharmacology and Therapeutics, 16*(9), 1603–1609.

Connor, K. M., & Davidson, J. R. (2003). Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC). *Depression and Anxiety*, *18*(2), 76–82.

Cosnes, J., Gower-Rousseau, C., Seksik, P., & Cortot, A. (2011). Epidemiology and natural history of inflammatory bowel diseases. *Gastroenterology*, *140*(6), 1785–1794.

Craig, C. L., Marshall, A. L., Sjostrom, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., … Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. *Medicine and Science in Sports and Exercise*, *35*(8), 1381–1395.

Crohn, B. B., Ginzburg, L., & Oppenheimer, G. D. (1932). Regional ileitis: A pathologic and clinical entity. *Journal of the American Medical Association*, *99*(16), 1323–1329.

Crohn's and Colitis Foundation of America. (2014). What is Crohn's disease? Retrieved from http://www.ccfa.org/what-are-crohns-and-colitis/what-is-crohns-disease/

Crohn's and Colitis Foundation of Canada. (2012). *The impact of inflammatory bowel disease in Canada: 2012 Final report and recommendations*. Toronto, Ontario: Crohn's and Colitis Foundation of Canada. Retrieved from http://www.isupportibd.ca/pdf/ccfc-ibd-impact-report-2012.pdf

Crohn's and Colitis UK. (2014). Understanding IBD. Retrieved from http://www.crohnsandcolitis.org.uk/information-and-support/information-about-ibd/what-is-IBD

Daperno, M., Sostegni, R., Scaglione, N., Ercole, E., Rigazio, C., Rocca, R., & Pera, A. (2004). Outcome of a conservative approach in severe ulcerative colitis. *Digestive and Liver Disease*, *36*(1), 21–28.

de Rooy, E. C., Toner, B. B., Maunder, R. G., Greenberg, G. R., Baron, D., Steinhart, A. H., … Cohen, Z. (2001). Concerns of patients with inflammatory bowel disease: Results from a clinical population. *American Journal of Gastroenterology, 96*(6), 1816–1821.

D'Inca, R., Varnier, M., Mestriner, C., Martines, D., D'Ordorico, A., & Sturniolo, G. C. (1999). Effect of moderate exercise on Crohn's disease patients in remission. *Italian Journal of Gastroenterology and Hepatology, 31*(3), 205–210.

Earvolino-Ramirez, M. (2007). Resilience: A concept analysis. *Nursing Forum*, *42*(2), 73–82.

El Sayed, E. Y. (2013). Overview on inflammatory bowel disease. *Nature and Science, 11*(8), 1–8.

Elsenbruch, S. (2011). Abdominal pain in irritable bowel syndrome: A review of putative psychological, neural and neuro-immune mechanisms. *Brain Behavior and Immunity, 25*(3), 386–394.

Elsenbruch, S., Langhorst, J., Popkirowa, K., Muller, T., Luedtke, R., Franken, U., … Dobos, G. J. (2005). Effects of mind-body therapy on quality of life and neuroendocrine and cellular immune functions in patients with ulcerative colitis. *Psychotherapy and Psychosomatics*, *74*(5), 277–287.

Farber, E. W., Schwartz, J. A., Schaper, P. E., Moonen, D. J., & McDaniel, J. S. (2000). Resilience factors associated with the adaptation to HIV disease. *Psychosomatics, 41*(2), 140–146.

Frazier, L. D. (2000). Coping with disease-related stressors in Parkinson's disease. *Gerontologist, 40*(1), 53–63.

Ghosh, S., & Mitchell, R. (2007). Impact of inflammatory bowel disease on quality of life: Results of the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) patient survey. *Journal of Crohn's and Colitis, 1*(1), 10–20.

Guthrie, E., Jackson, J., Shaffer, J., Thompson, D., Tomenson, B., & Creed, F. (2002). Psychological disorder and severity of inflammatory bowel disease predict health-related quality of life in ulcerative colitis and Crohn's disease. *American Journal of Gastroenterology, 97*(8), 1994–1999.

Guyatt, G. H., Deyo, R. A., Charlson, M., Levine, M. N., & Mitchell, A. (1989). Responsiveness and validity in health status measurement: A clarification. *Journal of Clinical Epidemiology, 42*(5), 403–408.

Hanauer, S. B. (2004). Update on the etiology, pathogenesis and diagnosis of ulcerative colitis. *Nature Clinical Practice Gastroenterology and Hepatology, 1*(1), 26–31.

Hanauer, S. B. (2006). Inflammatory bowel disease: Epidemiology, pathogenesis, and therapeutic opportunities. *Inflammatory Bowel Diseases, 12*(Suppl 1), 3–9.

Han, S. W., McColl, E., Steen, N., Barton, J. R., & Welfare, M. R. (1998). The inflammatory bowel disease questionnaire: A valid and reliable measure in ulcerative colitis patients in the North East of England. *Scandanavian Journal of Gastroenterology, 33*(9), 961–966.

Hjortswang, H., Jarnerot, G., Curman, B., Sandberg-Gertzen, H., Tysk, C., Blomberg, B., … Strom, M. (2003). The influence of demographic and disease-related factors on health-related quality of life in patients with ulcerative colitis. *European Journal of Gastroenterology and Hepatology, 15*(9), 1011–1020.

Husain, A., & Triadafilopoulos, G. (2004). Communicating with patients with inflammatory bowel disease. *Inflammatory Bowel Diseases*, *10*(4), 444–450.

Irvine, E. J. (1997). Quality of life issues in patients with inflammatory bowel disease. *American Journal of Gastroenterology*, *92*(Suppl 12), 18–24.

Jaccard, J., & Wan, C. K. (1995). Measurement error in the analysis of interaction effects between continuous predictors using multiple regression: Multiple indicator and structural equation approaches. *Psychological Bulletin*, *117*(2), 348–357.

Kaleth, A. S., Ang, D. C., Chakr, R., & Tong, Y. (2010). Validity and reliability of community health activities model program for seniors and short-form international physical activity questionnaire as physical activity assessment tools in patients with fibromyalgia. *Disability Rehabilitation*, *32*(5), 353–359.

Keller, W., Pritsch, M., von Wietersheim, J., Scheib, P., Osborn, W., Balck, F., … Deter, H.-C. (2004). Effect of psychotherapy and relaxation on the psychosocial and somatic course of Crohn's disease: Main results of the German Prospective Multicenter Psychotherapy Treatment Study on Crohn's Disease. *Journal of Psychosomatic Research*, *56*(6), 687–696.

Kennedy, A. P., Nelson, E., Reeves, D., Richardson, G., Roberts, C., Robinson, A., … North-West Regional Gastrointestinal Research Group. (2004). A randomised controlled trial to assess the effectiveness and cost of a patient orientated self management approach to chronic inflammatory bowel disease. *Gut*, *53*(11), 1639–1645.

Kline, R. B. (2010). *Principles and practice of structural equation modeling* (3rd ed.). New York, NY: Guilford Press.

Knowles, S. R., Wilson, J. L., Connell, W. R., & Kamm, M. A. (2011). Preliminary examination of the relations between disease activity, illness perceptions, coping strategies, and psychological morbidity in Crohn's disease guided by the common sense model of illness. *Inflammatory Bowel Diseases*, *17*(12), 2551–2557.

Kornbluth, A., & Sachar, D. (2010). Ulcerative colitis practice guidelines in adults: American College of Gastroenterology, Practice Parameters Committee. *American Journal of Gastroenterology, 105*(3), 501–523.

Kubzansky, L. D., Sparrow, D., Vokonas, P., & Kawachi, I. (2001). Is the glass half empty or full? A prospective study of optimism and coronary heart disease in the normative aging study. *Psychosomatic Medicine*, *63*(6), 910–916.

Larsson, K., Sundberg, H. M., Karlblom, U., Nordin, K., Anderberg, U. M., & Loof, L. (2003). A group-based patient education programme for high-anxiety patients with Crohn's disease or ulcerative colitis. *Scandanavian Journal of Gastroenterology*, *38*(7), 763–769.

Lee, N., Radford-Smith, G., & Taaffe, D. (2005). Bone loss in Crohn's disease: exercise as a potential countermeasure. *Inflammatory Bowel Diseases*, *11*(12), 1108–1118.

Lennard-Jones, J. (1989). Classification of inflammatory bowel disease. *Scandanavian Journal of Gastroenterology, 24*(Suppl 170), 2–6.

Leone, V., Chang, E. B., & Devkota, S. (2013). Diet, microbes, and host genetics: the perfect sotrm in inflammatory bowel diseases. *Journal of Gastroenterology*, *48*(3), 315–321.

Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Andreoli, A., Luzi, C., … Marcheggiano, A. (2000). Stress and exacerbation in ulcerative colitis: A prospective study of patients enrolled in remission. *American Journal of Gastroenterology*, *95*(5), 1213–1220.

Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Berto, E., Luzi, C., & Andreoli, A. (1993). Development of the perceived stress questionnaire: A new tool for psychosomatic research. *Journal of Psychosomatic Research*, *37*(1), 19–32.

Loftus, E. J. (2004). Clinical epidemiology of inflammatory boerl disease: Incidence, prevalence, and environmental influences. *Gastroenterology*, *126*(6), 1504–1517.

Loudon, C. P., Corroll, V., Butcher, J., Rawsthorne, P., & Bernstein, C. N. (1999). The effects of physical exercise on patients with Crohn's disease. *American Journal of Gastroenterology*, *94*(3), 697–703.

Mack, D. E., Wilson, P. M., Gilmore, J. C., & Gunnell, K. E. (2011). Leisure-time physical activity in Canadians living with Crohn disease and ulcerative colitis: Population-based estimates. *Gastroenterology Nursing*, *34*(4), 288–294.

Mannerkorpi, K. (2005). Exercise in fibromyalgia. *Current Opinion in Rheumatology*, *17*(2), 190–194.

Martin, A., Leone, L., Fries, W., & Naccarato, R. (1995). Quality of life in inflammatory bowel disease. *Italian Journal of Gastroenterology*, *27*(8), 450–454.

Martin, D. (2011). Physical activity benefits and risks on the gastrointestinal system. *Southern Medical Journal*, *104*(12), 831–837.

Maunder, R. G., & Esplen, M. J. (2001). Supportive-expressive group psychotherapy for persons with inflammatory bowel disease. *Canadian Journal of Psychiatry*, *46*(7), 622–626.

McCombie, A. M., Mulder, R. T., & Gearry, R. B. (2013). How IBD patients cope with IBD: A systematic review. *Journal of Crohn's and Colitis*, *7*(2), 89–106.

McHorney, C. A., Ware, J. E. J., Rogers, W., Raczek, A. E., & Lu, J. F. (1992). The validitiy and relative precision of MOS short-and long-form health status scales and Dartmouth COOP charts: Results from the Medical Outcomes Study. *Medical Care*, *30*(Suppl 5), 253–265.

Mitchell, A., Guyatt, G., Singer, J., Irvine, E. J., Goodacre, R., Tompkins, C., … Wagner, F. (1988). Quality of life in patients with inflammatory bowel disease. *Journal of Clinical Gastroenterology*, *10*(3), 306–310.

Mittermaier, C., Dejaco, C., Waldhoer, T., Oefferlbauer-Ernst, A., Miehsler, W., Beier, M., … Moser, G. (2004). Impact of depressive mood on relapse in patients with inflammatory bowel disease: A prospective 18-month follow-up study. *Psychosomatic Medicine*, *66*(1), 79–84.

Molodecky, N. A., Soon, I. S., Rabi, D. M., Ghali, W. A., Ferris, M., Chernoff, G., … Kaplan, G. G. (2012). Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterology*, *142*(1), 46–54.

Moradkhani, A., Beckman, L. J., & Tabibian, J. H. (2013). Health-related quality of life in inflammatory bowel disease: Psychosocial, clinical, socioeconomic, and demographic predictors. *Journal of Crohn's and Colitis*, *7*(6), 467–473.

Mulder, D. J., Noble, A. J., Justinich, C. J., & Duffin, J. M. (2014). A tale of two diseases: The history of inflammatory bowel disease. *Journal of Crohn's and Colitis, 8*(5), 341–348.

Naliboff, B. D., Kim, S. E., Bolus, R., Bernstein, C. N., Mayer, E. A., & Chang, L. (2012). Gastrointestinal and psychological mediatory of health-related quality of life in IBS and IBD: A structural equation modeling analysis. *American Journal of Gastroenterology, 107*(3), 451–459.

Narula, N., & Fedorak, R. (2008). Exercise and inflammatory bowel disease. *Canadian Journal of Gastroenterology, 22*(5), 497–504.

Nathan, I., Norton, C., Czuber-Dochan, W., & Forbes, A. (2013). Exercise in individuals with inflammatory bowel disease. *Gastroenterology Nursing, 36*(6), 437–442.

Navuluri, R. B. (2000). Gender differences in the factors related to physical activity among adults with diabetes. *Nursing and Health Sciences, 2*(4), 191–199.

Ng, V., Millard, W., Lebrun, C., & Howard, J. (2007). Low-intensity exercise improves quality of life in patients with Crohn's disease. *Clinical Journal of Sports Medicine, 17*(5), 384–388.

Otto, J. M., O'Doherty, A. F., Hennis, P. J., Mitchell, K., Pate, J. S., Cooper, J. A., … Montogomery, H. E. (2012). Preoperative exercise capacity in adult inflammatory bowel disease sufferers, determined by cardiopulmonary exercise testing. *International Journal of Colorectal Disease, 27*(11), 1485–1491.

Packer, N., Hoffman-Goetz, L., & Ward, G. (2010). Does physical activity affect quality of life, disease symptoms and immune measures in patients with inflammatory bowel disease? A systematic review. *Journal of Sports Medicine and Physical Fitness*, *50*(1), 1–18.

Parkin, D. M. (2011). Cancers attributable to inadequate physical exercise in the UK in 2010. *British Journal of Cancer*, *105*(Suppl 2), 38–41.

Ploeger, H., Obeid, J., Nguyen, T., Takken, T., Issenman, R., de Greef, M., & Timmons, B. (2012). Exercise and inflammation in pediatric Crohn's disease. *International Journal of Sports Medicine*, *33*(8), 671–679.

Ploeger, H., Takken, T., Wilk, B., Issenman, R., Sears, R., Suri, S., & Timmons, B. W. (2011). Exercise capacity in pediatric patients with inflammatory bowel disease. *Journal of Pediatrics*, *158*(5), 814–819.

Podolsky, D. (2002). Inflammatory bowel disease. *New England Journal of Medicine*, *347*(6), 417–429.

Richardson, G. E. (2002). The metatheory of resilience and resiliency. *Journal of Clinical Psychology*, *58*(3), 307–321.

Robinson, R. J., Krzywicki, T., Almond, L., al-Azzawi, F., Abrams, K., Iqbal, S. J., & Mayberry, J. F. (1998). Effect of a low-impact exercise program on bone mineral density in Crohn's disease: A randomized controlled trial. *Gastroenterology*, *115*(1), 36–41.

Robinson-Smith, G., Johnston, M. V., & Allen, J. (2000). Self-care, self-efficacy, quality of life, and depression after stroke. *Archives of Physical Medicine and Rehabilitation*, *81*(4), 460–464.

Robottom, B. J., Gruber-Baldini, A. L., Anderson, K. E., Reich, S. G., Fishman, P. S., Weiner, W. J., & Shulman, L. M. (2012). What determines resilience in patients with Parkinson's disease? *Parkinsonism and Related Disorders*, *18*(2), 174–177.

Rutter, M. (1985). Resilience in the face of adversity: Protective factors and resistance to psychiatric disorder. *British Journal of Psychiatry*, *147*(6), 598–611.

Sainsbury, A., & Heatley, R. V. (2005). Review article: Psychosocial factors in the quality of life of patients with inflammatory bowel disease. *Alimentary Pharmacology and Therapeutics*, *21*(5), 499–508.

Scott, E. M., Gaywood, I., & Scott, B. B. (2000). Guidelines for osteoporosis in coeliac disease and inflammatory bowel disease. *Gut*, *46*(Suppl 1), 1–8.

Sellar, C. M., & Courneya, K. S. (2011). Physical activity and gastrointestinal cancer survivorship. *Resent Results Cancer Research*, *186*, 237–253.

Seres, G., Kovacs, Z., Kovacs, A., Kerekgyarto, O., Sardi, K., Demeter, P., … Tury, F. (2008). Different associations of health related quality of life with pain, psychological distress and coping strategies in patients with irritable bowel syndrome and inflammatory bowel disease. *Journal of Clinical Psychology in Medical Settings*, *15*(4), 287–295.

Sewitch, M. J., Abrahamowicz, M., Bitton, A., Daly, D., Wild, G. E., Cohen, A., … Dobkin, P. L. (2001). Psychological distress, social support, and disease activity in patients with inflammatory bowel disease. *American Journal of Gastroenterology*, *96*(5), 1470–1479.

Shanahan, F. (2012). The microbiota in inflammatory bowel disease: friend, bystander, and sometime-villain. *Nutrition Reviews*, *7*(Suppl 1), 31–37.

Smith, B. W., Tooley, E. M., Montague, E. Q., Robinson, A. E., Cosper, C. J., & Mullins, P. G. (2009). The role of resilience and purpose in life in habituation to heat and cold pain. *Journal of Pain, 10*(5), 493–500.

Snyder, L. C. R. (1999). *Coping: The psychology of what works*. Oxford: Oxford University Press.

Soderstrom, M., Dolbier, C., Leiferman, J., & Steinhardt, M. (2000). The relationship of hardiness, coping strategies, and perceived stress to symptoms of illness. *Journal of Behavioral Medicine, 23*(3), 311–328.

Steinhardt, M. A., Mamerow, M. M., Brown, S. A., & Jolly, C. A. (2009). A resilience intervention in African American adults with type 2 diabetes. *The Diabetes Educator, 35*(2), 274–284.

Sullivan, S. N., & Wong, C. (1992). Runners' diarrhea: Different patterns and associated factors. *Journal of Clinical Gastroenterology*, *14*(2), 101–104.

Tsai, C., Bayliss, M. S., & Ware, J. E. (1997). *SF-36 Health survey annotated bibliography* (2nd ed.). Boston, MA: Health Assessment Lab, New England Medican Center.

Vaishnavi, S., Connor, K., & Davidson, J. R. T. (2007). An abbreviated version of the Connor-Davidson Resilience Scale (CD-RISC), the CD-RISC2: Psychometric properties and applications in psychopharmacological trials. *Psychiatry Research, 152*(2-3), 293–297.

van der Eijk, I., Stockbrugger, R., & Russel, M. (2000). Influence of quality of care on quality of life in inflammatory bowel disease (IBD): Literature review and studies planned. *European Journal of Internal Medicine*, *11*(4), 228–234.

van der Have, M., van der Aalst, K. S., Kaptein, A. A., Leenders, M., Siersema, P. D., Oldenburg, B., & Fidder, H. H. (2014). Determinants of health-related quality of life in Crohn's disease: A systematic review and meta-analysis. *Journal of Crohn's and Colitis, 8*(2), 93–106.

van Poppel, M. N., Chinapaw, M. J., Mokkink, L. B., van Mechelen, W., & Terwee, C. B. (2010). Physical activity questionnaires for adults: A systematic review of measurement properties. *Sports Medicine, 40*(7), 565–600.

Verma, S., Tsai, H. H., & Giaffer, M. H. (2001). Does better disease-related education improve quality of life? A survey of IBD patients. *Digestive Diseases and Sciences, 46*(4), 865–869.

Warburton, D. E. R., Nicol, C. W., & Bredin, S. S. D. (2006). Health benefits of physical activity: The evidence. *Canadian Medical Association Journal, 174*(6), 801–809.

Ware, J. E., Gandek, B., & IQOLA Project Group. (1994). The SF-36 health survey: Development and use in mental health research and the IQOLA project. *International Journal of Mental Health, 23*(2), 49–73.

Ware, J. E., Snow, K. K., Kosinski, M., & Gandek, B. (1993). *SF-36 health survey: Manual and interpretation guide*. Boston, MA: The Health Institute, New England Medical Center.

Waters, B. M., Jensen, L., & Fedorak, R. N. (2005). Effects of formal education for patients with inflammatory bowel disease: A randomized controlled trial. *Canadian Journal of Gastroenterology, 19*(4), 235–244.

Werner, E. E., & Smith, R. S. (1992). *Overcoming the odds: High risk children from birth to adulthood*. Ithaca, NY: Cornell University Press.

Westerhuis, W., Zijlmans, M., Fischer, K., van Andel, J., & Leijten, F. S. S. (2011). Coping style and quality of life in patients with epilepsy: A cross-sectional study. *Journal of Neurology*, *258*(1), 37–43.

Yazdi-Ravandi, S., Taslimi, Z., Saberi, H., Shams, J., Osanlo, S., Nori, G., & Haghparast, A. (2013). The role of resilience and age on quality of life in patients with pain disorders. *Basic and Clinical Neuroscience*, *4*(1), 24–30.

Yi, J. P., Vitaliano, P. P., Smith, R. E., Yi, J. C., & Weinger, K. (2008). The role of resilience on psychological adjustment and physical health in patients with diabetes. *British Journal of Health Psychology*, *13*(2), 311–325.

Zahn, A., Hinz, U., Karner, M., Ehehalt, R., & Stremmel, W. (2006). Health-related quality of life correlated with clinical and endoscopic activity indexes but not with demographic features in patients with ulcerative colitis. *Inflammatory Bowel Diseases*, *12*(11), 1058–1067.

Zarpour, S., & Besharat, M. A. (2011). Comparison of personality characteristics of individuals with irritable bowel syndrome and healthy individuals. *Social and Behavioral Sciences*, *30*, 84–88.

Zhou, Y., Ren, W., Irvine, E. J., & Yang, D. (2009). Assessing health-related quality of life in patients with inflammatory bowel disease in Zhejiang, China. *Journal of Clinical Nursing*, *19*(1-2), 79–88.

Zoccali, R., Muscatello, M. R., Bruno, A., Barilla, G., Campolo, D., Meduri, M., … Scaffidi, M. (2006). Anger and ego-defence mechanisms in non-psychiatric patients with irritable bowel syndrome. *Digestive and Liver Disease*, *38*(3), 195–200.

Chapter Four: Manuscript One

Confirmatory Factor Analysis of the Connor-Davidson Resilience Scale in a Cohort of People with Inflammatory Bowel Disease

In preparation for publication to the Journal of Psychiatry Research

Katrina Taylor, Philip W. Scruggs, Michelle M. Wiest, Onesmo B. Balemba, Chantal A. Vella

Abstract

Inflammatory bowel disease (IBD), a group of autoimmune diseases that affect the gastrointestinal tract, is known to negatively affect a person's physical and mental health-related quality of life (HRQOL). Resilience has recently been found to be related to higher HRQOL in people with select chronic diseases. However, there is no research regarding resilience levels in people with IBD. The aim of the current study was to validate the Connor-Davidson Resilience Scale (CD-RISC) in people with IBD and to understand resilience levels in this population. Participants with IBD (n = 125) were recruited to complete an online-survey using the CD-RISC to measure resilience. Confirmatory factor analysis was used to determine whether the 25-item or the 10-item version of the CD-RISC was a better representation of resilience in people with IBD. Analyses were conducted in SPSS v24.0 and AMOS v20.0. Results from the confirmatory factor analysis showed that the 10-item CD-RISC was a better representation of resilience in people with IBD than the 25-item instrument. Scores (mean ± SD) from the 10-item instrument were 26.4 ± 6.7 for people with

IBD, which is lower than previously reported data in the general population (31.8 ± 5.4). In conclusion, the current study shows that the 10-item CD-RISC is a valid instrument for measuring resilience in people with IBD. Furthermore, resilience levels seemed to be lower in people with IBD than the general population; however, future research is warranted comparing these groups and investigating whether there is a relationship between resilience and HRQOL in this population.

Keywords: Resilience, Inflammatory Bowel Disease, Crohn's Disease, Ulcerative Colitis

Introduction

Inflammatory bowel disease (IBD) is a group of autoimmune diseases, such as Crohn's disease and ulcerative colitis, which affect the gastrointestinal tract. IBD affects 3.6 million people in Europe and the United States (Loftus, 2004; Molodecky et al. 2012), has no known medical cure, and can cause lifelong debilitating illness. IBD is commonly recognized by signs and symptoms such as weight loss, gastrointestinal bleeding, bloody diarrhea, abdominal pain, and intestinal obstructions. Furthermore, IBD is characterized by a cyclical nature with a series of exacerbations followed by periods of remission.

Previous research has suggested that patients with IBD have a decreased quality of life due to the severe nature of the disease (Moradkhani et al. 2013) and one of the main treatment goals for these patients is to increase their health-related quality of life (HRQOL). Psychological outcomes, such as quality of life, in people with IBD can be predicted by several factors, such as disease severity, illness perceptions, and coping styles (McCombie et al. 2013). The main aim of the coping mechanism is to diminish the physical, emotional, and

psychological burden that is associated with chronic disease (Snyder, 1999), and thus understanding appropriate psychological factors that can act as coping measures in people with IBD is of high importance.

A developing psychological construct in the scientific literature is resilience and the effect it can have on chronic illness and disease. Resilience is the ability to 'bounce-back' from adversity and overcome challenges (Earvolino-Ramirez, 2007). Resilience refers to an individual's capacity to maintain psychological and physical quality of life in the face of adversity (Yi et al. 2008). Connor and Davidson (2003) have also defined the concept of resilience as individual qualities that enable a person to thrive in the face of adversity and also as a measure of coping ability.

Research in the general population has shown that higher ratings of resilience have a positive effect on perceived stress and are related to positive self-ratings of physical health and symptoms (Soderstrom et al. 2000). Recently, research has begun to try and understand the relationships between resilience and mental and physical illnesses, including physical symptoms and quality of life (Richardson, 2002). Resilience has been shown to be related to decreased disease susceptibility, improved disease outcomes, and better treatment management in an array of chronic diseases, such as cancer (Carver, 2005), HIV (Farber et al. 2005), cardiac disease (Kubzansky et al. 2001), and diabetes (Yi et al. 2008). However, in many of these populations the surveys used to measure resilience (such as the Connor-Davidson Resilience Scale [CD-RISC]) have not been previously validated.

Research indicates that patients with irritable bowel syndrome, a functional disorder of the colon that is known to be less damaging than IBD, scored low on the resilience scale, with corresponding high levels of neuroticism (Zarpour and Besharat, 2011), anger, and fear

(Elsenbruch, 2005; Zoccali et al. 2006). However, to our knowledge there is no research to date that investigates the levels of resilience exhibited by people with IBD. Given that previous research has shown irritable bowel syndrome patients are more prone to catastrophize their symptoms and HRQOL in comparison to people with IBD, assumptions cannot be made that IBD patients would exhibit similar levels of resilience (Seres et al. 2008). Therefore, before undertaking research that aims to characterize resilience in people with IBD, it is important to validate the CD-RISC in this population.

The aim of the current study was to determine whether the 10-item and 25-item CD-RISC are valid in a cohort of people with IBD. A secondary aim was to understand resilience levels in people with IBD in comparison to previously published data in the general population. It was hypothesized that the single-factor structure of the 10-item CD-RISC would be more appropriate in IBD participants in comparison to the 25-item version of this instrument. It was further hypothesized that people with IBD would have lower resilience levels than those reported in the general population.

Materials and Methods

Participants.

One hundred and twenty-five participants, between the ages of 18 and 65 years, with a self-reported, confirmed diagnosis of IBD were recruited for the study. All participants volunteered as part of a larger, online survey study using Qualtrics survey software (Qualtrics LLC, Provo, Utah, USA) with the survey taking 10 - 15 minutes to complete. A random subsample of the larger sample was taken to conduct the confirmatory factor analysis.

Participants were recruited through online social networking sites and specific groups for people with IBD. Additionally, recruitment of participants for the study included ResearchMatch, a national health volunteer registry that was created by several academic institutions and supported by the US National Institutes of Health as part of the Clinical Translational Science Award (CTSA) program. ResearchMatch has a large population of volunteers who have consented to be contacted by researchers about health studies for which they may be eligible. Review and approval for this study and all procedures was obtained from the University of Idaho's Institutional Review Board and the study was performed in line with the principles outlined in the Declaration of Helsinki. Informed consent was obtained from all participants enrolled in the study.

Instrumentation.

Resilience was measured using the CD-RISC, which was originally created as 25-item instrument to measure resilience. The CD-RISC includes 25 items that represent a myriad of different resilience characteristics (i.e., goal-setting, faith, humor, tolerance of negative affect, and patience). Recently, Campbell-Sills and Stein (2007) suggested that a 10-item, single construct version of the CD-RISC is a more valid instrument with an improved factor structure in comparison to 25-item CD-RISC in the general population. Responses for the survey are measured on a 5-point Likert scale, based on the participant's feelings over the past month. Scores are recorded as not true at all (0), rarely true (1), sometimes true (2), often true (3), and true nearly all of the time (4). Total scores for the 25-item CD-RISC range from 0 - 100 and 0 – 40 for the 10-item CD-RISC, with higher scores indicating greater resilience.

Sample Size Estimates

A-priori sample size calculations were conducted to estimate an appropriate sample size for the confirmatory factor analysis of the CD-RISC using the n:q rule, (i.e., the number of observations in relation to the number of items), which should be at least 5:1 (Kline, 2010). The CD-RISC has a maximum of 25 items; therefore 125 participants with IBD were required for adequate power.

Statistical Analyses

Data were initially screened for multicollinearity and multivariate outliers. Confirmatory factor analysis, using maximum likelihood estimation, was used to determine whether the 25-item CD-RISC or the 10-item CD-RISC was a better representation of resilience in IBD participants. The confirmatory factor analysis component of structural equation modeling produces the strongest combination of items in each category to form a latent variable such as resilience.

Model 1: Measurement Model of the 25-item CD-RISC

In this model, all 25-items from the original CD-RISC were included in the measurement model in accordance with the five-factor structure previously determined (Connor and Davidson, 2003). The five factors used in the 25-item measurement model were competence, tolerance, security, control, and spiritual.

Model 2: Measurement Model of the 10-item CD-RISC

In this model, the 10-items previously suggested to represent a better overall fit of latent variable resilience were included in the measurement model (Campbell-Sills and Stein,

2007). These items reflect tolerance including illness, personal issues, and painful feelings, and they are considered a unidimensional construct of resilience.

The chi-square (χ^2) test, p-value, and the ratio of χ^2 to degrees of freedom (χ^2/df) were used to assess overall model fit of the two models. Due to the known sensitivity to sample size, additional goodness of fit statistics were evaluated including the Comparative Fit Index (CFI) and Root Mean Square Error Approximation (RMSEA). Each of these fit indices provided different, important information regarding model fit (Jaccard and Wan, 1995). The final acceptance or rejection of each of the two models was based on (i) conventional criteria for good model fit (χ^2 p-value > 0.05, RMSEA < 0.08, CFI > 0.90, χ^2/df $\leq$ 2), (ii) the strength of the parameter estimates (i.e., factor loadings > 0.40), and (iii) the ability to interpret the solution on a conceptual level.

All data were prepared and screened using the statistical software package, SPSS version 24.0 (IBM Corporation, Armonk, New York, USA). All confirmatory factor analyses were conducted with the sample variance-covariance matrices being analyzed using the latent variable software program, Analysis of Moment Structures, version 20.0 (AMOS; Arbuckle, 2011).

Results

The assumptions of multivariate normality and linearity were assessed using box plots and Mahalanobis distance. There were no univariate or multivariate outliers in the data and both the 10-item and 25-item CD-RISC were normally distributed. With no missing data, the final data set included 125 responses.

Descriptive statistics show that in the current population (age 37.2 ± 12.7 years; 54.7% in remission; 81.6% females) the mean score for the 25-item CD-RISC was 65.7 ± 13.7 (range: 32 – 98; 95% confidence interval [CI]: 63.3 – 68.1), and the mean score for the 10-item CD-RISC was 26.4 ± 6.7 (range: 9 – 39; 95% CI: 25.2 – 27.6). Previous research has shown that in the general population scores for the 25-item CD-RISC were 80.4 ± 12.8 (95% CI: 79.4 – 81.4; Connor & Davidson, 2003) and 31.8 ± 5.4 (95% CI: 31.4 – 32.2; Campbell-Sillis et al. 2009) for the 10-item CD-RISC, indicating that people with IBD have lower resilience levels than previously reported data in the general population. Means, standard deviations, and Pearson correlations for the item-total and factor-total correlations is shown in Table 4.1.

The 25-item CFA model had five latent constructs (i.e., competence, tolerance, security, control, and spiritual) and 25 observed variables. An initial test of the 25-item measurement model was not a successful fit of the data with (χ^2 (265) = 564.26, $p < 0.001$; $\chi^2/df = 2.13$; RMSEA = 0.07; and CFI = 0.83) (See Figure 4.1). The spiritual factor was not significantly correlated with three of the other four factors in the 25-item CD-RISC and displayed the weakest correlation with the overall instrument.

The 10-item CFA model had one latent construct and 10 observed variables. The 10-item CD-RISC measurement model was a satisfactory fit to the data with (χ^2 (35) = 49.41, $p = 0.05$; $\chi^2/df = 1.41$; RMSEA = 0.04; and CFI = 0.98) (See Figure 4.2). Each of the criteria for good model fit was met with the 10-item measurement model. All the factor loadings for the indicators on the latent variable were significant ($p < 0.001$). This suggests that the latent construct was well represented by its indicators. The means and standard deviations along with the item-total correlations for the 10-item CD-RISC are shown in Table 4.2.

The 10-item and 25-item models were not nested within one another as they contained different items; therefore, the Akaike information criterion (AIC) was used to determine the difference between the two models. The 25-item CD-RISC had a higher AIC (734.3) than the 10-item CD-RISC (109.4), suggesting that the 10-item CD-RISC is a better fit to the data in the current population. Additionally, Cronbach's alpha (α) for the items in the 10-item CD-RISC was 0.88 while the 25-item CD-RISC had α=0.90. Both of these values suggest good internal consistency in the instruments; however, it should be noted that the 25-item CD-RISC has more items than the 10-item instrument, which may have led to an increased Cronbach's alpha (Cortina, 1993).

Discussion

The aim of the current study was to determine whether both the 10-item and 25-item CD-RISC were valid in a cohort of people with IBD. We hypothesized that the 10-item CD-RISC with a single-factor structure would be more valid and have better model fit of the data in a cohort of IBD participants than the 25-item version of the instrument. A secondary aim of the study was to determine the level of resilience of people with IBD in comparison to previously reported data in the general population.

Following confirmatory factor analysis, the results of the 25-item CD-RISC measurement model suggest that this factor structure does not fit the data well in a cohort of people with IBD. However, confirmatory factor analysis of the 10-item CD-RISC measurement model revealed that this adequately fit the data with overall improvement in comparison to the 25-item model as indicated by the reduction in AIC. These findings are consistent with Campbell-Sills and Stein's (2007) suggestion that the 10-item CD-RISC has

an improved factor structure and psychometric properties in comparison to the 25-item CD-RISC. The ‘spiritual’ factor was observed to have low covariances with other factors in the 25-item model as well as the items representing this factor having low correlations with the total score. Therefore, the low correlations and covariances, which have also been reported in previous research (Connor and Davidson, 2003; Yu et al., 2011), may have contributed to the poor model fit for the 25-item instrument in people with IBD.

A considerable proportion of the research that has been conducted on the factor structure of the CD-RISC has found consistently that the five-factor structure does not fit the data (Campbell-Sills and Stein, 2007; Green et al. 2014; Jorgensen and Seedat, 2008; Karairmak, 2010; Lamond et al. 2008; Yu and Zhang, 2007). The 10-item CD-RISC includes items related to tolerance, competence, and security (i.e., change, personal problems, illness, pressure, failure, and painful feelings). These items are all associated with the ability to bounce back (Campbell-Sills and Stein, 2007). Due to the cyclical nature of IBD (i.e., periods of disease flare followed by periods of remission), it is not surprising that items such as illness, personal problems, and change provide good overall fit to the data in these participants.

In comparison to previously published resilience scores in the general population, people with IBD seem to score lower on resilience. With the 10-item CD-RISC, Campbell-Sills et al. (2009) found that the average resilience score in a large sample of US adults was 31.8 ± 5.4. In the current study, IBD participants reported an average score 26.4 ± 6.7, which was significantly lower than reported in the general population. Furthermore, resilience levels in our sample of people with IBD were similar to those reported in people with multiple sclerosis (Black and Dorstyn, 2015) but slightly higher than reported in patients with

fibromyalgia (Notario-Pacheco et al., 2014). It seems important to consider the role that resilience may play in the lives of people with IBD and whether this impacts HRQOL or coping mechanisms. Additionally, it would be beneficial to understand whether there are mechanisms to improve resilience in this population (e.g., through mental skills training).

To our knowledge this is the first study to determine resilience levels in participants with IBD as well as evaluate the validity of the CD-RISC in this population. Although there has been research conducted reporting the psychometric properties of the CD-RISC in a variety of different countries, there has been minimal research in different disease populations. The development of an instrument specific to resilience levels in chronic disease populations may be beneficial. Measuring resilience in people with IBD could prove beneficial in understanding the psychosocial aspect of the disease as well as people's ability to cope with the disease. It is understood that a diagnosis of IBD impacts quality of life (Moradkhani et al. 2013); however, knowledge regarding the ability to cope is weak. Future research aimed at understanding the relationship between resilience and HRQOL in people with IBD and how this compares to healthy controls is needed. Additionally, it would be beneficial to understand how resilience levels in IBD patients may change during remission in comparison to a disease flare.

Limitations within our study include that participants were a convenience sample, which limits the generalizability of our findings. However, a random sample of our total sample of participants was used in order to conduct the confirmatory factor analysis. Additionally, the cohort was mostly female which may impact the ability to generalize our findings to people with IBD. Invariance analysis should be conducted to see whether the models hold true across sexes, disease states (i.e., disease-flare versus remission), and types of

inflammatory bowel disease (i.e., Crohn's disease versus ulcerative colitis). Future research in the area of resilience and inflammatory bowel disease has the potential to benefit patients and caregivers in determining whether mental skills training, particularly involving resilience, will improve HRQOL in those with IBD.

In conclusion, the current study shows that in a population of people with IBD the 10-item CD-RISC is a valid instrument to measure resilience. Furthermore, our findings indicate the 25-item survey is not a valid measure of resilience for this sample. People with IBD may present with low levels of resilience; however, it is unknown as to whether this directly impacts HRQOL. Further research is warranted in this area and would likely be beneficial to people who suffer with IBD.

References

Arbuckle, J.L., 2011. *AMOS* (version 20.0) [Computer program]. Chicago, IL: SPSS.

Black, R., Dorstyn, D. 2015. A biopsychosocial model of resilience for multiple sclerosis. J Health Psychol. 20(11), 1434-1444.

Campbell-Sills, L., Stein, M.B., 2007. Psychometric analysis and refinement of the Connor-Davidson Resilience Scale (CD-RISC): Validation of a 10-item measure of resilience. J. Trauma Stress. 20(6), 1019-1028.

Campbell-Sills, L., Forde, D.E., Stein, M.B., 2009. Demographic and childhood environmental predictors of resilience in a community sample. J. Psychiatry Res. 4(12), 1007-1012.

Carver, C.S., 2005. Enhancing adaptation during treatment and the role of individual differences. Cancer. 104(S11), 2602-2607.

Connor, K.M., Davidson, J.R., 2003. Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC). Depress. Anxiety. 18(2), 76-82.

Cortina, J.M., 1993. What is coefficient alpha? An examination of theory and applications. J. Appl. Psychol. 78(1), 98 – 104.

Earvolino-Ramirez, M., 2007. Resilience: A concept analysis. Nurs. Forum. 42(2), 73-82.

Elsenbruch, S., Langhorst, J., Popkirowa, K., Muller, T., Luedtke, R., Franken, U., Paul, A., Spahn, G., Michalsen, A., Janssen, O.E., Schedlowski, M., Dobos, G.J., 2005. Effects of mind-body therapy on quality of life and neuroendocrine and cellular immune functions in patients with ulcerative colitis. Psychother. Psychosom. 74(5), 277-287.

Farber, E.W., Schwartz, J.A., Schaper, P.E., Moonen, D.J., McDaniel, J.S., 2000. Resilience factors associated with the adaptation to HIV disease. Psychother. Psychosom. 41(2), 140-146.

Green, K.T., Hayward, L.C., Williams, A.M., Dennis, P.A., Bryan, B.C., Taber, K.H., Davidson, J.R.T., Beckham, J.C., Calhoun, P.S., 2014. Examining the factor structure of the Connor-Davidson Resilience Scale (CD-RISC) in a post-9/11 U.S. military veteran sample. Assessment. 21(4), 443-451.

Jaccard, J., Wan, C.K., 1995. Measurement error in the analysis of interaction effects between continuous predictors using multiple regression: Multiple indicator and structural equation approaches. Psychol. Bull. 117(2), 348-357.

Jorgensen, I.E., Seedat, S., 2008. Factor structure of the Connor-Davidson Resilience Scale in South African adolescents. Int. J. Adolesc. Med. Health. 20(1), 23-32.

Karairmak, O., 2010. Establishing the psychometrics qualities of the Connor-Davidson Resilience Scale (CD-RISC) using exploratory and confirmatory factor analysis in a trauma survivor sample. J. Psychiatry Res. 179(3), 350-356.

Kline, R.B., 2010. Principles and practice of structural equation modeling (3rd ed). New York, NY: Guilford Press.

Kubzansky, L.D., Sparrow, D., Vokonas, P., Kawachi, I., 2001. Is the glass half empty or full? A prospective study of optimism and coronary heart disease in the normative aging study. Psychosom. Med. 63(6), 910-916.

Lamond, A., Depp, C., Allison, M., Langer, R., Reichstadt, J., Moore, D., Golshan, S., Ganiats, T.G., Jeste, D.V., 2008. Measurement and predictors of resilience among community-dwelling older women. J. Psychiatry Res. 43(2), 148-154.

Loftus, E.J., 2004. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology. 126(6), 1504-1517.

McCombie, A.M., Mulder, R.T., Gearry, R.B., 2013. How IBD patients cope with IBD: A systematic review. J. Crohns Colitis. 7(2), 89-106.

Molodecky, N.A., Soon, I.S., Rabi, D.M., Ghali, W.A., Ferris, M., Chernoff, G., Benchimol, E.I., Panaccione, R., Ghosh, S., Barkema, H.W., Kaplan, G.G., 2012. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology. 142(1), 46-54.

Moradkhani, A., Beckman, L.J., Tabibian, J.H., 2013. Health-related quality of life in inflammatory bowel disease: Psychosocial, clinical, socioeconomic, and demographic predictors. J. Crohns Colitis. 7(6), 467-473.

Notario-Pacheco, B., Martinez-Vizcaino, V., Trill-Calvo, E., Perez-Yus, M.C., Serrano-Parra, D., Garcia-Campayo, J., 2014. Validity and reliability of the Spanish version of the 10-item CD-RISC in patients with fibromyalgia. Health Qual Life Outcomes. 12, 14-23.

Richardson, G.E., 2002. The meta-theory of resilience and resiliency. J. Clin. Psychol. 58(3), 307-321.

Seres, G., Kovacs, Z., Kovacs, A., Kerekgyarto, O., Sardi, K., Demeter, P., Meszaros, E., Tury, F., 2008. Different associations of health related quality of life with pain, psychological distress and coping strategies in patients with irritable bowel syndrome and inflammatory bowel disorder. J. Clin. Psychol. Med. Settings. 15(4), 287-295.

Snyder, L.C.R., 1999. Coping: The psychology of what works. Oxford: Oxford University Press.

Soderstrom, M., Dolbier, C., Leiferman, J., Steinhardt, M., 2000. The relationship of hardiness, coping strategies, and perceived stress to symptoms of illness. J. Behav. Med. 23(3), 311-328.

Yi, J.P., Vitaliano, P.P., Smith, R.E., Yi, J.C., Weinger, K., 2008. The role of resilience on psychological adjustment and physical health in patients with diabetes. Br. J. Health Psychol. 13(2), 311-325.

Yu, X., Lau, J.T.F., Mak, W.W.S., Zhang, J., Lui, W.W.S., Zhang, J., 2011. Factor structure and psychometric properties of the Connor-Davidson Resilience Scale among Chinese adolescents. Compr. Psychiatry. 52(2), 218-224.

Yu, X., Zhang, J., 2007. Factor analysis and psychometric evaluation of the Connor-Davidson Resilience Scale (CD-RISC) with Chinese people. Soc. Behav. Pers. 35(1), 19-30.

Zarpour, S., Besharat, M.A., 2011. Comparison of personality characteristics of individuals with irritable bowel syndrome and healthy individuals. Soc. Behav. Sci. 30, 84-88.

Zoccali, R., Muscatello, M.R., Bruno, A., Barilla, G., Campolo, D., Meduri, M., Familiar, L., Bonica, M., Consolo, P., Scaffidi, M., 2006. Anger and ego-defence mechanisms in non-psychiatric patients with irritable bowel syndrome. Dig. Liver Dis. 38(3), 195-200.

Table 4.1. Score means, standard deviations (SD), and item-total correlations for each of the 25 items and the factor-total correlations for the five factors of the 25-item CD-RISC.

Item	Mean	SD	Item-Total Correlation
Competence*	22.6	5.2	0.90[b]
10	3.1	0.9	0.52[b]
11	2.8	0.9	0.65[b]
12	2.9	0.9	0.72[b]
16	2.4	1.0	0.66[b]
17	3.0	0.9	0.72[b]
23	2.3	1.0	0.60[b]
24	2.7	0.9	0.73[b]
25	3.2	0.8	0.56[b]
Control*	7.2	2.5	0.76[b]
13	2.9	0.9	0.46[b]
21	2.3	1.1	0.71[b]
22	2.0	1.1	0.65[b]
Security*	14.0	3.4	0.81[b]
1	2.6	0.9	0.53[b]
2	3.4	0.9	0.27[b]
4	2.7	0.9	0.66[b]
5	2.7	0.9	0.71[b]
8	2.6	1.0	0.67[b]
Spiritual*	4.0	2.4	0.27[b]
3	1.6	1.5	0.25[b]
9	2.3	1.3	0.20[a]
Tolerance*	17.9	4.5	0.88[b]
6	2.8	1.0	0.55[b]
7	2.4	1.0	0.62[b]
14	2.4	0.9	0.63[b]
15	2.7	1.1	0.57[b]
18	2.5	1.1	0.50[b]
19	2.6	0.9	0.67[b]
20	2.6	0.9	0.48[b]

*composite factors calculated from the items listed below each factor [a]indicates that the two-tailed Pearson correlation is significant at $p \leq 0.05$; [b]indicates that the two-tailed Pearson correlation is significant at $p \leq 0.01$.

Table 4.2. Score means, standard deviations (SD), and item-total correlations for the unidimensional 10-item CD-RISC.

Item	Mean	SD	Item-Total Correlation
1	2.6	0.9	0.66[b]
4	2.7	0.9	0.79[b]
6	2.8	1.0	0.60[b]
7	2.4	1.0	0.67[b]
8	2.6	1.0	0.73[b]
11	2.8	0.9	0.67[b]
14	2.4	0.9	0.66[b]
16	2.4	1.0	0.70[b]
17	3.0	0.9	0.77[b]
19	2.6	0.9	0.73[b]

[a]indicates that the two-tailed Pearson correlation is significant at $p \leq 0.05$; [b]indicates that the two-tailed Pearson correlation is significant at $p \leq 0.01$.

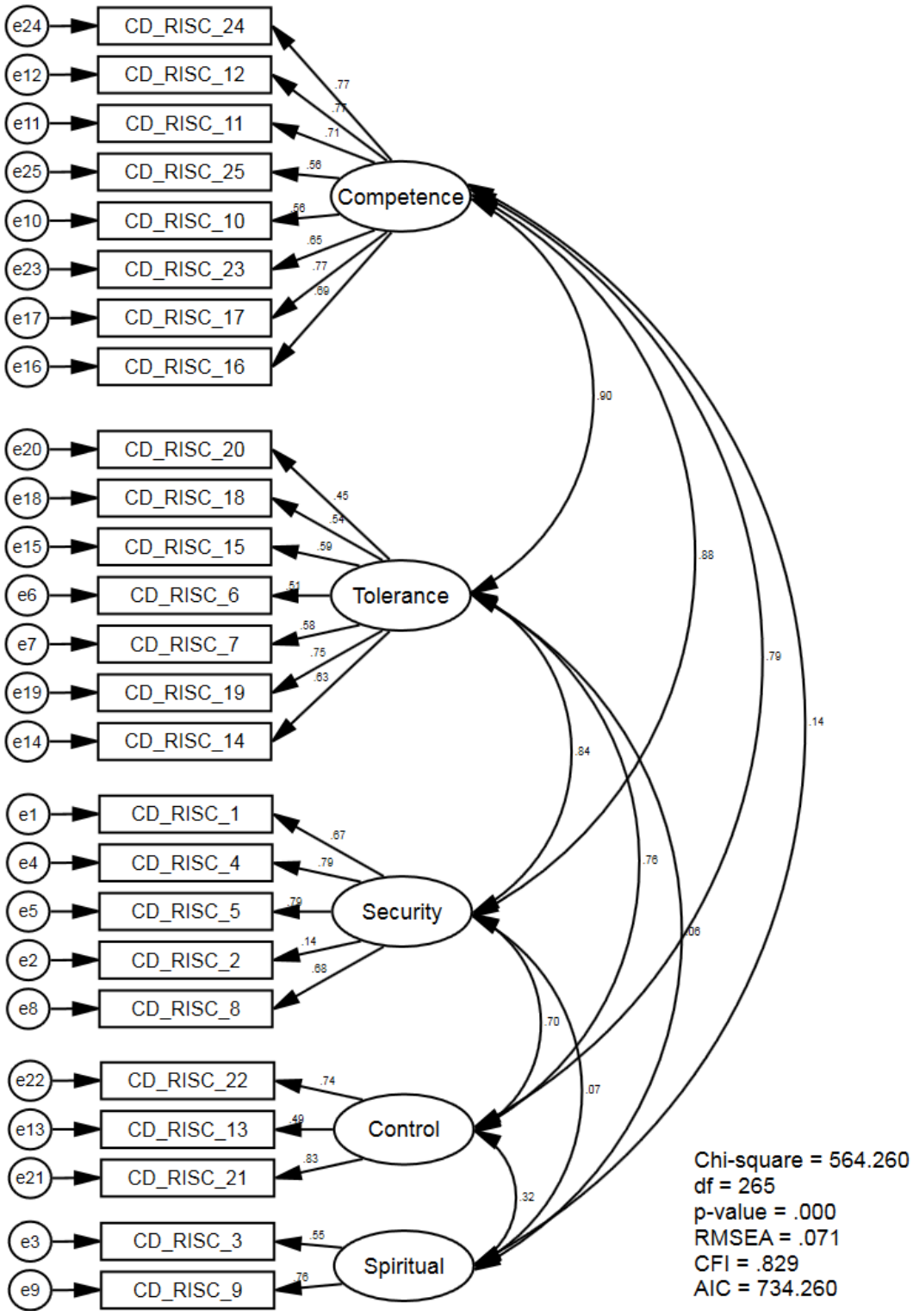

Figure 4.1. Standardized estimates of the 25-item CD-RISC measurement model with a five factor structure and corresponding model fit statistics.

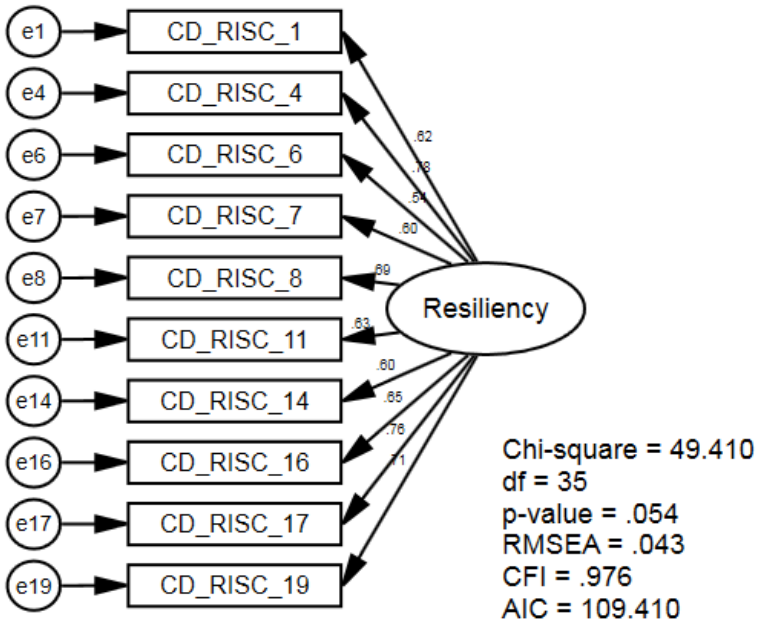

Figure 4.2. Standardized estimates of the 10-item CD-RISC unidimensional measurement model and corresponding model fit statistics.

Chapter Five: Manuscript Two

Differences in Quality of Life, Physical Activity, Sitting, and Resilience Levels between People with Inflammatory Bowel Disease and Healthy Controls

In preparation for publication to the American Journal of Gastroenterology

Katrina Taylor, Philip W. Scruggs, Onesmo B. Balemba, Michelle M. Wiest, Chantal A. Vella

Abstract

Inflammatory bowel disease (IBD) is an autoimmune disease characterized by the cyclical nature of flare and remission periods that impact health-related quality of life (HRQOL); however, there is limited research regarding HRQOL, physical activity, sitting, and resilience levels in this population. PURPOSE: To characterize physical activity, sitting, HRQOL, and resilience levels in people with IBD (in remission and disease flare) compared to healthy controls. METHODS: Participants with IBD (n=242; 96 in disease flare [IBD-flare] and 146 in disease remission [IBD-remission]), and healthy controls (n=265) were recruited to complete an online survey regarding HRQOL, physical activity, sitting, and resilience levels. Data were analyzed using analysis of covariance, with age, sex, education status, disease history, and smoking habits as covariates. RESULTS: Physical and mental HRQOL were different across the three groups with both groups of IBD participants reporting lower levels of HRQOL than healthy controls ($p<0.001$). Furthermore, IBD-flare and IBD-remission participants reported lower levels of all physical activity variables and resilience scores than

healthy controls but there were no differences between IBD participants ($p<0.05$). Time spent sitting was not different across the three groups ($p=0.07$). CONCLUSION: Our findings suggest that people with IBD report lower levels of HRQOL, physical activity, and resilience than healthy controls but no differences in time spent sitting. There were no negative consequences of a disease flare on physical activity and resilience levels; however, the presence of a disease flare did impact HRQOL in this cohort.

Introduction

Inflammatory bowel disease (IBD) is a group of debilitating autoimmune diseases, such as Crohn's disease and ulcerative colitis, which affect the gastrointestinal tract. IBD is recognized by symptoms that include weight loss, gastrointestinal bleeding, bloody diarrhea, and abdominal pain but there is no medical cure for the disease that is typically diagnosed between the ages of 15 and 30 years (1). IBD is further characterized by the cyclical nature of disease flares and remission periods, with many patients experiencing disease flares at least every few months (2).

People with IBD have been shown to have a lower health-related quality of life (HRQOL) compared to healthy populations (3), likely due to the combination of disease impact on the body, debilitating symptoms, diagnosis at an early age, lack of a medical cure, side effects associated with palliative medications, and cyclical nature of the disease (4-5). Research has begun to investigate physical activity and exercise as an approach to improve HRQOL in people with IBD (6-8). It has been suggested that low- to moderate-intensity physical activity, particularly walking, is safe (9-10), tolerated (11), and beneficial to HRQOL in people with IBD (12). Despite this evidence, physicians do not recommend exercise to IBD

patients due to fears of symptom exacerbation (6). However, there is currently no evidence to suggest that sedentary behavior is advised in people with IBD. Recent research within healthy populations has shown that sedentary behavior is negatively associated with HRQOL (13-14). There is currently a lack of research regarding the amount of time spent in physical activity and sedentary behaviors, such as sitting, in people with IBD. Additionally, it is unknown whether there are differences in levels of physical activity and time spent sitting between disease states in IBD as well as in comparison to healthy controls.

Findings have shown that in the general population HRQOL is associated with resilience (15). Resilience is a psychological construct understood to be the ability to bounce-back from adversity and is often considered a measure of coping ability (16). Additionally, increased levels of resilience are associated with improved health outcomes and HRQOL in diseased populations such as cancer (17), human immunodeficiency virus (HIV) (18), Parkinson's disease (19), and diabetes (20). However, there is currently no research that investigates resilience levels in people with IBD compared to healthy controls.

Therefore, the current study aims were to characterize physical activity, sitting, HRQOL, and resilience levels in people with IBD (in remission and disease flare) and compare them to healthy controls.

Methods

Study participants and setting.

Participants, aged 18 to 65 years, who were diagnosed with IBD or healthy controls, were recruited to complete an online survey. The online survey, delivered through Qualtrics survey software (Qualtrics LLC, Provo, Utah, USA), included questions from the

International Physical Activity Questionnaire (IPAQ) short version, the Short Form-36 (SF-36), and the Connor-Davidson Resilience Scale (CD-RISC), and took approximately 10 to 15 minutes to complete. IBD participants were recruited through online social networking sites for those with IBD and ResearchMatch. Healthy controls were recruited through word-of-mouth, academic institutions, and ResearchMatch. ResearchMatch is a national health volunteer registry that was created by several academic institutions and supported by the US National Institutes of Health as part of the Clinical Translational Science Award (CTSA) program. ResearchMatch has a large population of volunteers who have consented to be contacted by researchers about health studies for which they may be eligible.

Of the 793 participants who started the survey, 328 participants with self-reported IBD and 318 healthy controls were enrolled in the study as described in Figure 5.1. The study was certified exempt by the University's Institutional Review Board.

Instrumentation

Health-related quality of life (HRQOL).

HRQOL was measured with the SF-36, which has been previously designed to assess functional status, wellbeing, and general perceptions of health. The SF-36 is a generic, multidimensional instrument that consists of 36 questions representing eight subscales: physical functioning, bodily pain, vitality, social functioning, mental health, general health, role limitations due to physical problems, and role limitations due to emotional issues. Scores from the SF-36 range from 0–100 with higher scores indicating higher levels of HRQOL. The SF-36 has been validated and shown to be reliable in the general population (21) and also shown to be reliable in people with IBD. Cronbach's alpha for the SF-36 in IBD patients has

been found to range from 0.72 to 0.90 in Crohn's disease patients and from 0.74 to 0.91 in patients with ulcerative colitis (3).

Physical activity and sitting.

Physical activity and time spent sitting were measured using the IPAQ short version. The survey is comprised of seven items that measure physical activity at various intensities and sedentary behavior: 1) vigorous-intensity activity, 2) moderate-intensity activity, 3) walking, and 4) sitting. The IPAQ is the most widely used physical activity questionnaire (22), and has been shown to be reliable (23) and at least as valid as other established self-report physical activity instruments in adult populations (24).

Resilience.

The 10-item CD-RISC, a single construct instrument, was used to measure resilience in the current study. The 10-item CD-RISC has been shown to be a more valid instrument with an improved factor structure than the original 25-item CD-RISC in both the general population (25) and IBD participants (unpublished data). Responses are measured on a 5-point Likert scale ranging from 0-not true at all to 4-true nearly all of the time. Total scores for the 10-item CD-RISC range from 0 to 40, with higher scores indicating greater levels of resilience.

Demographics.

Demographic information from the survey included age, sex, smoking habits, and education status. These basic demographic variables were in addition to IBD-specific questions such as the number of years diagnosed with the disease (i.e., disease history), the specific diagnosis of IBD (i.e., Crohn's disease versus ulcerative colitis), and participant's current disease state (i.e., disease-flare versus remission).

Statistical Analyses

Data were initially screened for missing data, normality, and outliers. Data cleaning identified 86 responses from IBD participants and 53 responses from healthy controls that were missing data and overall scores for at least two instruments, thus these cases were removed from the database (See Figure 5.1). Physical activity variables (walking, moderate-intensity physical activity, moderate-to-vigorous physical activity, and vigorous-intensity physical activity in both minutes per week and MET-minutes per week) were non-normally distributed and were square root transformed for all analyses, although non-transformed data are presented in the results section for ease of interpretation.

Data were further analyzed for univariate and multivariate outliers using z-scores and Mahalanobis distance, respectively. Seven cases were removed from the analysis as outliers with z-scores greater than |3.3| and cases from the Mahalanobis distance scores that were significant at $p<0.01$ (26). Final sample sizes included data from 242 IBD participants (96 IBD participants in a disease flare [IBD-flare] and 146 IBD participants in disease remission [IBD-remission]) and 265 healthy controls.

Data were reported as mean and standard deviations (mean±SD) unless otherwise stated. Analysis of covariance (ANCOVA) tests with Bonferroni pairwise comparisons were used to compare IBD-flare, IBD-remission, and healthy controls on physical activity, sitting, HRQOL, and resilience as well as demographic variables. Age, sex, disease history, smoking status, and education level were used as covariates. All analyses were conducted in SPSS v24.0 (IBM Corporation, Armonk, New York, USA) with an alpha level set at 0.05.

Results

General participant characteristics.

Participants self-reported that they were free of any cardiovascular, pulmonary, or metabolic diseases (healthy controls), or that they had a physician diagnosis of IBD (IBD participants) who were then subdivided based on their current reported disease state (i.e., disease-flare versus remission). All participant characteristics are displayed in Table 5.1. Groups differed on age, sex, smoking status, and disease history, therefore these variables were used as covariates in all of the ANCOVA analyses.

IBD participants were predominantly female (80.2%) with an average age of 39.6 years. IBD participants also self-reported an average of 11.9 years since their diagnosis with IBD-remission having reported a longer diagnosis of IBD (13.1±12.4 years) compared to the IBD-flare participants (9.9±10.3 years). Overall, 45% of people with IBD met the physical activity recommendations for health (27). When groups were divided into IBD-flare and IBD-remission, we found that 42% (n=40) of people in IBD-flare met physical activity guidelines whereas 48% (n=70) of IBD-remission met the guidelines of 150 minutes/week. Participants with IBD also reported spending approximately 7.0 hours sitting on a typical weekday (423.7±195.7 minutes/day).

Healthy controls (n=265) were also predominantly female (75.9%) with an average age of 36.5 years which was significantly lower than that of the IBD participants. Of the healthy control participants, 73% (n=193) met the current physical activity recommendations for health. Healthy controls spent approximately 6.5 hours sitting on a typical weekday (394.5±182.3 minutes/day).

Differences in HRQOL across groups.

All data and results for differences across groups for HRQOL, physical activity, sitting, and resilience are shown in Table 5.2. There was a significant main effect for physical HRQOL across the three groups ($p<0.001$), with IBD-flare participants reporting the lowest levels of physical HRQOL (38.9±8.3). IBD-flare participants had significantly lower levels of physical HRQOL than both IBD-remission ($p<0.001$) and healthy controls ($p<0.001$). Additionally, IBD-remission participants (47.6±9.4) reported significantly lower levels of physical HRQOL than healthy controls (55.9±6.0) ($p<0.001$). When examining the specific subscales of physical HRQOL, the largest difference between groups was in general health perceptions with IBD-flare (33.3±9.4) scoring more than 20 points lower than healthy controls (54.4±8.7).

There was a significant main effect for mental HRQOL across the three groups ($p<0.001$) with IBD-flare participants reporting the lowest levels of mental HRQOL compared to both IBD-remission ($p<0.001$) and healthy controls ($p<0.001$). IBD-remission reported significantly lower mental HRQOL than healthy controls ($p<0.001$). Interestingly, the largest difference in the mental HRQOL subscales was in social functioning with IBD-flare participants (33.4±10.5) reporting considerably lower scores than healthy controls (51.5±8.5).

Differences in physical activity and sitting across groups.

There was a significant main effect for walking across the three groups ($p=0.032$) with pairwise comparisons showing that IBD-flare reported participating in lower volumes of walking than healthy controls ($p=0.026$). On average, IBD-flare participants (301.1±466.4 minutes/week) reported walking over 170 minutes/week less than healthy controls. There

were no differences between IBD-flare and IBD-remission participants ($p=0.433$), nor were there differences between IBD-remission participants and healthy controls ($p=0.572$).

Moderate-intensity physical activity showed a significant main effect across the three groups ($p=0.003$) with IBD-flare ($p=0.003$) and IBD-remission ($p=0.028$) participants reporting less moderate-intensity physical activity than healthy controls ($p=0.003$). Healthy controls reported engaging in higher levels of moderate-intensity physical activity with the greatest difference between IBD-flare and healthy controls (130.6 minutes/week); however, there were no differences between IBD-flare and IBD-remission participants. There was also a significant main effect for vigorous-intensity physical activity across groups ($p<0.001$). There were no differences between IBD-flare (90.5±195.7 minutes/week) and IBD-remission (116.7±190.4 minutes/week) participants; however, both groups reported lower vigorous-intensity physical activity than healthy controls ($p<0.001$ for both).

When combined, the volume of MVPA (minutes/week) and the energy cost associated with MVPA (MET-minutes/week) there was a significant main effect across groups ($p<0.001$ for both). Healthy controls reported higher levels of MVPA (minutes/week and MET-minutes/week) than both IBD-flare and IBD-remission participants ($p<0.001$ for both). There were no differences between IBD-flare and IBD-remission participants ($p>0.05$). Additionally, on average IBD-flare expended the least amount of energy through MVPA with more than 1500 MET-minute/week difference between IBD-flare and healthy control participants.

Self-reported time spent sitting was not different among groups ($p>0.05$), with IBD-flare report on average 1 more hour per day of sitting than healthy controls and approximately 45 minutes more per day than IBD-remission.

Differences in resilience across groups.

There was also a significant main effect across groups ($p<0.001$) for resilience scores. IBD-flare participants ($p<0.001$) and IBD-remission participants ($p=0.006$) reported significantly lower resilience scores than healthy controls. However, there were no differences between IBD-flare and IBD-remission participants ($p=0.461$).

Discussion

The aim of the current study was to characterize physical activity, sitting, and resilience levels in people with IBD (in remission and disease flare) and compare them to healthy controls. It was hypothesized that HRQOL would be lower in those with IBD than healthy controls, with IBD-flare participants reporting lower HRQOL than IBD-remission and healthy controls. Furthermore, it was hypothesized that resilience levels would be lower in both groups of IBD participants than healthy controls but that IBD-remission participants would score higher than IBD-flare participants. Finally, it was hypothesized that there would be no differences in physical activity and sitting across groups.

The findings from the current study showed that there are a number of differences between the two groups of IBD participants (i.e., IBD-remission and IBD-flare) and in comparison to healthy controls. IBD-remission participants on average have been diagnosed with the disease longer than IBD-flare participants at the time of the study. This suggests that increased time since diagnosis may allow for the discovery of an appropriate treatment approach to control the disease and improve coping strategies. Previous research has shown that almost 60% of people with IBD undergo surgical treatment (28), which may contribute to

improved disease management. It is important to note that the current study did not control for surgical treatment or medical interventions.

Importantly, both groups of IBD participants exhibited lower levels of both physical and mental HRQOL than healthy controls, which supports previous findings in this area (2, 29). Further analyses showed that both physical and mental HRQOL were significantly lower in IBD participants in a disease-flare than those in remission. These results correspond with the findings of other research in this area (3, 30-34) and suggest that a disease flare can negatively impact HRQOL in people with IBD. Our results indicate that general health perceptions for physical HRQOL and social functioning scores for mental HRQOL show the greatest differences to healthy controls. IBD is known to impact many aspects of a person's health, particularly gastrointestinal health, but can also lead to extraintestinal issues such as fatigue, anemia, and bone mineral loss (35). Many of these extraintestinal issues may have a considerable impact on a person's physical HRQOL and perception of their general health. Survey research has also shown that people with IBD are concerned about losing control of their bowel movements, producing unpleasant smells, feeling dirty, and experiencing issues with sexual relationships (36). This research supports the decrease in the social functioning aspect of mental HRQOL in the current study, suggesting that there are not only physical consequences of the disease but impacts on mental and social well-being as well.

Research is beginning to suggest that physical activity is beneficial to the IBD population, particularly in terms of improving HRQOL (8, 37). However, previous studies on IBD and physical activity have been limited by small sample sizes and little is known about how much physical activity people with IBD engage in on a regular basis. The current study shows that levels of light (walking), moderate, and vigorous physical activity are lower in

people with IBD compared to healthy controls with healthy controls engaging in over 160 minutes/week more MVPA than IBD participants in remission. Walking showed the least difference between healthy controls and IBD participants with less than 150 minutes/week difference between healthy controls and IBD-remission. Both groups of IBD participants were lower on all aspects of physical activity than healthy controls, yet IBD-flare and IBD-remission were not different from another. Although those in a disease flare on average reported less physical activity than those in remission, this difference was not significant. This suggests that disease flares may not significantly impact physical activity levels in this population and people with IBD are able to continue some level of physical activity despite the cyclical nature of the disease. This is inconsistent with previous research which suggests that more than 75% of people with IBD report reduced leisure activities due to disease activity (28). Ghosh and Mitchell (28) asked participants "how do your symptoms affect your ability to enjoy leisure activities (e.g., travel, dining, sports)?" This question is inclusive of leisure activities that do not involve physical activity and may explain the difference in findings. Although research investigating the benefits of physical activity in people with IBD has grown over the last decade, there is still a paucity of data, particularly regarding the type and amount of physical activity that is beneficial for improved health outcomes.

Our results are the first to show that the amount of time spent sitting was not significantly different across the three groups. Although not significant, IBD-flare participants spent 50 minutes/day more sitting than healthy controls. These findings suggest that despite the debilitating symptoms associated with IBD, it may not necessarily impact the amount of time spent sitting in this sample. However, these findings should be interpreted with caution due to the possible under-reporting of time spent sitting. To our knowledge there is currently

no research in the area of sedentary behavior and IBD; however, previous research has shown that sedentary behaviors, such as sitting, are related to decreased levels of quality of life in the general population (13-14) and colorectal cancer survivors (38). Future research investigating the relationship between objectively measured sedentary behaviors, particularly time spent sitting, and HRQOL in people with IBD would be beneficial for understanding the impact of sitting on health outcomes in people with IBD.

A unique finding in this study was that resilience levels were significantly lower in the two groups of IBD participants compared to healthy controls. Furthermore, although we found that both groups of IBD participants had lower resilience levels than healthy controls, the two IBD groups were not different from one another. These findings suggest that people with IBD have a lower ability to bounce-back from adversity than healthy controls, although this difference on average was only 2.8 points indicating that despite the debilitating disease these patients still have relatively high resilience levels. Resilience scores from IBD participants in the current sample are similar to previous research in adults with multiple sclerosis (39) as well as adult females with HIV (40). However, IBD participants seemed to have slightly higher levels of resilience compared to patients with fibromyalgia (41). Interestingly, our healthy controls reported lower resilience scores than other healthy adults that have been studied (42), which might explain the small, but significant difference between people with IBD and healthy controls.

Despite the important findings in the current study, there are limitations that should be recognized when interpreting the results. Our findings are limited by a convenience sample and self-reported levels of HRQOL, physical activity, sitting, and resilience. All participants were volunteers, which limits the generalizability of the current findings. Furthermore, it is

understood that there is some bias with self-reported variables, particularly with the overestimation of physical activity and underestimation of time spent sitting (43). However, both groups likely over- and under-estimated to a similar extent. Time spent sitting was used as a measure of sedentary behavior; however, there are additional sedentary behaviors, such as lying down, which may not have been captured from the survey. Future research would be beneficial in looking at different sedentary activities in people with IBD. An additional limitation in the current study is that we did not measure the type and frequency of medical treatments being used by IBD participants or whether participants had undergone surgical interventions to manage the disease.

To our knowledge this is one of the first research studies comparing physical activity, sitting, and HRQOL in people with IBD, both in remission and disease flare, and healthy controls. Our findings have important implications for future research in this area. We have confirmed previous findings of differences in both physical and mental HRQOL between IBD and healthy controls, as well as provided new evidence to show levels of physical activity, sitting, and resilience in a relatively large sample of people with IBD. Future research should examine the possible inter-relationships among physical activity, sitting, resilience, and HRQOL. Research investigating different doses and modes of exercise for people with IBD are needed to understand appropriate exercise prescriptions that do not exacerbate the symptoms associated with IBD.

In conclusion, our findings suggest that people with IBD, either in disease-flare or remission, report lower levels of physical and mental HRQOL compared to healthy controls. People with IBD in a disease flare report lower levels of physical and mental HRQOL, particularly general health perceptions and social functioning respectively, than those in

remission. Furthermore, IBD participants in both disease states engage in lower levels of physical activity, report lower resilience scores but show no differences in the amount of time spent sitting. There were no negative impacts of a disease-flare versus remission on resilience, physical activity, and sitting in this cohort.

Study Highlights

What is current knowledge?

- Health-related quality of life is lower in people with inflammatory bowel disease than healthy controls.
- A disease flare can further negatively impact health-related quality of life in people with inflammatory bowel disease.

What is new here?

- Physical activity and resilience levels are lower in people with inflammatory bowel disease compared to healthy controls.
- Disease state does not affect physical activity or resilience levels in people with inflammatory bowel disease.
- There are no differences in time spent sitting between people with inflammatory bowel disease and healthy controls.

References

1. Bernstein CN, Rawsthorne P, Cheang M et al. A population-based case control study of potential risk factors for IBD. Am J Gastroenterol 2006;101:993-1002.

2. Moradkhani A, Beckman LJ, Tabibian JH. Health-related quality of life in inflammatory bowel disease: Psychosocial, clinical, socioeconomic, and demographic predictors. J Crohns Colitis 2013;7:467-73.

3. Bernklev T, Jahnsen J, Lygren I et al. Health-related quality of life in patients with inflammatory bowel disease measured with the Short Form-36: Psychometric assessments and a comparison with general population norms. Inflamm Bowel Dis 2005;11:909-18.

4. Casellas F, Lopez-Vivancos J, Badia X et al. Impact of surgery for Crohn's disease on health-related quality of life. Am J Gastroenterol 2000;95:177-82.

5. Hjortswang H, Jarnerot G, Curman B, et al. The influence of demographic and disease-related factors on health-related quality of life in patients with ulcerative colitis. Eur J Gastroenterol Hepatol 2003;15:1011-20.

6. Ng V, Millard W, Lebrun C et al. Low-intensity exercise improves quality of life in patients with Crohn's disease. Clin J Sports Med 2007;17:384-88.

7. Vogelaar L, van den Berg-Emons R, Bussmann H et al. Physical fitness and physical activity in fatigued and non-fatigued inflammatory bowel disease patients. Scand J Gastroenterol 2015;50:1357-67.

8. Klare P, Nigg J, Nold J, et al. The impact of a ten-week physical exercise program on health-related quality of life in patients with inflammatory bowel disease: A prospective randomized controlled trial. Digestion 2015;91:239-47.

9. Martin D. Physical activity benefits and risks on the gastrointestinal system. South Med J 2011;104:831-37.

10. Packer N, Hoffman-Goetz L, Ward G. Does physical activity affect quality of life, disease symptoms and immune measures in patients with inflammatory bowel disease? A systematic review. J Sports Med Phys Fitness 2010;50:1-18.

11. Nathan I, Norton C, Czuber-Dochan W et al. Exercise in individuals with inflammatory bowel disease. Gastroenterol Nurs 2013;36:437-42.

12. Narula N, Fedorak R. Exercise and inflammatory bowel disease. Can J Gastroenterol 2008;22:497-504.

13. Omorou AY, Vuillemin A, Menai M et al. 10-year cumulative and bidirectional associations of domain-specific physical activity and sedentary behavior with health-related quality of life in French adults: Results from the SU.VI.MAX studies. Prev Med 2016;88:66-72.

14. Rebar AL, Duncan MJ, Short C et al. Differences in health-related quality of life between three clusters of physical activity, sitting time, depression, anxiety, and stress. BMC Public Health 2014;14:1088-94.

15. Soderstrom M, Dolbier C, Leiferman J et al. The relationship of hardiness, coping strategies, and perceived stress to symptoms of illness. J Behav Med 2000;23:311-28.

16. Connor KM, Davidson JR. Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC). Depress Anxiety 2003;18:76-82.

17. Carver CS. Enhancing adaptation during treatment and the role of individual differences. Cancer 2005;104:2602-07.

18. Farber EW, Schwartz JA, Schaper PE et al. Resilience factors associated with the adaptation to HIV disease. Psychosomatics 2000;41:140-6.

19. Robottom BJ, Gruber-Baldini AL, Anderson KE et al. What determines resilience in patients with Parkinson’s disease? Parkinsonism Relat Disord 2012;18:174-7.

20. Yi JP, Vitaliano PP, Smith RE, Yi JC et al. The role of resilience on psychological adjustment and physical health in patients with diabetes. Br J Health Psychol 2008;13:311-25.

21. McHorney CA, Ware JEJ, Rogers W et al. The validity and relative precision of MOS short- and long-form health status scales and Dartmouth COOP charts: Results from the Medical Outcomes Study. Med Care 1992;30:253-65.

22. van Poppel MN, Chinapaw MJ, Mokkink LB et al. Physical activity questionnaires for adults: A systematic review of measurement properties. Sports Med 2010;40:565-600.

23. Craig CL, Marshall AL, Sjostrom M et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003;35:1381-95.

24. Kaleth AS, Ang DC, Chakr R et al. Validity and reliability of community health activities model program for seniors and short-form international physical activity questionnaire as physical activity assessment tools in patients with fibromyalgia. Disabil Rehabil 2010;32:353-9.

25. Campbell-Sills L, Stein MB. Psychometric analysis and refinement of the Connor-Davidson Resilience Scale (CD-RISC): Validation of a 10 item measure of resilience. J Trauma Stress 2007;20:1019-28.

26. Tabachnick BG, Fidell LS. Using multivariate statistics, 6th edn. Pearson: Boston, 2012.

27. Garber CE, Blissmer B, Descehenes MR, Franklin BA, Lamonte MJ, Lee IM, Nieman DC, Swain DP. American College of Sports Medicine position stand: Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. Med Sci Sports Exerc 2011;43:1334-1359.

28. Ghosh S, Mitchell R. Impact of inflammatory bowel disease on quality of life: Results of the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) patient survey. J Crohns Colitis 2007;1:10-20.

29. Verma S, Tsai HH, Giaffer MH. Does better disease-related education improve quality of life? A survey of IBD patients. Dig Dis Sci 2001;46:865-9.

30. Cohen R. The quality of life in patients with Crohn's disease. Aliment Pharmacol Ther 2002;16:1603-9.

31. Andersson P, Olaison G, Bendsten P et al. Health related quality of life in Crohn's proctocolitis does not differ from a general population when in remission. Colorectal Dis 2003;5:56-62.

32. Bernklev T, Jahnsen J, Henriksen M et al. Relationship between sick leave, unemployment, disability, and health-related quality of life in patients with inflammatory bowel disease. Inflamm Bowel Dis 2006;12:402-12.

33. Guthrie E, Jackson J, Shaffer J et al. Psychological disorder and severity of inflammatory bowel disease predict health-related quality of life in ulcerative colitis and Crohn's disease. Am J Gastroenterol 2002;97(8):1994-9.

34. Zhou Y, Ren W, Irvine EJ et al. Assessing health-related quality of life in patients with inflammatory bowel disease in Zhejiang, China. J Clin Nurs 2010;19:79-88.

35. Bi L, Triadafilopoulos G. Exercise and gastrointestinal function and disease: An evidence-based review of risks and benefits. Clin Gastroenterol Hepatol 2003;1:345-55.

36. de Rooy EC, Toner BB, Maunder RG et al. Concerns of patients with inflammatory bowel disease: Results from a clinical population. Am J Gastroenterol 2001;96:1816-21.

37. Loudon CP, Corroll V, Butcher J et al. The effects of physical exercise on patients with Crohn's disease. Am J Gastroenterol 1999;94:697-703.

38. van Roekel EH, Bours MJ, Breedveld-Peters JJ et al. Modeling how substitution of sedentary behavior with standing or physical activity is associated with health-related quality of life in colorectal cancer survivors. Cancer Causes Control 2016;27:513-25.

39. Black R, Dorstyn D. A biopsychosocial model of resilience for multiple sclerosis. J Health Psychol 2015;20:1434-44.

40. Dale SK, Cohen MH, Kelso GA et al. Resilience among women with HIV: Impact of silencing the self and socioeconomic factors. Sex Roles 2014;70:221-31.

41. Notario-Pacheco B, Martinez-Vizcaino V, Trillo-Calvo E et al. Validity and reliability of the Spanish version of the 10-item CD-RISC in patients with fibromyalgia. Health and Quality of Life Outcomes 2014;12:14-23.

42. Paulus MP, Flagan T, Simmons AN et al. Subjecting elite athletes to inspiratory breathing load reveals behavioral and neural signatures of optimal performers in extreme environments. PLoS One 2012;7:e29394.

43. Sallis JF, Saelens BE. Assessment of physical activity by self-report: Status, limitations, and future directions. Res Q Exerc Sport 2000;71:1-14.

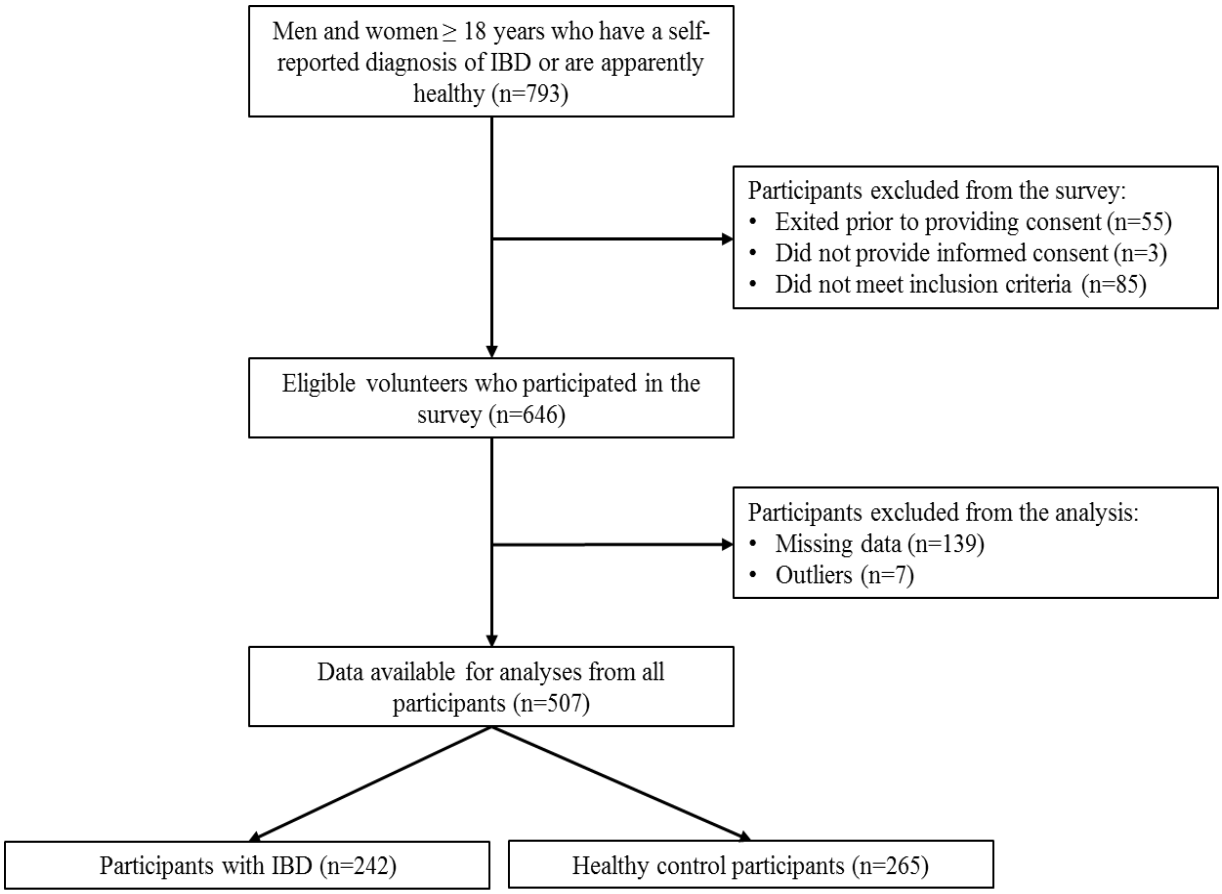

Figure 5.1. Study schematic of inclusion of individuals into the study.

Table 5.1. Characteristics of IBD participants and healthy controls (data presented as mean±SD unless otherwise stated).

Variable	**All IBD Participants (n=242)**	**IBD-Remission (n=146)**	**IBD-Flare (n=96)**	**Healthy Controls (n=265)**	**P-value**
Age	39.6 ± 14.3	40.4 ± 15.1	38.5 ± 12.8	36.5 ± 14.4[a,b]	< 0.001
Sex, number of males (%)	48 (19.8)	36 (24.7)	12 (12.5)	64 (24.2)	0.061
Disease history, years	11.9 ± 11.7	13.1 ± 12.4	9.9 ± 10.3[b]	-	< 0.001
Met PA guidelines, number (%)	110 (45.4)	70 (47.9)	40 (42)	193 (73)	
Education, frequency (%)					0.763
Less than high school	18 (7.4)	13 (8.9)	5 (5.2)	6 (2.3)	
High school	39 (16.1)	24 (16.4)	15 (15.6)	46 (17.4)	
Some college/university	170 (70.3)	100 (68.5)	70 (72.9)	206 (77.7)	
Postgraduate education	15 (6.2)	9 (6.2)	6 (6.3)	7 (2.6)	
Smoking status, frequency (%)					< 0.001
Never smoked	135 (55.8)	89 (61.0)	42 (43.8)	215 (81.1)	
Ex-smoker	83 (34.3)	43 (29.5)	42 (43.8)	37 (14.0)	
Current smoker	24 (9.9)	14 (9.5)	12 (12.4)	13 (4.9)	

[a]significantly different than IBD-remission ($p<0.05$); [b]significantly different than IBD-flare ($p<0.05$); PA, physical activity.

Table 5.2. Differences across groups (healthy controls vs. IBD-flare vs. IBD-remission) after adjusting for age, sex, disease history, education status, and smoking habits (data presented as mean±SD).

Variable	All IBD participants	IBD-remission	IBD-flare	Healthy controls	*P* value
Resilience	27.0 ± 6.5	27.6 ± 6.7	26.1 ± 6.0	29.8 ± 5.5[a,b]	< 0.001
HRQOL					
Physical functioning composite score	44.2 ± 9.7	47.6 ± 9.4	38.9 ± 8.3[a]	55.9 ± 6.0[a,b]	< 0.001
Physical functioning	48.2 ± 9.1	50.5 ± 8.4	44.6 ± 9.3	55.1 ± 4.7	-
Role limitation due to physical health	42.4 ± 10.9	46.5 ± 10.0	36.1 ± 9.7	54.3 ± 5.3	-
Bodily pain	43.6 ± 9.8	47.5 ± 9.1	37.4 ± 7.9	52.8 ± 7.1	-
General health perceptions	37.7 ± 11.2	40.8 ± 11.4	33.3 ± 9.4	54.4 ± 8.7	-
Mental functioning composite score	40.7 ± 11.7	43.6 ± 11.0	36.4 ± 11.6[a]	48.1 ± 10.0[a,b]	< 0.001
Vitality	40.3 ± 11.3	43.6 ± 11.5	35.5 ± 9.5	51.0 ± 9.2	-
Social functioning	40.2 ± 11.7	44.5 ± 10.7	33.4 ± 10.5	51.5 ± 8.5	-
Role limitation due to emotion	42.1 ± 12.3	45.1 ± 11.1	37.8 ± 12.9	49.1 ± 8.6	-
Mental health	43.5 ± 10.9	46.0 ± 10.0	40.0 ± 11.2	49.7 ± 8.8	-
Physical activity & Sitting Time					
Walking, minutes/week	328.6 ± 421.8	334.5 ± 368.0	301.1 ± 466.4	476.5 ± 535.8[a,b]	0.032
Moderate, minutes/week	173.0 ± 304.4	214.0 ± 363.1	137.2 ± 210.8	267.8 ± 370.5[a,b]	0.003
Vigorous, minutes/week	105.5 ± 186.9	115.9 ± 189.0	89.5 ± 194.9	213.5 ± 261.8[a,b]	< 0.001
MVPA, minutes/week	278.5 ± 411.7	329.9 ± 481.2	226.7 ± 315.4	481.3 ± 528.9[a,b]	< 0.001
MVPA, MET-minutes/week	1536.1 ± 2712.4	1783.0 ± 2540.8	1265.0 ± 1920.3	2779.3 ± 2991.5[a,b]	< 0.001
Sitting, minutes/day	423.7 ± 195.7	403.6 ± 191.5	447.6 ± 195.0	394.5 ± 182.3	0.071

[a]significantly different than IBD-remission ($p<0.05$); [b]significantly different than IBD-flare ($p<0.05$). HRQOL health-related quality of life; MVPA moderate-to-vigorous physical activity.

Chapter Six: Manuscript Three

Associations of Physical Activity, Resilience, and Quality of Life in people with IBD

In preparation for publication to Medicine and Science in Sports and Exercise

Katrina Taylor, Philip W. Scruggs, Onesmo B. Balemba, Michelle M. Wiest, Chantal A. Vella

Abstract

Inflammatory bowel disease (IBD) is a debilitating autoimmune disease that negatively impacts health-related quality of life (HRQOL) due to the damage to the gastrointestinal system and extraintestinal manifestations associated with the disease. Recent research has suggested that low- to moderate-intensity physical activity can be beneficial to HRQOL in people with IBD; however, studies associating higher intensities of physical activity with HRQOL in this population are lacking. PURPOSE: To understand the relationships among physical activity (walking and moderate-to-vigorous physical activity [MVPA]), resilience, and HRQOL in people with IBD. METHODS: People with IBD (n = 242) were recruited to complete an online survey with questions about physical activity, resilience, and HRQOL. Pearson-product moment correlations and multiple regression analyses were used to identify associations between physical activity levels and HRQOL.. Analysis of covariance was used to compare physical and mental HRQOL over quartiles of walking and MVPA. Demographics, disease state, diagnosis history, resilience, and time spent sitting were controlled for in the models/were used as covariates. RESULTS: Multiple regression analyses showed that walking and MVPA were independently associated with

physical ($p \leq 0.001$) but not mental HRQOL ($p > 0.05$). Higher volumes of MVPA were significantly associated with physical HRQOL ($p < 0.001$) while higher volumes of walking were significantly associated with both physical and mental HRQOL ($p \leq 0.01$). CONCLUSIONS: Our findings suggest that engaging in higher volumes of walking above 60 minutes/week and MVPA above 150 minutes/week were beneficial to HRQOL, particularly physical HRQOL, in people with IBD.

Keywords: walking, moderate-to-vigorous physical activity, Crohn's disease, ulcerative colitis

Introduction

Inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis affect more than 3.6 million people in the United States (13, 17). Little is known about the cause of these autoimmune diseases that have no cure but have major symptoms and extraintestinal manifestations that impact health-related quality of life (HRQOL) (4, 10). Furthermore, emotional and social burdens of the disease negatively impact HRQOL in these patients (18). The goal of treatment management in people with IBD is to improve and/or maintain HRQOL. Recently, physical activity has emerged as a non-pharmacological approach to increase HRQOL in people with IBD (22), with sedentary behavior believed to be detrimental to people with IBD (20).

Low- to moderate-intensity physical activity has shown to be beneficial for HRQOL in people with IBD (7, 14, 19); however, there is a paucity of data on this topic particularly regarding higher intensities of physical activity. Currently, only one in four people with IBD

participate in the recommended levels of physical activity to benefit health (15), yet emerging research suggests that low- to moderate-intensity physical activity is safe (16, 23) and beneficial to HRQOL in this population (19). Previous research has reported walking to be beneficial to HRQOL in a small sample of Crohn's disease patients (22). Similarly, Loudon et al. (14) reported significant increases in HRQOL following a 12-week walking program in Crohn's disease patients. Although these studies have provided important information they were limited by small sample sizes, restricted to people with Crohn's disease, and only investigated low-intensity physical activity (i.e., walking). Previous research in colorectal cancer survivors, a disease that is related to IBD, has shown that light physical activity (27) and MVPA are positively associated with HRQOL (3).

Resilience, defined as the ability to bounce back from adversity, is associated with improved HRQOL in people with chronic diseases such as Parkinson's disease (24), HIV (9), and irritable bowel syndrome (8, 29). Furthermore, resilience has been associated with physical activity in healthy populations (21). However, there is no research regarding resilience levels in people with IBD and whether resilience mediates the possible relationship between physical activity and HRQOL in this population.

Therefore, the aim of the current study was to understand the relationships among differing intensities of physical activity, resilience, and HRQOL in people with IBD. It was hypothesized that both walking and MVPA would be independently associated with physical and mental HRQOL. Furthermore, it was hypothesized that increased volumes of walking and MVPA would be related to increased physical and mental HRQOL scores.

Methods

Study participants and setting.

Participants, aged 18 to 65 years who were diagnosed with IBD, were recruited to complete an online survey. The online survey, delivered through Qualtrics survey software (Qualtrics LLC, Provo, Utah, USA), included questions from the International Physical Activity Questionnaire (IPAQ) short version, the Short Form-36 (SF-36), and the Connor-Davidson Resilience Scale (CD-RISC), and took approximately 10 to 15 minutes to complete. Participants were recruited through online social networking sites and ResearchMatch. ResearchMatch is a national health volunteer registry that was created by several academic institutions and supported by the US National Institutes of Health as part of the Clinical Translational Science Award (CTSA) program. ResearchMatch has a large population of volunteers who have consented to be contacted by researchers about health studies for which they may be eligible.

Of the 375 IBD participants who started the survey, 37 exited the survey prior to completing the informed consent, and three participants did not provide their consent to be in the study. Finally, 328 participants with self-reported IBD were enrolled in the study. The study was certified exempt by the University's Institutional Review Board and performed in line with the principles outlined in the Declaration of Helsinki. Informed consent was obtained from all participants enrolled in the study.

Instrumentation

Health-related quality of life (HRQOL).

The SF-36, a generic, multidimensional instrument assessing functional status, wellbeing, and general perceptions of health, was used to measure HRQOL. The SF-36 consists of 36 questions across two major subscales: physical functioning and mental functioning composite scores. Scores range from 0 – 100 with higher scores indicating higher levels of HRQOL. The SF-36 has been previously validated in people with IBD with Cronbach's alpha ranging from 0.72 to 0.90 in Crohn's disease patients and from 0.74 to 0.91 in patients with ulcerative colitis (2).

Physical activity and sitting.

The IPAQ short version, which consists of seven items, was used to measure physical activity and time spent sitting. Participants recorded their activity at varying intensities: 1) vigorous-intensity physical activity, 2) moderate-intensity physical activity, 3) walking, and 4) sitting. MVPA was calculated as the sum of moderate- and vigorous-intensity physical activity. The outcome variables were reported in minutes/week and MET-minutes/week. The IPAQ is the most widely used physical activity questionnaire (26) and has shown to be reliable in adult populations (6).

Resilience.

The 10-item CD-RISC, a single construct instrument, was used to measure resilience. The 10-item CD-RISC has been shown to be a more valid instrument with an improved factor structure than the 25-item CD-RISC in IBD participants (unpublished data). Total scores for the 10-item CD-RISC range from 0 to 40, with higher scores indicating higher levels of resilience.

Demographics.

Demographic information from the survey included age, sex, educational status, and smoking habits. These basic demographic variables were in additional to IBD-specific variables such as the number of years since disease diagnosis (diagnosis history), the specific IBD diagnosis (Crohn's disease, ulcerative colitis, or undetermined), and the participant's current disease state (disease-flare or disease remission).

Sample Size Estimates

A priori sample size estimates were generated using G*Power 3.1.9.2. Using linear multiple regression sample size calculations and estimating a small effect size (0.10) with nine predictor variables, 207 participants would result in a power of 0.90 and an alpha of 0.05.

Statistical Analyses

Data were initially screened for missing data, normality, and outliers. Data cleaning identified missing data (i.e., did not have overall scores for at least two instruments) from 86 cases and these cases were removed from the database leaving a final sample size of 242 participants. Physical activity variables (walking, moderate-intensity physical activity, vigorous-intensity physical activity, and MVPA in both minutes/week and MET-minutes/week) were non-normally distributed and were square root transformed for all analyses. Non-transformed data are presented for ease of interpretation.

Pearson product-moment correlation analyses were used to establish associations between physical activity, resilience, and HRQOL. Multivariate linear regression analyses, using the Enter method, were used to establish the independent contributions of physical

activity on the dependent variables (physical and mental HRQOL). Several regression models were analyzed and included age, sex, education, smoking habits, disease state, diagnosis history, resilience, and time spent sitting as covariates to determine whether measures of physical activity were independently related to HRQOL. Analysis of covariance (ANCOVA) tests with Bonferroni pairwise comparisons were used to detect differences in physical and mental HRQOL across quartiles of walking and MVPA with age, sex, education status, smoking habits, disease state, and diagnosis history used as covariates. All analyses were conducted in SPSS version 24.0 (IBM Corporation, Armonk, New York, USA) with an alpha level set at 0.05.

Results

Participant characteristics.

Participants self-reported that they had a physician diagnosis of IBD with all participant characteristics displayed in Table 6.1. Participants had a mean age of 39.6 years and had been diagnosed with IBD for an average of 11.9 years. The majority of participants were female (80.2%) with 39.7% participants being diagnosis with Crohn's disease and 59.9% participants diagnosed with ulcerative colitis. There were no differences in HRQOL and physical activity between disease diagnoses. Less than 1% of participants reported a diagnosis of IBD that had not been specific to Crohn's disease or ulcerative colitis at the time of the survey.

Correlations between physical activity, resilience, and HRQOL.

All correlations are presented in Table 6.2. MVPA, walking, and resilience were positively correlated with physical HRQOL ($p \leq 0.001$). Time spent sitting was negatively

correlated with physical HRQOL, but the strength of the association was weak ($p = 0.015$). There was a significant but moderate, positive correlation between resilience and mental HRQOL ($p \leq 0.001$), while sitting trended towards a negative correlation with mental HRQOL ($p = 0.07$). There were no relationships between MVPA, walking, and mental HRQOL ($p > 0.05$).

Linear regression analysis.

Regression analyses are presented in Table 6.3. The linear regression results were similar when using MVPA in minutes/week compared to MET-minutes/week; however, slightly more variance was explained by the model using MVPA in MET-minutes/week for physical HRQOL; therefore, those results are presented. Results from the linear regression analysis indicated that MVPA was associated with physical HRQOL independent of age, sex, disease state, and diagnosis history ($\beta = 0.098$, $p < 0.001$) with MVPA explaining 10% of the variance in physical HRQOL. After adjusting for resilience and sitting, MVPA remained significantly associated with physical HRQOL ($\beta = 0.094$, $p < 0.001$). Walking (minutes/week) was associated with physical HRQOL after adjusting for age, sex, disease state, and diagnosis history ($\beta = 0.220$, $p < 0.001$). When resilience and time spent sitting were added into the model, the relationship between walking and physical HRQOL was slightly attenuated but remained independent ($\beta = 0.195$, $p \leq 0.001$). Walking explained 9% of the variance in physical HRQOL and walking, smoking habits, and disease state were the strongest contributors to physical HRQOL in this model explaining 28% of the variance.

Further analysis showed that neither walking or MVPA were associated with mental HRQOL independent of age, sex, disease state, and diagnosis history ($p > 0.05$), or after adjustment for resilience and sitting ($p > 0.05$).

Differences in HRQOL across quartiles of MVPA and walking.

There was a significant main effect of MVPA quartile for physical HRQOL ($p < 0.001$) but not mental HRQOL ($p = 0.08$) after adjusting for age, sex, education, smoking habits, disease state, and diagnosis history (Figure 6.1). Compared to quartile 1, quartiles 3 ($p = 0.002$) and 4 ($p < 0.001$) had significantly higher physical HRQOL. There were also increases in physical HRQOL from quartile 2 to quartile 4 ($p = 0.02$) but no other differences across quartiles ($p > 0.05$). MVPA quartile 4 had the highest physical HRQOL (47.4 ± 9.0) compared to quartile 1 with the lowest physical HRQOL (40.3 ± 9.0) with more than a 7-point difference. There were no differences across MVPA quartiles for mental HRQOL (Figure 6.1).

There was a significant main effect of walking quartiles for physical HRQOL ($p < 0.001$) (See Figure 6.2). There were differences in physical HRQOL between quartile 1 and quartiles 2, 3, and 4 ($p < 0.001$ for all) with quartile 1 reporting the lowest physical HRQOL. There were no differences between any of the other quartiles ($p > 0.05$). There was at least a 9-point increase in physical HRQOL (quartile 1: 36.4 ± 9.0) vs. quartile 2: 45.4 ± 9.5) when walking more than 60 minutes/week.

There was also a significant main effect of walking quartiles for mental HRQOL ($p = 0.01$). Quartile 1 reported the lowest mental HRQOL (36.1 ± 12.2) compared to the highest scores of mental HRQOL in quartile 3 (43.2 ± 10.9) ($p = 0.008$). There were no other differences between quartiles for mental HRQOL.

Discussion

The aim of the current study was to understand the relationships among differing intensities of physical activity (i.e., walking and MVPA), resilience, and HRQOL in people with IBD. It was hypothesized that both walking and MVPA would be independently associated with physical and mental HRQOL. Furthermore, it was hypothesized that increased volumes of walking and MVPA would be related to increased physical and mental HRQOL scores.

Our results demonstrate that in people with IBD, MVPA was significantly and positively associated with physical HRQOL independent of demographic variables, resilience, and sitting time. Walking was positively associated with physical HRQOL independent of demographics, resilience, and sitting time. Furthermore, increased volumes of MVPA were associated with increased physical HRQOL, while increased volumes of walking were associated with both increased physical and mental HRQOL. These findings show that engaging in higher amounts of MVPA is related to increased physical HRQOL in people with IBD, particularly when participating in more than 150 minutes/week of MVPA, which is equivalent to the current physical activity recommendations for health. In addition, walking more than 60 minutes/week was related to higher physical HRQOL in this cohort, while walking for 180 – 420 minutes/week (approximately 30 – 60 minutes per day for 7 days) seems to be favorable for improved mental HRQOL scores. Moreover, similar physical HRQOL scores were found across the two sets of quartiles for walking and MVPA.

Research has shown that HRQOL is impaired in people with IBD (4, 18), with improving and/or maintaining HRQOL one of the main treatment goals in this population. Previous approaches to enhance HRQOL in people with IBD have included medications and

surgical interventions; however, these are often expensive and with their own complications (Cohen et al., 2000). Recently, research has begun to investigate non-pharmacological treatment approaches, such as physical activity, to improve HRQOL in people with IBD (12, 22, 28). Findings have shown that low- to moderate-intensity physical activity is beneficial for improving HRQOL in people with IBD (14), yet there is a lack of research concerning the impact of higher levels of physical activity on HRQOL in this population.

Previous research in colorectal cancer survivors has shown that MVPA is beneficial to HRQOL (3). IBD is considered a high-risk condition for developing colorectal cancer due to the chronic inflammation (11), suggesting that the beneficial effects of physical activity in one disease may carry to the other. Our findings indicate that walking and MVPA were both associated with increased physical HRQOL; however, there did not seem to be any relationship with physical activity and mental HRQOL. These findings support previous research in colorectal cancer survivors, which show positive associations between physical activity and physical HRQOL but not mental HRQOL (3). An interesting finding in the current study is that disease state (i.e., disease flare versus disease remission) substantially contributed to each of the regression models, explaining 14% of the variance. This finding supports the understanding that disease state impacts HRQOL in people with IBD (1-2, 5). Therefore, disease state should be considered when recommending physical activity to improve HRQOL in people with IBD, future research investigating the benefits of physical activity during a disease flare is warranted.

To our knowledge, this study is the first to investigate the role of resilience on HRQOL in people with IBD. Our study shows that the positive relationships between MVPA, walking and physical HRQOL were independent of resilience scores. However, resilience was

positively correlated with both physical and mental HRQOL in this population. These findings are in support of previous research in other chronic diseases such as HIV/AIDS (9) and Parkinson's disease (24), which have shown that increased resilience levels are related to higher perceived physical and mental HRQOL. Our data further indicate that resilience had a stronger association with mental HRQOL than physical HRQOL, suggesting that the ability to bounce-back from adversity may be more beneficial to mental than physical HRQOL in this sample.

There are limitations in the current study that should be recognized when interpreting the results. Our findings are limited by a convenience sample and self-reported levels of HRQOL, physical activity, sitting, and resilience. Our participants were a predominantly female convenience sample of volunteers, which may limit the generalizability of our findings to all people with IBD. The self-reported variables in the study may be biased, particularly with the overestimation of physical activity (25).

Despite these limitations, to our knowledge this is the first study to investigate the associations between MVPA and HRQOL in people with IBD. By quantifying these relationships, we can improve our understanding of the benefits of MVPA on HRQOL, particularly the physical component of HRQOL. Future research is needed to confirm these findings with a random sample of IBD participants and with objective measures of physical activity. The current study is not causative in nature; therefore, longitudinal research in this area is warranted to investigate whether increasing levels of MVPA is beneficial to HRQOL in people with IBD.

In conclusion, we have found that walking and MVPA are independently and positively associated with physical but not mental HRQOL. Furthermore, increased volumes

of walking and MVPA are related to higher levels of HRQOL in this cohort. Our findings show that walking more than 60 minutes/week can have beneficial effects on physical and mental HRQOL while participating in higher volumes of MVPA, preferably greater than 150 minutes/week, is beneficial to physical HRQOL in people with IBD.

Acknowledgements: This study was funded by the Gatorade Sports Science Institute Student Award program.

Conflicts of Interest: None. The results of the present study do not constitute endorsement by the American College of Sports Medicine (ACSM). The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

References

1. Bernklev T, Jahnsen J, Henriksen M, et al. Relationship between sick leave, unemployment, disability, and health-related quality of life in patients with inflammatory bowel disease. *Inflamm Bowel Dis.* 2006;12(5):402-12.

2. Bernklev T, Jahnsen J, Lygren I, Henriksen M, Vatn M, Moum B. Health-related quality of life in patients with inflammatory bowel disease measure with the short form-36: Psychometric assessments and a comparison with general population norms. *Inflamm Bowel Dis.* 2005;11(10):909-18.

3. Buffart LM, Thong MS, Schep G, Chinapaw MJ, Brug J, van de Poll-Franse LV. Self-reported physical activity: its correlates and relationship with health-related quality of life in a large cohort of colorectal cancer survivors. *PLoS One.* 2012;7(5):e36164.

4. Casati J, Toner BB. Psychosocial aspects of inflammatory bowel disease. *Biomed Pharmacother.* 2000;54(7):388-393.

5. Cohen RD, Larson LR, Roth JM, Becker RV, Mummert LL. The cost of hospitalization in Crohn's disease. *Am J Gastroenterol.* 2000;95(2):524-30.

6. Craig CL, Marshall AL, Sjostrom M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* 2003;35(8):1381-95.

7. Elsenbruch S, Langhorst J, Popkirowa K, et al. Effects of mind-body therapy on quality of life and neuroendocrine and cellular immune functions in patients with ulcerative colitis. *Psychother Psychosom.* 2005; 74(5):277-87.

8. Elsenbruch S. Abdominal pain in irritable bowel syndrome: A review of putative psychological, neural and neuro-immune mechanisms. *Brain Behav Immun.* 2011;25(3):386-94.

9. Farber EW, Schwartz JA, Schaper PE, Moonen DJ, McDaniel JS. Resilience factors associated with the adaptation to HIV disease. *Psychosomatics.* 2000;41(2):140-6.

10. Husain A, Triadafilopoulos G. Communicating with patients with inflammatory bowel disease. *Inflamm Bowel Dis.* 2004;10(4):444-50.

11. Itzkowitz SH, Yio X. Inflammation and cancer IV. Colorectal cancer in inflammatory bowel disease: The role of inflammation. *Am J Physiol Gastrointest Liver Physiol.* 2004;287(1):7-17.

12. Klare P, Nigg J, Nold J, et al. The impact of a ten-week physical exercise program on health-related quality of life in patients with inflammatory bowel disease: A prospective randomized controlled trial. *Digestion.* 2015;91(3):239-47.

13. Loftus EV. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterol.* 2004;126(6):1504-17.

14. Loudon CP, Corroll V, Butcher J, Rawsthorne P, Bernstein CN. The effects of physical exercise on patients with Crohn's disease. *Am J Gastroenterol.* 1999;94(3):697-703.

15. Mack DE, Wilson PM, Gilmore JC, Gunnell KE. Leisure-time physical activity in Canadians living with Crohn's disease and ulcerative colitis: Population-based estimates. *Gastroenterol Nurs.* 2011;34(4):288-94.

16. Martin D. Physical activity benefits and risks on the gastrointestinal system. *South Med J.* 2011;104(12):831-7.

17. Molodecky NA, Soon IS, Rabi DM, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterol.* 2012;142(1):46-52.

18. Moradkhani A, Beckman LJ, Tabibian JH. Health-related quality of life in inflammatory bowel disease: Psychosocial, clinical, socioeconomic, and demographic predictors. *J Crohns Colitis.* 2013;7(6):467-73.

19. Narula N, Fedorak R. Exercise and inflammatory bowel disease. *Can J Gastroenterol.* 2008;22(5):497-504.

20. Nathan I, Norton C, Czuber-Dochan W, Forbes A. Exercise in individuals with inflammatory bowel disease. *Gastroenterol Nurs.* 2013;36(6):437-42.

21. Navuluri RB. Gender differences in the factors related to physical activity among adults with diabetes. *Nurs Health Sci.* 2000;2(4):191-9.

22. Ng V, Millard W, Lebrun C, Howard J. Low-intensity exercise improves quality of life in patients with Crohn's disease. *Clin J Sport Med.* 2007;17(5):384-8.

23. Packer N, Hoffman-Goetz L, Ward G. Does physical activity affect quality of life, disease symptoms and immune measures in patients with inflammatory bowel disease? A systematic review. *J Sports Med Phys Fitness.* 2010;50(1):1-18.

24. Robottom BJ, Gruber-Baldini AL, Anderson KE, et al. What determines resilience in patients with Parkinson's disease? *Parkinsonism Relat Disord.* 2012;18(2):174-7.

25. Sallis JF, Saelens BE. Assessment of physical activity by self-report: Status, limitations, and future directions. *Res Q Exerc Sport.* 2000;71(2 Suppl):S1-14.

26. van Poppel MN, Chinapaw MJ, Mokkink LB, van Mechelen W, Terwee CB. Physical activity questionnaires for adults: A systematic review of measurement properties. *Sports Med.* 2010;40(7):565-600.

27. van Roekel EH, Bours MJ, Breedveld-Peters JJ, et al. Modeling how substitution of sedentary behavior with standing or physical activity is associated with health-related quality of life in colorectal cancer survivors. *Cancer Causes Control.* 2016;27(4):513-25.

28. Vogelaar L, vant Spijker A, Timman R, et al. Fatigue management in patients with IBD: A randomized controlled trial. *Gut.* 2014;63(6):911-8.

29. Zoccali R, Muscatello MRA, Bruno A, et al. Anger and ego-defence mechanisms in non-psychiatric patients with irritable bowel syndrome. *Dig Liver Dis.* 2006;38(3):195-200.

Table 6.1. Participant characteristics (n = 242).

Variable	**Mean ± SD***
Sex, frequency of males (%)	48 (19.8)
Age, years	39.6 ± 14.3
Diagnosis history (years)	11.9 ± 11.7
IBD Diagnosis, frequency (%)	
Crohn's disease	96 (39.7)
Ulcerative colitis	145 (59.9)
Undetermined diagnosis	1 (0.4)
Disease State, frequency (%)	
Disease-flare	96 (39.7)
Disease remission	146 (60.3)
Resilience	27.0 ± 6.5
Sitting, minutes/day	423.7 ± 195.7
Education, frequency (%)	
Less than high school	18 (7.4)
High school	39 (16.1)
Some college/university	170 (70.3)
Postgraduate education	15 (6.2)
Smoking status, frequency (%)	
Never smoked	135 (55.8)
Ex-smoker	83 (34.3)
Current smoker	24 (9.9)
HRQOL	
Physical functioning composite score	44.2 ± 9.7
Physical functioning	48.2 ± 9.1
Role limitations due to physical health	42.4 ± 10.9
Bodily pain	43.6 ± 9.8
General health perceptions	37.7 ± 11.2
Mental functioning composite score	40.7 ± 11.7
Vitality	40.3 ± 11.3
Social functioning	40.2 ± 11.7
Role limitations due to emotional problems	42.1 ± 12.3
Mental health	43.5 ± 10.9
Physical activity*	
Vigorous-intensity, minutes/week	105.5 ± 186.9
Vigorous-intensity, MET-minutes/week	843.9 ± 1495.0
Moderate-intensity, minutes/week	173.0 ± 304.4
Moderate-intensity, MET-minutes/week	692.2 ± 1217.4
MVPA, minutes/week	278.5 ± 411.7
MVPA, MET-minutes/week	1536.1 ± 2712.4
Walking, minutes/week	328.6 ± 421.8
Walking, MET-minutes/week	1084.5 ± 1391.9

*Square-root transformed variables

Table 6.2. Correlations between physical activity variables, resilience, and HRQOL.

	Age	Diagnosis History	Physical HRQOL	Mental HRQOL
Time spent sitting	0.002	0.01	-0.16	-0.12
Walking*	-0.19[a]	-0.14[a]	0.30[b]	0.04
MVPA*	-0.02	-0.01	0.31[b]	0.07
Resilience	0.28[b]	0.09	0.23[b]	0.54[b]

*Square-root transformed. [a]$p \leq 0.05$. [b]$p \leq 0.001$.

Table 6.3. Multiple linear regression analyses to examine the independent associations between physical activity and physical and mental HRQOL.

Dependent variable	AIC	Independent variables*	B ± SE of the estimate	Standardized beta	P
Physical HRQOL					
Model 1 $R^2 = 0.31$	1013.79	MVPA	0.10 ± 0.02	0.27	<0.001
Model 2 $R^2 = 0.34$	1001.72	MVPA	0.09 ± 0.02	0.26	<0.001
Model 3 $R^2 = 0.35$	961.65	MVPA	0.09 ± 0.02	0.26	<0.001
Physical HRQOL					
Model 1 $R^2 = 0.30$	1009.65	Walking	0.22 ± 0.05	0.24	<0.001
Model 2 $R^2 = 0.32$	999.12	Walking	0.20 ± 0.05	0.22	<0.001
Model 3 $R^2 = 0.33$	965.23	Walking	0.20 ± 0.06	0.21	0.001
Mental HRQOL					
Model 1 $R^2 = 0.21$	1133.74	MVPA	0.03 ± 0.03	0.06	0.35
Model 2 $R^2 = 0.39$	1069.98	MVPA	0.01 ± 0.02	0.02	0.67
Model 3 $R^2 = 0.37$	1028.20	MVPA	0.01 ± 0.03	0.02	0.79
Mental HRQOL					
Model 1 $R^2 = 0.21$	1123.49	Walking	0.11 ± 0.07	0.10	0.10
Model 2 $R^2 = 0.39$	1060.84	Walking	0.02 ± 0.06	0.02	0.78
Model 3 $R^2 = 0.37$	1024.75	Walking	0.01 ± 0.06	0.01	0.83

*All independent variables listed were square-root transformed. Model 1 adjusted for age, sex, education, smoking habits, disease state, and diagnosis history; Model 2 adjusted for age, sex, education, smoking habits, disease state, diagnosis history, and resilience; Model 3 adjusted for age, sex, education, smoking habits, disease state, diagnosis history, resilience, and sitting time.

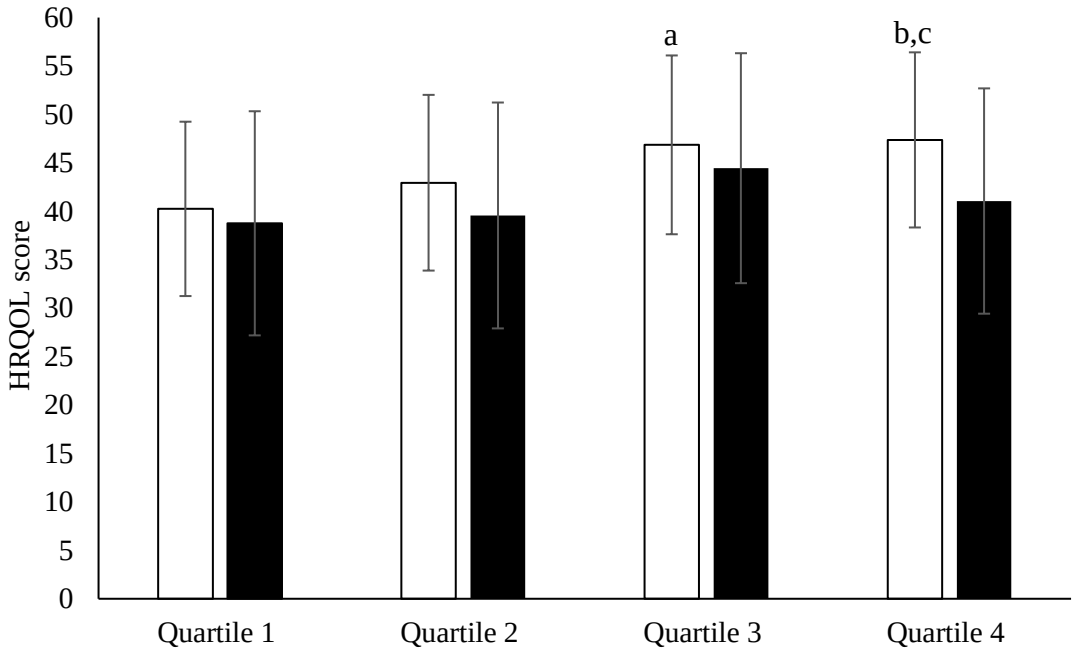

Figure 6.1. Associations between MVPA quartiles and physical (white) and mental (black) HRQOL (quartile 1: 0 minutes/week [n = 68]; quartile 2: 1 – 149 minutes/week [n = 77]; quartile 3: 150 – 299 minutes/week [n = 41]; quartile 4: > 300 minutes/week [n = 79]). [a]significantly different to quartile 1 ($p \leq 0.05$); [b]significantly different to quartile 1 ($p \leq 0.001$); [c]significantly different to quartile 2 ($p \leq 0.05$).

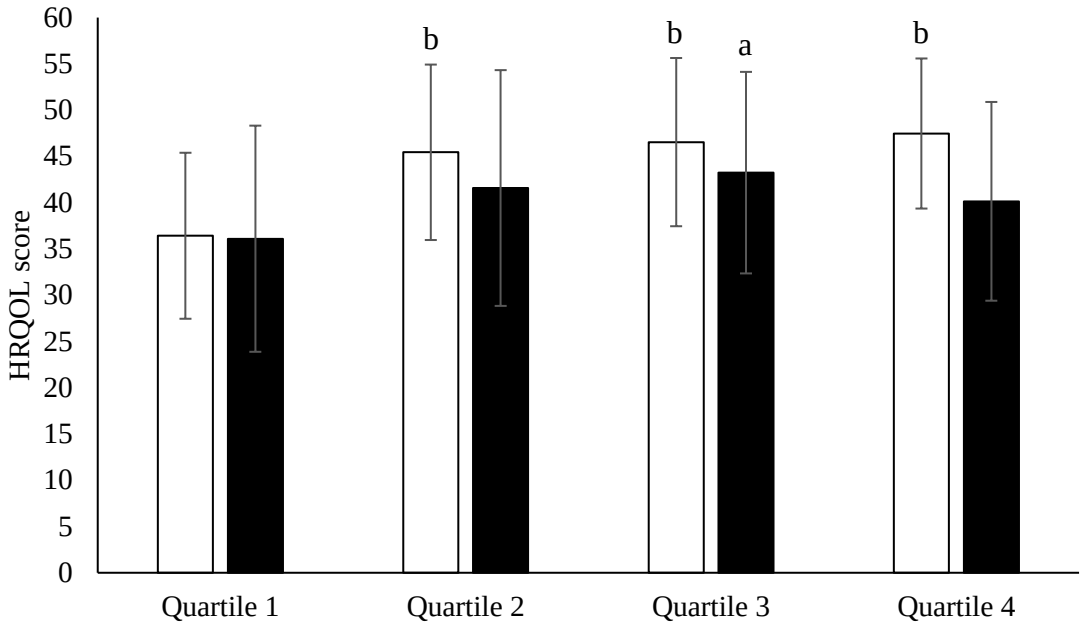

Figure 6.2. Association between walking quartiles and physical (white) and mental (black) HRQOL (quartile 1: < 60 minutes/week [n = 55]; quartile 2: 60 – 180 minutes/week [n = 70]; quartile 3: 181 – 420 minutes/week [n = 61]; quartile 4: > 420 minutes/week [n = 56]). [a]significantly different to quartile 1 ($p \leq 0.05$); [b]significantly different to quartile 1 ($p \leq 0.001$).

Appendix A: IRB exempt certification

University of Idaho
Office of Research Assurances
Institutional Review Board
875 Perimeter Drive, MS 3010
Moscow ID 83844-3010
Phone: 208-885-6162
Fax: 208-885-5752
irb@uidaho.edu

To: Chantal Vella

From: Leontina M. Hormel, Ph.D.
Chair, University of Idaho Institutional Review Board
University Research Office
Moscow, ID 83844-3010

Date: 10/13/2014 11:40:03 AM

Title: Relationship between physical activity, quality of life, and resilience in patients with Inflammatory Bowel Diseases

Project: 14-442

Certified: Certified as exempt under category 2 at 45 CFR 46.101(b)(2).

On behalf of the Institutional Review Board at the University of Idaho, I am pleased to inform you that the protocol for the above-named research project has been certified as exempt under category 2 at 45 CFR 46.101(b)(2).

This study may be conducted according to the protocol described in the Application without further review by the IRB. As specific instruments are developed, modify the protocol and upload the instruments in the portal. Every effort should be made to ensure that the project is conducted in a manner consistent with the three fundamental principles identified in the Belmont Report: respect for persons; beneficence; and justice.

It is important to note that certification of exemption is NOT approval by the IRB. Do not include the statement that the UI IRB has reviewed and approved the study for human subject participation. Remove all statements of IRB Approval and IRB contact information from study materials that will be disseminated to participants. Instead please indicate, 'The University of Idaho Institutional Review Board has Certified this project as Exempt.'

Certification of exemption is not to be construed as authorization to recruit participants or conduct research in schools or other institutions, including on Native Reserved lands or within Native Institutions, which have their own policies that require approvals before Human Subjects Research Projects can begin. This authorization must be obtained from the appropriate Tribal Government (or equivalent) and/or Institutional Administration. This may include independent review by a tribal or institutional IRB or equivalent. It is the investigator's responsibility to obtain all such necessary approvals and provide copies of these approvals to ORA, in order to allow the IRB to maintain current records.

As Principal Investigator, you are responsible for ensuring compliance with all applicable FERPA regulations, University of Idaho policies, state and federal regulations.

This certification is valid only for the study protocol as it was submitted to the ORA. Studies certified as Exempt are not subject to continuing review (this Certification does not expire). If any changes are made to the study protocol, you must submit the changes to the ORA for determination that the study remains Exempt before implementing the changes. Should there be significant changes in the protocol for this project, it will be necessary for you to submit an amendment to this protocol for review by the Committee using the Portal. If you have any additional questions about this process, please contact me through the portal's messaging system by clicking the 'Reply' button at either the top or bottom of this message.

Leontina M. Hormel, Ph.D.