Living With Ulcerative Colitis: Exploring Dietary Inflammatory Intake, Physical Activity, and Methods to Manage the Burden of Illness

Kelli E. DuBois

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Living with Ulcerative Colitis: Exploring Dietary Inflammatory Intake, Physical Activity, and Methods to Manage the Burden of Illness

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ABSTRACT

Ulcerative Colitis (UC) is a chronic illness under the umbrella of Inflammatory Bowel Disease (IBD). IBD is becoming a global health issue as incidence rates are rising throughout the world. UC is characterized by chronic inflammation and ulcerations in the colon’s mucosal lining due to abnormal inflammatory and immune system responses. Patients with UC experience a range of gastrointestinal and extraintestinal symptoms as well as psychosocial challenges throughout the course of illness that generate a significant burden on daily life. Periods of active disease, or flares, present exacerbations of disease symptoms and the greatest burden on daily functioning, yet disease activity often fluctuates in symptom severity over the disease course and much of the extraintestinal burden continues throughout periods of remission as well. Many of those diagnosed with UC seek out a combination of medical, lifestyle, and/or alternative treatment and management methods in efforts to mitigate disease symptoms, reduce dependence upon pharmaceuticals, and respond to the challenges of living with chronic health condition.

Current literature is lacking sufficient description of how individuals use treatment and management methods on a daily basis and over the disease course, as well as examination of the perspectives, resources, and motivations supporting utilization of various methods. Despite limited evidence to support consistent dietary recommendations for the management of UC, dietary change is a popular self-management method among UC patients. Popular diets currently recommended for UC
lack evidence of effective healing of the inflamed and ulcerated mucosal lining of the colon. The Energy-Adjusted Dietary Inflammatory Index (E-DII™) measures the inflammatory potential of food intake and has never been studied among the UC population. Additionally, physical activity is highly likely to contribute to a reduced burden of illness among individuals with UC, yet few studies have examined physical activity among this population. Recommendations for physical activity among the UC population do not currently exist. Two specific aims were proposed for this dissertation and addressed using two distinct studies.

The specific aim of study 1 was to examine how treatment and management methods are used by individuals who have been living with UC for at least 5 years and how patients make decisions regarding the use of these treatment and management methods for UC. Qualitative data were collected using individual semi-structured interviews addressing the participant’s retrospective illness trajectory, the impact of UC on daily life, experiences with medical and complementary or alternative treatment methods used to control disease activity, methods for self-managing the impact of UC on daily living, and processes of making decisions regarding treatment and management of UC of the course of illness. Eligibility criteria included: 1) diagnosis of UC; 2) duration of illness ≥5 years; and 3) a minimum of one disease flare during the course of illness. Patients (n=21) were recruited in collaboration with a large gastroenterology clinic in South Carolina, a support group for individuals experiencing Crohn’s and UC, an integrative medicine clinic in South Carolina, and through posting study fliers in two UC focused Facebook support groups. Thematic analysis was conducted using NVivo 12
software. Iterative coding led to the organization of meaningful themes and sub-themes across all interviews to capture key elements the participants’ experiences.

The specific aim of study 2 was to examine associations between dietary inflammatory potential, physical activity, and health outcomes associated with the burden of living with UC. Data obtained from participants in the IBD Partners e-cohort who self-reported UC (n=2,052) were analyzed using a cross-sectional, secondary data analysis. Dietary data collected through a National Cancer Institute dietary screener were converted into an E-DII score. Physical activity data were collected using the Godin-Shephard Leisure Time Activity Index. Outcome variables included the Simple Clinical Colitis Activity Index (SCCAI), Short Inflammatory Bowel Disease Questionnaire (SIBDQ), and PROMIS domains of anxiety, depression, fatigue, sleep disturbance, and social satisfaction. Multivariable regression models controlled for age, sex, body mass index (BMI), race, education, diet, physical activity, smoking status, medication class, and disease duration.

From study 1, we observed that decisions are shaped by a patient’s approach towards disease management, personal experiences, sources of information, and individual motivating factors. A driving factor in decision making is personal suffering. Patients are willing to try new methods of management and overlook long-term implications in order to reduce suffering and be able to ‘function’ in the present day. Suffering may motivate long term behavior change, but the majority of participants tend to utilize most treatment and management methods as responses to flares and UC suffering instead of as preventative health behaviors. While patients identify some medications and overall stress reduction as important methods to avoid UC flares,
treatment and management methods are predominantly employed as efforts to recover from flares and reduce existing symptoms.

Findings from study 2 showed that pro-inflammatory dietary intake, indicated by E-DII score, was associated with increased disease activity ($\beta=0.166; p<0.001$), anxiety ($\beta=0.342; p=0.006$), depression ($\beta=0.408; p=0.004$), fatigue ($\beta=0.386; p=0.005$), sleep disturbance ($\beta=0.339; p=0.003$), and decreased social satisfaction ($\beta=-0.370; p=0.004$) and IBD-related quality of life ($\beta=-0.056; p<0.001$). Leisure time activity was inversely associated with disease activity ($\beta=-0.108; p<0.001$), anxiety ($\beta=-0.025; p=0.001$), depression ($\beta=-0.025; p=0.001$), fatigue ($\beta=-0.058; p<0.001$), and sleep disturbance ($\beta=-0.019; p=0.008$), while positively associated with social satisfaction ($\beta=0.063; p<0.001$), and IBD-related quality of life ($\beta=0.005; p<0.001$). The benefit among health outcomes, excluding depression, was greater for strenuous exercise intensity than for moderate or mild intensities. For all outcomes, interaction effects between E-DII and physical activity were not significant.

This dissertation offers added insight into how and why treatment and management methods are used to reduce the physical and psychosocial burden of illness associated with UC. Findings suggest that an anti-inflammatory diet and physical activity are each complementary lifestyle methods that may contribute to decreases in disease activity, anxiety, depression, and fatigue, and improvements in health-related quality of life, sleep, and social satisfaction. Such modalities may aid in managing systemic and localized inflammation associated with UC and reduce the burden of UC on daily living. More research in this area will contribute to creating evidence-based dietary and physical activity recommendations for the UC population. Findings from this
dissertation can aid in framing patient education and behavioral interventions that assist patients with UC in adopting and sustaining self-management behaviors to reduce and prevent disease activity. Future research is needed to design and evaluate ways to shift treatment and management approaches away from reactive behaviors and promote preventative self-management.
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CHAPTER 1

INTRODUCTION

Ulcerative Colitis (UC) is a chronic illness under the umbrella of Inflammatory Bowel Disease (IBD) characterized by chronic inflammation and ulcerations of the colon’s mucosal lining due to abnormal immune system responses (Crohn’s and Colitis Foundation, 2022; Porter et al., 2020). Reports estimate that over 6.8 million people are living with IBD across the world and indicate over 2 million Europeans and 1.5 million North Americans are currently diagnosed with IBD (Alatab et al., 2020; Jairath & Feagan, 2020; Ng et al., 2017). Despite the complexity of the condition and irregularities in reporting and data collection (Mulder et al., 2014), IBD is becoming a global health issue as incidence rates are rising throughout the world (Jairath & Feagan, 2020; Windsor & Kaplan, 2019). North America is reported to hold one of the highest reported prevalence values of Ulcerative Colitis in the world, with 286 cases per 100,000 people (Ng et al., 2017). Reports suggest that incidence rates are stabilizing in western countries while prevalence continues to rise due to improved survival, and rising incidence rates are evident across, South America, Eastern Europe, Asia, and Africa (Alatab et al., 2020; Ng et al., 2017; Olfatifar et al., 2021). The cause of UC is unknown. Current frameworks suggest the development and progression of UC is a complex combination of environmental factors, abnormal immune response, gut microbiota, and genetic predisposition (Porter et al., 2020).
Individuals with UC experience lifelong unpredictable fluctuations between periods of disease remission and exacerbations of disease activity (Falvo & Holland, 2018). Disease activity generates physical symptoms such as abdominal pain, rectal bleeding, bowel urgency, bowel frequency, diarrhea, and fatigue, along with various extraintestinal manifestations of disease, which interfere with maintaining normal daily activities (Fourie et al., 2018; Hall et al., 2005; Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008). Regardless of whether disease is active, the majority of individuals with UC report decreased work productivity, anxiety and depression, isolation, strained relationships, ‘brain fog’, poor sleep quality, and negative body image (Falvo & Holland, 2018; Fedosiejew et al., 2016; López-Sanromán et al., 2017; McMullan et al., 2017). UC has been found to influence choices regarding employment status, career planning and development, family planning, and social engagement (Fourie et al., 2018; Hall et al., 2005; Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008).

Medical treatments for UC aim to reduce symptoms and induce a state of remission through reducing inflammation using pharmaceutical therapies. While certain drugs can lead to improvements in reducing disease activity, many patients report that pharmaceuticals, overall, provide insufficient treatment to induce or maintain remission and overcome the burden of UC in everyday life (Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008). Additionally, the cost of medication is a key driver of healthcare spending on UC (Beard et al., 2020), which has implications for patient affordability and access to new medicines.
Many of those diagnosed with UC seek out a combination of medical, lifestyle (e.g., diet, physical activity), and/or alternative treatment and management methods in efforts to mitigate disease symptoms, reduce dependence upon pharmaceuticals, avoid medication side effects, achieve disease remission, reduce the burden of illness on the activities of every-day life, and improve overall quality of life (Fourie et al., 2018; le Berre et al., 2020; McCormick et al., 2012; McMullan et al., 2017; Wolfe & Sirois, 2008). While existing research has indicated the use of various treatment and management methods among individuals with UC, current literature is lacking sufficient description of how individuals use treatment and management methods on a daily basis and over the disease course, and examination of the perspectives, resources, and motivations supporting utilization of various methods (Crooks et al., 2021).

Despite limited evidence to support consistent dietary recommendations for the management of UC, dietary change is a popular self-management method among UC patients (Rizzello et al., 2019). With varying success, many patients attempt to identify and avoid foods that seem to trigger gastrointestinal symptoms or adopt highly restrictive diets in response to a disease flare (Cohen et al., 2014; Jowett et al., 2004). Exclusionary diet practices can result in healthier dietary intake, but also can result in malnutrition, disengagement from social activities, excessive cognitive energy spent on food choices, frustration with the desire for excluded foods, and significant distress after straying from dietary exclusion goals (Nazarenkov et al., 2019). Low fiber diets are often suggested to help ease the roughage passing through an inflamed colon during UC flares. Indeed, low-fiber and exclusion diets tend to be strongly pro-inflammatory (Khayyatzadeh et al., 2017; Krishnamurthy et al., 2012; Y. Ma et al., 2008). So, this prescription could tend to
exacerbate the problem and amplify symptoms when adopted for an extended period of time. There is very limited evidence about the effectiveness of these recommended exclusion diets in healing the inflamed and ulcerated mucosal lining of the colon.

A successful approach to food choice among individuals with UC may be the adoption of an anti-inflammatory dietary lifestyle to manage the burden of living with UC. Outside of the development of the IBD Anti-Inflammatory Diet (IBD-AID) protocol and subsequent examination of its interaction with the microbiome (Olendzki et al., 2022; Olendzki et al., 2014), the adoption of an anti-inflammatory dietary lifestyle has not been otherwise examined as a complementary treatment approach and self-management method for UC. An anti-inflammatory diet may play a role in managing the localized and systemic inflammation associated with UC and therefore may decrease disease activity and associated extraintestinal manifestations of illness.

The Dietary Inflammatory Index (DII®) is a literature-derived dietary index developed to measure the inflammatory potential of one’s food intake (Shivappa, et al., 2014a). Outside of a study showing that a pro-inflammatory diet was a risk factor for developing UC (Shivappa, et al., 2016a and another one producing suggestive results (Mirmiran et al., 2019), the DII has never been studied among the UC population.

In addition to diet, physical activity (PA) is another behavioral method UC patients use for reduction and management of the physical and psychosocial burden of illness. PA is widely known to reduce stress and depression, regulate systemic inflammation, reduce the risk of co-morbidities, improve social relationships, and demonstrate quality of life benefits among the general population. Physical activity is highly likely to contribute to a reduced burden of illness among individuals with UC, yet
few studies have examined PA among this population. Existing studies on PA and IBD suggest that although patients struggle with motivation to exercise during periods of active disease, engagement in PA or structured exercise is associated with improvements in quality of life, fatigue, and mental health (Eckert et al., 2019; Lamers et al., 2021; Raman et al., 2021; Wiestler et al., 2019). Additionally, evidence suggests that physical activity also may be an effective modifier in the disease course of UC (Eckert et al., 2019; Engles et al., 2018). However, recommendations for PA and maintenance of health among the UC population do not currently exist. Research is needed to determine the magnitude of effect physical activity has on decreasing the burden of illness associated with UC. Additionally, recent reviews call for data on the intensity and frequency of exercise that would generate the greatest benefit among individuals with UC in order to determine exercise recommendations for this population (Eckert et al., 2019; Engles et al., 2018; Nathan et al., 2013; Raman et al., 2021).

This work is a mixed-methods design that utilizes both qualitative and quantitative approaches to understand the effect of treatment and management methods on the daily burden of Ulcerative Colitis. To address the aims of this dissertation two separate studies are presented. Study 1 examines how treatment and management methods are used by individuals with UC and how patients make decisions regarding the use of these methods throughout the disease course. Study 2 examines associations between diet-related inflammation, as indicated by the DII, physical activity at varying intensities, and both physical and psychosocial health outcomes associated with the burden of living with UC.
This study offers added insight regarding why patients use various treatment and management methods and how behavioral methods of diet and physical activity may impact the physical and psychosocial burden of illness on daily life. To our knowledge, this is the first study to use the DII to examine dietary inflammatory potential and UC-related physical and psychosocial health outcomes. Findings from this study contribute to the development of dietary and physical activity recommendations for the UC population and may inform evidence-based models of patient care and behavioral health methods for reducing the burden of UC in daily life.

**Research Objectives and Aims**

This research aims to:

1. Examine how treatment and management methods are used by individuals who have been living with UC for at least 5 years and how patients make decisions regarding the use of these treatment and management methods for UC.
   
   a. What treatment and management methods do those living with UC for at least 5 years report using over the disease course?
   
   b. In what ways do patients utilize treatment and management methods in their daily life?
   
   c. In what ways do patients with UC perceive the influence of treatment and management methods on the burden of illness associated with UC?
      
      i. How do individuals with UC describe the impact of illness on their quality of life?
   
   d. How do those living with UC for at least 5 years make decisions about the use of treatment and management methods for UC?
i. How do individuals living with UC perceive their self-efficacy and agency in self-managing their illness experience?

ii. Where do individuals with UC learn about treatment and management methods?

iii. How do those living with UC describe the incentives for the use of treatment and management methods?

iv. How do those living with UC describe the deterrents and barriers for the use of treatment and management methods?

2. Examine associations between dietary inflammatory potential, physical activity, and health outcomes associated with the burden of living with UC.

**Hypothesis 1.** Anti-inflammatory dietary intake will be negatively associated with disease activity scores, symptoms of anxiety, symptoms of depression, fatigue, and sleep disturbance, and positively associated with satisfaction with social role, and IBD-related quality of life.

**Hypothesis 2.** Physical activity will be negatively associated with disease activity scores, symptoms of anxiety, symptoms of depression, fatigue, and sleep disturbance, and positively associated with satisfaction with social role, and IBD-related quality of life.

**Hypothesis 2a.** Increased engagement in physical activity at a moderate intensity will have a stronger inverse association with disease activity scores, anxiety, depression, fatigue, and sleep disturbance, and a stronger positive association with satisfaction with social role, and IBD-related quality of life than an increase in physical activity at a strenuous or mild intensity.
Hypothesis 3. Physical activity will amplify the relationship between an anti-inflammatory diet and disease activity scores, IBD-related quality of life, and patient reported outcomes (anxiety, depression, fatigue, sleep disturbance, and satisfaction with social role).

Hypothesis 3a. The interaction between moderate physical activity and high anti-inflammatory dietary intake will have the strongest associations with low disease activity scores, high IBD-related quality of life, low anxiety, low depression, low fatigue, low sleep disturbance, high satisfaction with social role.

Overview

The next chapter (Chapter 2) includes a review of the literature regarding Ulcerative Colitis, the burden of illness associated with UC, and treatment for the management of UC. Chapter 2 also describes the conceptual framework guiding this work and reviews the significance of this research contribution. Chapter 3 describes the study design and methodology used to address the aims of this research. Chapter 4 presents the results of the research in two distinct manuscripts. Chapter 5 presents a summary of the main findings and a discussion about the implications for future research.
CHAPTER 2
BACKGROUND AND SIGNIFICANCE

This chapter will describe Ulcerative Colitis (UC), the impact of UC on patients’ lives, and existing treatment and management methods. An overview of UC and rates of prevalence and incidence will be described, followed by a discussion of the potential etiology of UC. The burden of illness that accompanies UC is presented, followed by a discussion of treatment and management methods available to patients. The conceptual framework for this work is presented followed by a discussion of this dissertation’s significance.

Background

2.1 Ulcerative Colitis

Ulcerative Colitis (UC) is a chronic illness under the umbrella of Inflammatory Bowel Disease (IBD) characterized by chronic inflammation and ulcerations of the colon’s mucosal lining due to abnormal immune system responses (Crohn’s and Colitis Foundation, 2022; Porter et al., 2020). Individuals with UC may experience disease severity ranging from mild to moderate or severe (Peyrin-Biroulet et al., 2016) with lifelong unpredictable fluctuations between periods of disease remission and exacerbations of disease activity (Falvo & Holland, 2018). Patients suffer from gastrointestinal (GI) symptoms associated with UC, predominantly rectal bleeding, abdominal pain, bowel urgency, bowel frequency, and diarrhea that interfere with
maintaining normal daily activities (Fourie et al., 2018; Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016) as well as extraintestinal manifestations of illness affecting joints, skin, and the eyes (Ghosh et al., 2021; Wolfe & Sirois, 2008). Patients also report considerable physical and cognitive fatigue, isolation, reduced productivity, limited professional development, ‘brain fog’, diminished self-concept, anxiety, depression, strained relationships, as well as strained physical, emotional, and social functioning (Devlen et al., 2014; Fedosiejew et al., 2016; Fourie et al., 2018; López-Sanromán et al., 2017; Matini & Ogden, 2016; Yarlas et al., 2018). Overall, living with UC generates a significant burden on daily functioning and long-term well-being.

2.1.1 Prevalence/Incidence

Reports estimate that over 6.8 million people are living with IBD across the world, and indicate over 2 million Europeans and 1.5 million North Americans are currently diagnosed with IBD (Alatab et al., 2020; Jairath & Feagan, 2020; Ng et al., 2017). The majority of cases are currently diagnosed in Western societies, reflecting to some extent reporting and diagnosis bias (Delgado-Rodríguez & Llorca, 2004; Jairath & Feagan, 2020; Solomon, 1992). Despite the complexity of the condition and irregularities in reporting and data collection (Mulder et al., 2014), IBD is becoming a global health issue as incidence rates are rising throughout the world (Jairath & Feagan, 2020; Windsor & Kaplan, 2019). Reports suggest that incidence rates are stabilizing in western countries while prevalence continues to rise due to improved survival, while rising incidence rates are evident across South America, Eastern Europe, Asia, and Africa (Alatab et al., 2020; Ng et al., 2017). Indeed, IBD is known to be grossly underreported in India (Amarapurkar et al., 2018; Banarjee et al., 2020; Jain & Venkataraman, 2021;
Maroo et al., 1974; Olfatifar et al., 2021; Patel et al., 2013) where UC has been determined to be a “sleeping giant” (Juyal et al., 2018). Compounding prevalence is due, in part, to improved survival rates (due to development of new therapies and improved surgical outcomes), increases in early-onset IBD, and the resulting lengthened disease duration, creating a potential for complex disease trajectories (Jairath & Feagan, 2020; Kaplan & Windsor, 2021; Windsor & Kaplan, 2019).

In western regions (i.e. developed economies; regions predominantly colonized by Europeans), the incidence range for UC is 23.1-57.9 per 100,000 (Crohn’s disease range is 23.8-29.3 per 100,000) (Kaplan & Windsor, 2021; Ng et al., 2017). North America currently holds one of the highest reported prevalence values of Ulcerative Colitis in the world, with 286 cases per 100,000 people (Ng et al., 2017). Studies have previously found a higher prevalence of UC among high income White Americans, with prevalence rates among minority racial groups around 50-75% of those rates among White individuals (Aniwan et al., 2019; Sonnenberg et al., 2017), but adequate evaluation of current racial and ethnic distribution is lacking (Aniwan et al., 2019). Sonnenberg et al., (2017) found prevalence of IBD to be highest in individuals aged 20-29 years, though other studies have found the median age of diagnosis for UC to range from 28-34.9 years (Long et al., 2012; Shivashankar et al., 2017). Diagnoses of UC among men and women have been found to have a relatively equal distribution (Shivashankar et al., 2017; Sonnenberg et al., 2017).

2.1.2 Potential Etiology of Ulcerative Colitis

The cause of UC is unknown. Current frameworks suggest the development and progression of UC is a complex combination of environmental factors, abnormal immune
response, gut microbiota, and genetic predisposition (Porter et al., 2020). Environmental factors may include lifestyle behaviors such as smoking, sleep, stress, diet, and breastfeeding, ecological factors such as pollution, and pharmacologic agents such as antibiotics or vaccinations (Abegunde et al., 2016).

Some researchers parallel rapidly rising rates of UC with the adoption of the westernized diet and culture in Eastern countries (Kaplan & Windsor, 2021; Rizzello et al., 2019; Windsor & Kaplan, 2019). Processed foods, refined sugars, dairy, and less plant-based fiber consumption has been linked with rising incidence rates in newly industrialized nations (Jairath & Feagan, 2020; Windsor & Kaplan, 2019), giving rise to increased attention to the impact of diet and various lifestyle health behaviors on the UC disease course.

Stress is widely recognized to influence risk for digestive illnesses, and commonly believed by UC patients to be a precursor for disease flares. Prolonged stress can elicit numerous physiological reactions that contribute to immune dysfunction and increased inflammation (Glaser & Kiecolt-Glaser, 2005). Living with UC is, in itself, a chronic stressor. The burden of illness associated with UC contributes to the ongoing nature of the illness by adding prolonged stress and, therefore, systemic inflammation and a reduced immune system (Fedosiejew et al., 2016). Prolonged stress also contributes to imbalances in the microbiome and natural gut flora, shown to be associated with UC (Aleksandrova et al., 2017; Lane et al., 2017).

2.2 Burden of Illness Associated with Ulcerative Colitis

Living with UC often gives rise to a considerable personal burden of illness, compounded by the unpredictable fluctuations between periods of remission and disease
exacerbation. Periods of active disease, or flares, present exacerbations of gastrointestinal symptoms and carry the greatest burden on daily functioning, yet disease activity often fluctuates in symptom severity over the disease course and much of the extraintestinal and psychosocial burden continues throughout periods of remission as well.

2.2.1 Gastrointestinal Symptoms

The most prominent localized physical symptoms reported among individuals with UC include rectal bleeding, abdominal pain, bowel urgency, bowel frequency and diarrhea (Fourie et al., 2018; Hall et al., 2005; Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008). Such symptoms require proximity to a restroom and challenge one’s ability to run errands, go shopping, travel, or attend social events. Patients often refer to episodes of exacerbations of disease symptoms as ‘flares’ and periods of little to no gastrointestinal symptoms as ‘remission’, with varying descriptions of symptom severity between such states (Devlen et al., 2014). Flares have been referred to by individuals living with UC as ranging from ‘mild’ or ‘the beginnings of a flare’ to having a ‘bad’ or ‘gigantic’ flare (Devlen et al., 2014).

2.2.2 Pain and Extraintestinal Manifestations

Between 50 and 70% of patients with IBD experience pain over the disease course, with 20% of patients experiencing pain during periods of remission (Fedosiejew et al., 2016). Physical pain often accompanies the symptoms of UC, yet sometimes manifests despite remission of active GI symptoms. Pain is often reported locally in the abdomen region, as well as manifesting extra-intestinally as arthropathy (i.e., joint pain). In a study with over 2,500 participants diagnosed with UC, 47.2% of patients reported painful joints (Long, 2012). Other extraintestinal manifestations of illness, such as eye
inflammation, mouth ulcerations, or various skin conditions have also been reported (Long, 2012; Wolfe & Sirois, 2008).

2.2.3 Fatigue

Fatigue is a predominant burden of illness and can be worse when UC activity is in remission (Keefer et al., 2022; Matini & Ogden, 2016; McMullan et al., 2017). Physical symptoms leave UC patients feeling drained with little to no energy. Systemic inflammation and use of immunosuppressant medications also contribute to chronic fatigue that is often reported by patients as different than typical tiredness (Keefer et al., 2022; Lacourt et al., 2018; Villoria et al., 2017). Reports of tiredness and lack of energy may be compounded by difficulty sleeping reported by patients (Wickman et al., 2016). As a result, patients must prioritize where to allocate their limited energy and often feel restricted in their daily activities (Matini & Ogden, 2016). Patients have expressed the burden of cognitive fatigue as well, given the continual need to attend to symptoms, spend cognitive energy on disease management and prevention of worsening symptoms, and worry about future flares and cancer risks (Fedosiejew et al., 2016; Hall et al., 2005; Wolfe & Sirois, 2008). Patient reported ‘brain fog’ is also believed to limit cognitive productivity and memory (Keefer et al., 2022).

2.2.4 Mental Health and Emotional Distress

High rates of psychiatric disorders are prevalent among individuals with UC. Among patients with UC, research estimates an incidence rate ratio of 1.58 (95% CI:1.41-1.76) for depression and 1.39 (95%CI: 1.26-1.53) for anxiety compared to the general population (Bernstein et al., 2019; Engel et al., 2021). Regardless of active disease, symptoms of anxiety persist for many individuals throughout the disease course
(Faust et al., 2012). The nature of a chronic illness, the implications of UC on daily life, and the disease symptoms that accompany UC each contribute to depression, anxiety, and emotional distress. The majority of individuals with UC report varying levels of emotional distress, as making sense of a chronic illness with an unknown cause and no available cure can weigh heavily a patient’s emotional well-being (Fourie et al., 2018; Hall et al., 2005; Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008). Patients with UC report that the stressors of diagnostic procedures, uncomfortable or embarrassing symptoms, and limitations on daily activities are compounded by fear and anxiety toward the overarching uncertainty surrounding treatment efficacy and the future course of illness (Devlen et al., 2014; Fedosiejew et al., 2016; López-Sanromán et al., 2017; Matini & Ogden, 2016). In addition, the chronic nature of UC and the distressing implications can have a significant impact on an individual’s perception of life’s goals, meaning, and purpose, with feelings of loss revisited with each exacerbation of disease activity (Fedosiejew et al., 2016; Pereira, 1984).

UC has been described as an ‘invisible’ illness, where many patients feel that others, including health professionals, do not recognize, understand, or validate the gravity of their illness experience (Fourie et al., 2018; Hall et al., 2005; Wolfe & Sirois, 2008). Many patients express feelings of loneliness and difficulty sharing their feelings about UC with others and letting others into their illness experience (Wickman et al., 2016). Such social and emotional isolation contributes to depression and depressive symptoms. UC is often accompanied with diminished self-concept, guilt, anger, frustration, and self-blame (Fedosiejew et al., 2016; López-Sanromán et al., 2017).
Additionally, participants experience poor sleep, strained relationships, and significant social anxieties around symptom management, which heightens overall emotional distress.

2.2.5 Economic Burden

A report on the economic implications of IBD in the US estimated direct and indirect costs to range between at least $14.6 and $31.6 billion annually (Mehta, 2016). The direct and indirect costs of IBD, driven by medical therapies, hospitalizations, surgeries, lost work time, etc., generate a substantial economic burden on patients and health care systems with costs specifically for UC totaling nearly $15 billion annually (Beard et al., 2020). In the US, patients may be burdened with substantial direct costs for medications, physician appointments, diagnostic procedures, surgeries, and other associated hospital tests and treatments. A 2010 review estimated annual per-patient direct medical costs for UC patients to range from $6,217 to $11,477 in the US (Cohen et al., 2010). Multiple costly new medications, such as injection and infusion treatments, have been incorporated into patient care since these estimates were calculated. In 2015, a systematic review estimated annual per-patient indirect costs to range from $2,424.01 to $9,622.15 (Kawalec, 2016). Indirect costs are incurred by work absenteeism, decreased productivity, limited work capacity and professional development, as well as time spent attending to the disease. Psychological treatment and care and other complementary and alternative therapies can be very costly as well. Health insurance is pivotal for access to medical treatments and care. Reliance on supplemental coverage programs to reduce out of pocket costs is high among patients receiving injections, infusions, and other recently released pharmaceutical treatment options.
2.2.6 Impact on Daily Life

Due to the physical and emotional burden of UC, the majority of individuals with UC report decreased productivity at work and home, social isolation, and negative body image (Fourie et al., 2018). Many patients feel like a burden or disappointment to their family and friends, while others feel restricted from developing close relationships due to their illness (Fedosiejew et al., 2016; Fourie et al., 2018; Wolfe & Sirois, 2008). UC often restricts choices regarding employment status, career development, family planning, and social engagement (Devlen et al., 2014; Fedosiejew et al., 2016; Fourie et al., 2018; Matini & Ogden, 2016; McMullan et al., 2017). Despite best efforts to manage their chronic health condition, many patients report significant difficulty committing to social events or making plans for the future, due to the unpredictable nature of UC (Devlen et al., 2014; Matini & Ogden, 2016).

2.2.7 Quality of Life

Quality of Life (QoL) encompasses an individual’s perception of their position in life in relation to their values, goals, expectations, and standards (World Health Organization, 2022). IBD is associated with a decreased QoL, with patients experiencing a lower QoL than healthy individuals (Knowles et al., 2018). QoL among individuals with IBD is often described by physical, emotional, systemic, and social domains (Irvine, 1996). Health related quality of life (HRQoL) encompasses one’s physical and mental health impact on the ability to live a fulfilling life (Carr et al., 2001). Wolfe & Sirois (2008) identified patient-reported dimensions of HRQoL affected by IBD to include 1) physical, 2) emotional, 3) social, 4) cognitive 5) self-regulatory (feelings of control), and 6) practical (economic). Studies have shown a significant inverse
relationship between disease activity and HRQoL among the UC population (Faust et al., 2012). The burden of illness associated with UC, including GI symptoms, pain, fatigue, financial costs, emotional distress, etc., influences all dimensions of HRQOL. High anxiety and depression symptoms have been shown to significantly reduce HRQoL among patients with UC (Faust et al., 2012). The magnitude of UC’s burden on daily life and overall QoL is influenced by perceptions of control, coping skills, and social support (Wolfe & Sirois, 2008). In general, individuals with a chronic illness who can rely on family members or a support group tend to experience a higher QoL (Fedosiejew et al., 2016).

2.3 Treatment

Although there is currently no cure for UC, multiple methods exist to manage disease symptoms and reduce the burden of illness on every-day life. The main goal of medical treatments for UC is to reduce GI symptoms and induce a state of remission by regulating the immune system with pharmaceutical therapies (Crohn’s & Colitis Foundation, 2021; Falvo & Holland, 2018; Wickman et al., 2016). For the majority of individuals with UC, pharmacotherapy is insufficient to regain and maintain a ‘normal’ lifestyle (Fourie et al., 2018; Matini & Ogden, 2016; McMullan et al., 2017). Medications for UC can be very costly and bring a range of side effects (e.g., weight gain, fatigue, nausea, skin rashes, and musculoskeletal pain).

Many of those diagnosed with UC seek out a combination of medical, complimentary, and/or alternative treatment methods, as well as undertake social and lifestyle adaptations to self-manage disease symptoms, reduce dependence upon pharmaceuticals, and respond to the challenges of living with chronic illness.
Manipulations to diet intake, adjustments in physical activity, chiropractic treatment, probiotic use, and stress reduction techniques have been reported (Fourie et al., 2018; Hall et al., 2005; Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008). Seeking out new and personal preference-based self-management options for treatment of UC has been associated with a high QoL and successful self-management (Wickman et al., 2016).

2.3.1 Pharmacologic Treatment

The most common approach for treatment and management of UC symptoms is physician-prescribed pharmaceutical therapies. Pharmacological management of UC can include aminosalicylates, corticosteroids, immunomodulators, biologic or biosimilar therapies, and target synthetic small molecules (or Janus Kinase (JAK) Inhibitors) (Crohn’s & Colitis Foundation, 2021). Aminosalicylates contain 5-aminosalicylic acid (5-ASA) and target the surface lining of the colon to decrease inflammation.

Corticosteroids suppress the entire immune response and are often used in response to disease flares, though rarely used as long-term maintenance medication. Immunomodulators suppress the entire immune system and can increase the effectiveness of other UC medications, such as biologics. Biologics are protein-based antibodies that block inflammation-causing proteins in the body. JAK inhibitors target specific parts of the immune system to reduce inflammation. (Crohn’s & Colitis Foundation, 2021) Some medications are ingested in pill form, while others are administered through injections or infusions.

Medications for UC are prescribed in reaction to disease activity with the goal of decreasing GI symptoms, regulating the immune system, and moving toward healing the
inflamed mucosal lining of the colon. While pharmaceutical treatments provide beneficial improvements to disease activity, patients report pharmaceuticals overall as insufficient treatment (Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008). The use of multiple concurrent medications is not uncommon in attempts to control symptoms (Falvo & Holland, 2018; McMullan et al., 2017). Continuous medication use is accompanied by various side effects (e.g., weight gain, fatigue, nausea, skin rashes, and musculoskeletal pain) that may add to the burden of illness. Many medications used for treatment of UC suppress the immune system and can lead to additional health challenges. The majority of pharmaceutical treatments, particularly biologic therapies, are known to lose effectiveness over time, or when administered after the use of a similar biological agent (Cleveland et al., 2022). This loss of response to medication leads to disease relapse, emotional distress, and progressive use of stronger and more costly medications.

2.3.2 Surgery

Some patients with UC choose to undergo colectomy surgery to remove diseased portions of the colon. In cases when patients become unresponsive to available treatments or dangerously ill, surgery may be recommended or required (Crohn’s & Colitis Foundation, 2021). In many cases surgery provides relief to patients and improves HRQOL (Brown et al., 2015). For an ileostomy, a surgeon will create a small hole in the abdominal wall and invert a piece of the small intestine to expel waste into an ostomy pouch worn outside of the abdomen. More commonly today, patients choose a proctocolectomy ileal pouch-anal anastomosis. Typically performed in 3 stages of surgery, the colon and rectum are removed and the small intestine is attached to the anus.
with an internal pouch (J-pouch) created from the small intestine. This procedure still allows patients to have bowel movements and use the bathroom (Crohn’s & Colitis Foundation, 2021).

2.3.3 Diet and Ulcerative Colitis

Despite limited evidence to support consistent dietary recommendations for the management of UC, dietary change is a popular self-management method among UC patients (Rizzello et al., 2019). Clinical evidence is lacking on the impact of diet on disease activity, leaving physicians unable to provide dietary recommendations for their patients (Cohen et al., 2013; Sáez-González et al., 2019). Individuals with UC believe that their diets play a role in managing disease symptoms and have reported diet manipulation as a strategy for managing GI symptoms for quite some time (Hall et al., 2005). At the same time, research examining diet as a behavioral treatment and management method for mitigating disease activity is relatively new (Celiberto et al., 2018; Torres et al., 2019; Wark et al., 2021). Patients with severe cases of disease often rely on parenteral nutrition administered through a feeding tube in order to eliminate the passage of food substance through the intestines. Such a change in ‘normalcy’ is often associated with depression (Fedosiejew et al., 2016).

With varying success, many patients attempt to identify and avoid foods that seem to trigger GI symptoms or adopt highly restrictive diets (Cohen et al., 2014; Jowett et al., 2004). Many patients attribute symptom exacerbations to particular foods and adopt self-dictated exclusionary diet practices. Others struggle to identify beneficial dietary changes through exclusionary trial and error. Some patient-reported foods that are perceived to worsen symptoms (e.g., dairy, ice cream, soda, sugar, high-fiber foods, leafy
and non-leafy vegetables, gluten, fatty foods, corn, red meat, chocolate, nuts, fruits) overlap with foods also reported by other patients to improve symptoms (e.g., milk, cheese, cereal, whole grains, leafy and non-leafy vegetables, potatoes, rice, fruit) (Cohen et al., 2013). Patients have also reported that despite doing everything ‘right’ (i.e., food selection, managing symptoms), many still experience flares with significant accompanying discouragement and frustration (Devlen et al., 2014).

Popular diets currently recommended for UC, such as the Specific Carbohydrate Diet (SCD) (Cohen et al., 2014), Low-FODMAP diet (Carlson et al., 2015), and low-fiber recommendations, have received the most attention among the UC community and aim to reduce irritable bowel (note: irritable bowel vs inflammatory bowel) symptoms such as gassiness or diarrhea. Scientific studies have explored the influence of dietary manipulations on disease activity among UC patients with varying outcomes. Diet has been shown to improve outcomes associated with UC, but specific dietary recommendations continue to remain inconsistent across the field (Raman & Ghosh, 2019; Sáez-González et al., 2019; Wark et al., 2021).

The SCD diet excludes complex carbohydrates, sugar, and dairy products believed to contribute to intestinal inflammation and allows limited types of nuts and vegetables, fresh poultry and fish, and fermented yogurts (Cohen et al., 2014; Parrish & Rdn, 2019; Wark et al., 2021). Interventions among IBD patients tend to include samples with higher inclusion of Crohn’s Disease patients than UC patients (Kakodkar et al., 2015), and patients are guided by dieticians for optimal adherence and nutrient intake (Wark et al., 2021). Research on the SCD diet has been retrospective and lacking objective measures of disease activity, although a few small case series among IBD
patients have shown evidence of improved stool inflammatory markers (Wark et al., 2021).

Non-digestible short-chain carbohydrates are collectively known as FODMAPs. Low-FODMAP diets have generated evidence of reduced GI symptoms among patients with IBD, but lack evidence of change in inflammatory markers (Wark et al., 2021). A 6-week trial with 22 UC patients found improved disease activity scores and decreased median calprotectin scores after following a low-FODMAP diet (Bodini et al., 2019), but not all studies have found similar results (Cox et al., 2020). Research has found improvement to HRQoL after following a low FODMAP diet in patients with IBD, yet dietary studies are lacking large sample sizes of UC patients (Cox et al., 2020).

These exclusion-focused diets can help ease the burden of UC to an extent, yet are often reported as difficult to maintain (Nazarenkov et al., 2019). Exclusionary diet practices can result in healthier dietary intake, but also can result in malnutrition, disengagement from social activities, excessive cognitive energy spent on food choices, frustration with the desire for excluded foods, and significant distress after straying from dietary exclusion goals (Nazarenkov et al., 2019). Low-fiber diets are often suggested to help ease the roughage passing through an inflamed colon during UC flares. Indeed, low-fiber and exclusion diets tend to be strongly pro-inflammatory (Khayyatzadeh et al., 2017; Krishnamurthy et al., 2012; Y. Ma et al., 2008). So, this prescription could tend to exacerbate the problem and amplify symptoms when adopted for an extended period of time. There is very limited evidence in the effectiveness of these recommended exclusion diets in healing the inflamed and ulcerated mucosal lining of the colon.
A promising approach to food choice among individuals with UC may be the adoption of an anti-inflammatory dietary lifestyle to manage the burden of living with UC. Research suggests that a focus on removing ‘pro-inflammatory’ foods, such as refined carbohydrates and processed foods should guide exclusion diets among patients with UC (Marsh et al., 2022). Among the general population, an anti-inflammatory dietary intake has been shown to decrease anxiety, depression, and risk of colon cancer, among other health outcomes (Shivappa et al., 2017; Shivappa, et al., 2016b). This method of dietary intake expands food choices by incorporating aromatic spices, blends of colorful foods, and plentiful intake of fruits, vegetables, and healthy fats. Olendzki and colleagues (2021) developed the IBD Anti-Inflammatory Diet (IBD-AID) as a protocol built from the SCD diet that incorporates anti-inflammatory components to rebuild bacterial gut flora and mitigate disease activity (https://www.umassmed.edu/nutrition/ibd/ibdaid/). An associated study screened medical records for 10 IBD patients who followed the IBD-AID and found improvements in GI symptoms, yet the sample included only three cases of UC (Olendzki et al., 2014). Recent evidence indicates an association between the adoption of the IBD-AID and beneficial changes in the microbiome of IBD patients (Olendzki et al., 2022).

Outside of the development of the IBD-AID protocol and subsequent examination of its interaction with the microbiome, the adoption of an anti-inflammatory dietary lifestyle has not been otherwise examined as a complementary treatment approach and self-management method for UC. Though there is abundant evidence on the relationship between diet-associated inflammation and diseases of the gastro-intestinal tract, and suggestive links from work using the Dietary Inflammatory Index (DII®) (Marx et al.,
2021; Mirmiran et al., 2019; Phillips et al., 2019; Shivappa, et al., 2016a), additional carefully designed, ideally prospective studies need to be conducted in order to provide sufficient scientific evidence to support clear dietary recommendations for the management of UC.

2.3.4 Complementary and Alternative Therapies/ Lifestyle Change

Patients have reported the use of complementary and alternative therapies to manage their UC that either contribute to or replace treatment regimens recommended by their healthcare providers (McMullan et al., 2017; Wickman et al., 2016). Probiotic use has been promoted for improved gut health, yet no evidence currently exists to support this method in mitigating disease activity (Torres et al., 2019). Cannabis and other herbal therapies have been tried among the IBD population, but little evidence exists to show positive results (Torres et al., 2019). Vitamins and minerals are often used to supplement deficiencies, yet evidence to suggest the treatment effects of supplement use on disease activity is insufficient (Torres et al., 2019).

Many patients report stress reduction techniques to manage the burden of illness. Mindfulness, yoga, relaxation courses, and exercise has been reported by patients to be beneficial (McMullan et al., 2017). Relaxation and mindfulness techniques help patients overcome negative experiences and stimuli (Fedosiejew et al., 2016; Torres et al., 2019). Cognitive behavioural therapy has been found to improve short term QoL in adults with IBD, and some patients report using this type of psychotherapy, by trying to find a positive outlook in a challenging condition, as a way to cope with the burden of illness (Fedosiejew et al., 2016; Torres et al., 2019). Additional lifestyle changes for stress
management have also been reported by patients, such as increasing sleep and decreasing work hours (Wickman et al., 2016).

2.3.5 Physical Activity and Ulcerative Colitis

Physical activity (PA) is another behavioral method UC patients look to for reduction and management of the physical and psychosocial burden of illness. PA is widely known to reduce stress and depression, regulate systemic inflammation, reduce the risk of co-morbidities, improve social relationships, and demonstrate QoL benefits among the general population. PA is highly likely to contribute to a reduced burden of illness among individuals with UC, yet few studies have examined PA among this population. Existing studies on PA and UC suggest that although patients struggle with motivation to exercise during periods of active disease, engagement in PA or structured exercise is associated with improvements in QoL, fatigue, and mental health (Eckert et al., 2019; Lamers et al., 2021; Raman et al., 2021; Wiestler et al., 2019). Physical activity, for the majority of patients, has not been shown to worsen symptoms and is suggested as safe among the IBD population (Engles et al., 2018; Nathan et al., 2013).

Some research suggests that exercise may serve as a protective factor against disease activity (Jones et al., 2015), and reviews of evidence suggests that PA may be an effective modifier in the disease course of UC (Eckert et al., 2019; Engles et al., 2018), but studies on physical activity’s impact on disease activity are limited (Engles et al., 2018). Although patients with UC tend to report benefits of physical activity on well-being, participation in exercise is often difficult, given barriers associated with GI symptoms (Engles, 2018). Recommendations for PA and maintenance of health among
the UC population do not currently exist. Research is needed to determine the magnitude of effect physical activity has on decreasing the burden of illness associated with UC.

Conceptual Framework

This work is anchored in a biopsychosocial lens examining the illness experience associated with UC. The biopsychosocial model is a clinical and practical guide for understanding how suffering and illness is affected by an interaction between biological, psychological, and social influences (Borell-Carrió et al., 2004; Engel, 1977). The cause of UC is unknown, yet the combination of one’s genetics, environment, microbiome, and immune system are believed to play a prominent influential role in the development of UC. Patients with UC experience a significant physical, psychological, and social burden of illness. Due to the biopsychosocial nature of UC, this research is guided by a conceptual framework to understand the illness experience in whole and examine how treatment and management methods may play a role in reducing the biopsychosocial burden of illness (see Figure 2.1 Conceptual Framework).

UC is experienced in degrees of disease severity and extent with fluctuating degrees of disease activity, and characterized by localized inflammation evident in the colon and systemic inflammation throughout the body. As UC is associated with increased levels of localized and systemic inflammation, changes in localized and systemic inflammation can increase or decrease UC severity and activity. Increases and decreases in localized and systemic inflammation are mainly affected by the environment and the immune system.

The burden of illness is a cumulative biopsychosocial experience of physical gastrointestinal symptoms, extraintestinal manifestations of illness, pain, physical and
mental fatigue, stress and emotional distress, anxiety and depression, insufficient sleep, medication use and accompanying side effects, and the costs of health care. All of these experiences impact one another. The burden of illness impacts social, mental health-related, and biological aspects of daily life. Aspects of daily life effected by the burden associated with UC include work capacity and productivity, participation in social and leisure activities, isolation, relationships, self-image and risks for cancer and other comorbidities. These interrelated aspects of daily life often feed back into the burden of illness. For example, isolation from activities once enjoyed may increase feelings of depression, but new supportive relationships can decrease stress. Inflammation has a bi-directional relationship with aspects of the burden of illness.

Treatment and management methods may impact the overall experience of living with UC. Methods such as medication, diet change, physical activity, stress management, lifestyle changes, and other complementary and alternative treatments can have an impact on the magnitude of burden and the impact of such burden on everyday life. Treatment and management methods may also have direct impacts on inflammation. Treatment and management methods may also influence the immune system, microbiome, and environmental factors that influence disease severity and activity. Recent evidence suggests that many types of therapies may also change gene expression (Buric et al., 2017). Decisions to use various treatment and management methods are shaped by internal and external factors such as personal suffering, patient-provider relationships, knowledge and familiarity, perceptions/beliefs and attitudes, resources and barriers, social support and messages, and values and faith. Each of these factors influence one another as well.
Figure 2.1. Conceptual Framework
Significance

This dissertation draws attention to health behaviors as lifestyle methods that aid in managing the burden of illness associated with UC, as well as the potential of these methods to contribute to achieving reduced disease activity, disease remission, and healing of the colon’s mucosal lining. While existing research has indicated the use of various treatment and management methods among individuals with UC, current literature is lacking sufficient description of how and why individuals use treatment and management methods as they face the burden of illness in daily life and over the disease course, as well as examination of the perspectives, resources, and motivations that guide decisions regarding the use of various methods (Crooks et al., 2021).

Diet and physical activity are health behaviors commonly understood to improve overall health, and although dietary change is a predominant health behavior used by patients to self-manage their experience with UC, research on the impact of diet and physical activity on the disease course is limited and insufficient to support clear dietary and physical activity recommendations. In fact, no tailored recommendations for physical activity among the UC population currently exist. Research is needed to determine the magnitude of effect physical activity has on decreasing the burden of illness associated with UC. Additionally, recent reviews call for data on the intensity and frequency of exercise that would generate the greatest benefit among individuals with UC in order to determine exercise recommendations for this population (Eckert et al., 2019; Engles et al., 2018; Nathan et al., 2013; Raman et al., 2021). This study provides a unique examination of the associations between engagement of physical activity at varying intensities and UC related health outcomes.
This research is the first, to our knowledge, to examine how patients use treatment and management methods to manage the burden of illness and the factors that guide patient decision making in the use of such methods throughout the disease course. This is also the first work, to our knowledge, that examines the relationships between disease outcomes relevant to UC, dietary inflammatory potential, and physical activity. More specifically, this is the first study to use the DII to examine dietary inflammatory potential and UC-related physical and psychosocial health outcomes among a large cohort of UC patients.

Outside of the development of the IBD-AID protocol and subsequent examination of its interaction with the microbiome, the adoption of an anti-inflammatory dietary lifestyle has not been otherwise examined as a complementary treatment approach and self-management method for UC. An anti-inflammatory diet may play a significant role in self-managing the localized and systemic inflammation associated with UC and therefore may decrease disease activity and associated extraintestinal manifestations of illness.

Results of this study may provide additional insights to physicians and patients regarding diet and PA as complimentary self-management methods to mitigate disease activity and manage the burden of UC, as well as insights on patient perspectives and experiences that influence patient decision making and support improved patient-provider communication. Collaborative care between patients and providers helps patients feel a sense of control over their illness verses their illness controlling them, which, in turn, improves self-management overall (Plevinsky et al., 2016). This research can aid in framing patient education and contribute to the development of evidence-based
behavioral interventions that assist patients in adopting and sustaining self-management behaviors to reduce and prevent disease activity. This research can also inform evidence-based dietary and physical activity recommendations for the UC population. This work may assist providers in understanding complementary treatment methods that may be acceptable and desired by patients, which could also be incorporated into standard care. Seeking out personal preference-based management options for treatment of UC has been associated with a high QoL and successful self-management among the UC population (Wickman et al., 2016).
CHAPTER 3
RESEARCH DESIGN AND METHODS

Overall Dissertation Design

This dissertation follows a mixed-methods design that aimed to utilize both qualitative and quantitative approaches to understand the effect of treatment and management methods on the daily burden of UC. To achieve the aims of this dissertation two separate studies were conducted. Study 1 was a qualitative study that aimed to examine the perspectives of individuals with UC regarding the use of various treatment and management methods to reduce the burden of illness and the factors that guide decision making in the use of such methods. Study 2 was a secondary data analysis that aimed to analyze associations between diet and physical activity as self-management methods and disease outcomes relevant to the burden of illness among a large population.

Study 1

1.1 Research Design- Study 1

As patients cope with the burdens of living with UC, various treatment and management methods are often used to manage the impact of UC on daily life. Study 1 sought to understand how and why treatment and management methods are used to influence the burden of living with UC. Study 1 utilized a qualitative design to obtain rich, in-depth data reflecting the experiences and perspectives of participants. Data was obtained through individual semi-structured interviews (Creswell, 2007; Patton, 2015)
with patients diagnosed with UC. Each interview was scheduled and conducted by the researcher. Interviews were audio-recorded, transcribed verbatim, and uploaded into Nvivo software. Interviews were coded and organized into meaningful themes and sub-themes relevant to the study aims.

1.2 Setting- Study 1

Patient recruitment and data collection for Study 1 initially occurred in collaboration with the Greenville Health System/Prisma Health (GHS) Gastroenterology department in Greenville, South Carolina. Patients receiving care for UC at GHS were identified by a GHS gastroenterologist, Anjani Jammula, MD and invited to participate in this study. Patient recruitment was expanded through the South Carolina Center for Integrative Medicine (SCCIM), the Carolina’s Crohn’s and Colitis Foundation support group, and through posting study fliers in two Facebook support groups. In-depth, semi-structured interviews were conducted in person at the participant’s home, a private room on site at GHS, a private room at the local library, over a secure web-based platform (Skype), or over the phone according to participant preference. Data collection occurred outside of the clinical flow on site at GHS such that it did not disrupt clinical activities.

1.3 Sample- Study 1

This study included individuals with UC receiving care from either gastroenterologists at GHS or providers at SCCIM, along with individuals who engage with the Carolina’s Crohn’s and Colitis Foundation support group, or Facebook support groups. Participants met the following criteria to be eligible to participate in this study: 1) diagnosed with UC, 2) duration of illness ≥5 years, 3) experienced a minimum of one disease flare during the illness trajectory, and 4) speak English. Participants who were
referred to the study through GHS were screened for eligibility criteria through clinical records. All other participants met the eligibility criteria based on self-report.

Purposeful sampling was used to ensure variation in the final sample across race, ethnicity, gender, and current medication use (i.e., to represent mild, moderate, and severe cases of UC) in order to obtain variation in participant experiences (Creswell, 2007; Morse, 1998, 1999; Patton, 2015).

1.4 Recruitment- Study 1

Patient recruitment for Study 1 began in collaboration with the GHS Gastroenterology department in Greenville, South Carolina. Patients receiving care for UC at GHS were identified by a GHS gastroenterologist, Anjani Jammula, MD and invited to participate in this study. Two methods of recruitment occurred simultaneously:

1.) An invitation letter (see Appendix A) was mailed from GHS to each eligible patient to inform the patient of the study and invite them to participate. GHS identified 105 patients with UC in their records. Invitation letters were mailed to 44 patients, as the remaining 61 subjects did not meet the eligibility requirement of duration of UC >5 years, or subjects had been lost to follow up at GHS. Patients interested in participating were instructed to contact the researcher directly by phone or email. GHS staff mailed a 2nd copy of the invitation letter to 42 existing or newly identified eligible subjects two months later.

2.) Recruitment flyers (see Appendix B) were posted in the GHS patient waiting room, in patient care rooms, and near check-in and check-out areas. Additional copies of the flyer were available with office receptionists for distribution to interested patients. The flyer directed interested patients to contact the researcher by
The GHS physician encouraged eligible patients to participate in the study and provided additional copies of the flyers and invitation letters to eligible patients during patient care.

Seven subjects responded to the mailed invitation letter after the first distribution. Four additional subjects responded to the invitation letter after the second distribution, for a total of 11 respondents (10 of which completed an interview). Patient recruitment was expanded to collaborate with the South Carolina Center for Integrative Medicine (SCCIM) and the Carolina’s Crohn’s and Colitis Foundation support group. The researcher contacted each organization through email to describe the research study and invite each organization to refer eligible subjects. The recruitment flyer was attached to each email. The SCCIM referred one eligible subject. Carolina’s Crohn’s and Colitis Foundation referred two eligible subjects. These three subjects each complete an interview. At the same time, the researcher joined two UC support groups on Facebook (Ulcerative Colitis, and Ulcerative Colitis Support Group) and posted the recruitment flyer and a request for participation on each Facebook newsfeed. Of those who responded, eight eligible subjects from the Ulcerative Colitis group, and one eligible subject from the Ulcerative Colitis Support Group completed an interview.

Upon phone or email/messaging contact from an interested patient, the researcher followed a scripted protocol (see Appendix C) to inform patients about the study, screen for eligibility (see Appendix D), obtain verbal consent, and schedule an interview appointment. Additional snowball sampling was attempted to recruit participants, as the researcher encouraged patients to share the study information with any acquaintances who may be eligible and interested. A $25 cash gift card was offered to each participant.
as a gesture of gratitude for their time. Participant gift cards were funded by an Olga I. Ogoussan Doctoral Research Award from the University of South Carolina. Recruitment continued until saturation in the data was achieved (Morse, 1998, 2000).

1.5 Data Collection Procedures- Study 1

Data was obtained through in-depth individual semi-structured interviews (Creswell, 2007; Patton, 2015). Each interview was scheduled and conducted by the researcher. Interviews were conducted in person (n=10), over a secure web-based platform (n=4) (Skype), or over the phone (n=7) according to participant preference (Creswell, 2007). Interviews lasted approximately 60 minutes and followed a semi-structured interview guide (see Appendix E).

Interviews addressed the participant’s retrospective course of illness, the impact of UC on daily life, experiences with medical and complementary treatment methods used to control disease symptoms, methods for self-managing the impact of UC on daily living, and the processes of making decisions regarding treatment and management of UC over the course of illness. A brief survey to obtain demographic information (eg. age, gender, race, ethnicity, education, duration of illness) was also administered at the end of each interview (see Appendix E). Participants shared their experiences using treatment and self-management methods and described factors that contributed to their decisions to use such methods.

To facilitate a collaborative environment with the participant, the researcher consistently framed the interview experience as an opportunity to learn from the participant about the participant’s experiences. To establish a comfortable rapport with the participant, the researcher introduced herself as a student from the University of
South Carolina. She also expressed that she has a longstanding history with UC herself, and, knowing that she is not the only one who has struggled to manage the burden of illness, wants to hear the participant’s story. (See introduction of interview guide, Appendix E)

Upon data collection, the researcher was mindfully aware that the experiences of others would be different from her own and aimed to uphold an objective stance in the interview. The researcher maintained an understanding that some UC patients do not have a desire to make lifestyle improvements or seek complementary treatments to decrease the burden of illness, and that many patients would express experiences or opinions contrary to the researcher’s personal beliefs and experiences. The researcher attempted to the best of her ability to suspend her own biases and experiences in order to allow the participant to lead the conversation and feel comfortable and confident in voicing their own experiences and opinions.

Interviews were audio-recorded and transcribed verbatim by a professional transcription service (Rev.com) and then reviewed for accuracy by the primary researcher. Transcription costs were funded by a SPARC grant awarded to the researcher by the University of South Carolina. All identifying information was removed from transcriptions. Interview transcripts were uploaded into Nvivo 12 qualitative analysis software (QSR International, 2020).

Transcription and data analysis co-occurred with data collection. Memos were written throughout the data collection and analysis process to document insights and observations related to the research aims (Creswell, 2007; Miles & Huberman, 1994).
1.6 Data Analysis- Study 1

Data was analyzed using QRS International NVivo 12 software (QSR International, 2020) by researchers with training and experience conducting qualitative studies. Thematic analysis was conducted using a constant comparative approach. The primary coder (KD) led the analysis with input from a secondary coder (CB) throughout the process. KD coded passages of text relevant to the study’s aim to reflect the content and meaning of each passage. Content and meaning of passages were discussed and clarified in biweekly meetings with KD and CB to verify the analysis to ensure accurate representation of the data (Creswell, 2007; Miles & Huberman, 1994).

Multiple steps were taken to strengthen the integrity of the findings: 1.) Transcriptions were first read in whole to capture the overall context of passages (KD); 2.) An initial codebook was developed from analysis of the first five interviews using an emergent inductive approach and guided the coding of subsequent transcripts, allowing for additional codes to be added as they emerged in the data (Creswell, 2007; Miles & Huberman, 2013; Patton, 2015); 3.) The rest of the interviews were coded, identifying themes addressing the burden of illness, treatment and management methods, attributions of UC and disease activity, decision making process, motivating factors, sources of information, the impact of methods on daily life experiences and disease activity, and the disease course; 4.) Codes were iteratively organized into meaningful themes and sub-themes across all interviews to capture key elements of the participants’ experiences (Miles & Huberman, 1994, 2013); 5.) Themes on treatment and self-management methods used by participants were assessed and categorized as medical, lifestyle, or complementary/alternative methods; 6.) Memos were written to capture additional
insights and observations throughout data analysis; 7.) Disease trajectories were
delineated for approximately 1/3 of the participants in attempt to explore potential
patterns of disease flares among life events and treatment and management methods; 8.)
Queries were created to explore patterns of dietary behaviors among participants; 9.)
Contextual relationships were considered between treatment and management methods,
decision making approaches, sources of information, and motivating factors.

**Study 2**

2.1 *Research Design - Study 2*

This work is motivated by the underlying hypothesis that an anti-inflammatory
diet and physical activity can improve immune system functioning and overall health.
Choosing to consume foods with anti-inflammatory properties, while decreasing
consumption of pro-inflammatory foods may affect symptoms of UC. Dietary
inflammatory intake may have a direct impact on the localized and systemic
inflammation associated with UC. Such an impact could have direct and indirect effects
on disease activity, components of the burden of illness (e.g. fatigue, emotional distress)
and overall quality of life. PA may also be of particular benefit to individuals with UC,
given established associations with improved immune functioning, decreased fatigue, and
improvements in mental health, social functioning, and QoL. This research hypothesized
that an anti-inflammatory diet is associated with improved health outcomes associated
with UC. In addition, we hypothesized that PA is also associated with improved health
outcomes.

To test the associations between dietary inflammatory intake, physical activity,
and UC related health outcomes, data from the IBD Partners e-cohort was analyzed using
a cross-sectional design. Outcomes of interest included disease activity, IBD-related
QoL, and Patient Reported Outcome (PRO) domains of fatigue, anxiety, depression,
satisfaction with social role, and sleep disturbance. Disease activity was measured using
the Simple Clinical Colitis Activity Index (SCCAI). IBD-related quality of life was
measured using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ). Fatigue,
anxiety, depression, satisfaction with social role, and sleep disturbance were measured
using the Patient Reported Outcome Measurement Information System (PROMIS).

Associations were tested using multivariate regression models. Predictor
variables included dietary inflammatory intake and physical activity. Given the
established association between body mass index (BMI) and disease activity, BMI was
calculated using data on weight and height and included in the statistical model.
Additional confounders included age, sex, race, level of education, smoking status,
disease duration, and medication class. Dietary data were collected using a National
Cancer Food Frequency Questionnaire and converted into a Dietary Inflammatory Index
Score (DII®). Physical activity data were collected using the Godin-Shephard Leisure
Time Activity Index.

2.2 Data Set- Study 2

IBD Partners, previously named the Crohn’s and Colitis Foundation of America
(CCFA) Partners, is a longitudinal Internet-based cohort of patients with IBD. This
cohort was developed in response to needed patient reported data that is lacking in
administrative and clinical data from the IBD patient population, such as dietary patterns,
exercise, quality of life, and other important patient-reported outcomes (PROs) (Long et
IBD Partners serves as a facilitator for research studies using a large, diverse population and as a platform for additional disease related studies (Long et al., 2012). The initial CCFA Partners cohort included 7,819 individuals with self-reported IBD who joined through August 2011. A total of 96.4% of cohort members were from within the US, and 72.3% were female. Distribution of disease was as follows: Crohn’s Disease n=4933 (63.1%), Ulcerative Colitis n=2675 (34.2%), Indeterminate colitis/IBD unspecified n=211 (2.7%). Patients were recruited through the Crohn’s and Colitis Foundation of America email roster, social media, CCFA website promotion, word of mouth, and promotion at CCFA events. Eligible participants were required to be over the age of 18 years with self-reported IBD (Crohn’s Disease, Ulcerative Colitis, or indeterminate colitis) and access to the internet.

All initial participants received Module 1, providing information on demographics, disease phenotype, disease activity, and medication use, among others. Participants were randomized to complete their 2nd module, either Module 2 or Module 3. Participants were then given an option to complete a 3rd module, which was the Module 2 or Module 3 they had not yet completed (Long et al., 2012). Module 2 assessed diet and exercise. Module 3 consisted of patient-reported outcomes (PROs), which are health data provided by the patient regarding their feelings as they deal with chronic conditions (Long et al., 2012). Additionally, Module 3 included the Short IBD Questionnaire (SIBDQ) to collect data on IBD-specific QoL.

2.3 Population of Interest- Study 2

This research included patients over 18 years of age who self-reported UC and completed modules 1, 2, and 3 (as described above in 2.2 Data Set-Study 2). Patients
who had undergone UC-related intestinal surgery were excluded. Studies have shown that patients who receive surgical treatment to remove portions of their diseased colon have significantly reduced disease severity and activity, and experience challenges separate from the scope of this research.

2.4 Variables and Measures- Study 2

The following variables were abstracted from validated measures administered within the IBD Partners surveys.

2.4.1 Outcome Variables

Disease Activity

Disease activity was measured using the Simple Clinical Colitis Activity Index (SCCAI) (Long et al., 2012; Walmsley et al., 1998). This measure assesses five clinical criteria and general wellbeing to generate a summed activity index score. Strong psychometric validity and performance validity was found for the SCCAI in a repeated measures longitudinal study of patients with UC (Higgins et al., 2007). The SCCAI has been validated for use as a self-report measure (Jowett et al., 2003).

Patients are asked to rate 1) bowel frequency during the day 2) bowel frequency at night 3) urgency of defecation 4) blood in stool, 5) general well-being and 6) extracolonic manifestations (see Appendix F). Items 1-5 are scored individually using Likert-scale type response options, then summed into a disease activity score. An additional 1 point per extracolonic manifestation is added to the total SCCAI score. Scores range from 0-15+ points. Remission in UC is associated with a SCCAI score <2; clinical relapse is defined by a SCCAI score ≥5 (Jowett et al., 2003; Turner et al., 2009).
Disease-related Quality of Life

The Short Inflammatory Bowel Disease Questionnaire (SIBDQ) is a 10-item questionnaire used to assess disease-related quality of life among individuals with IBD (Irvine et al., 1996). The SIBDQ assesses four domains, including bowel symptoms, emotional health, systemic systems, and social function, to generate a summed quality of life score relative to the two weeks prior to self-report. The SIBDQ correlates to disease activity in patients with UC and demonstrates good test-retest reliability (Irvine et al., 1996). The 10-item questionnaire is highly correlated with the full 32-item Inflammatory Bowel Disease Questionnaire (IBDQ) (Irvine et al., 1996).

Individuals are asked to answer questions relative to how they have felt in the last two weeks. Questions address 1) feelings of fatigue or being worn out, 2) canceling a social engagement because of bowel disease, 3) difficulty doing desired leisure or sports activities, 4) pain in the abdomen, 5) feeling depressed or discouraged, 6) passing gas, 7) maintaining or gaining weight, 8) feeling relaxed and free of tension, 9) a feeling of having to go to the bathroom even though bowels were empty, and 10) feelings of anger as a result of illness. (see Appendix G)

Seven response options were provided as follows: All of the time, most of the time, a good bit of time, some of the time, a little of the time, hardly any of the time, none of the time. Each item is scored by a 7-point scale, from 1 being a severe problem to 7 indicating no problem at all. An absolute score ranges from 10 to 70, with 70 indicating optimum HRQOL. Scores can be averaged by dividing each absolute score by the number of items (10) so that all scores range from 1 to 7, with 1 indicating poor HRQOL and 7 indicating optimum HRQOL.
Patient Reported Outcomes

The National Institutes of Health Patient Reported Outcome Measurement Information System (PROMIS) is a system of precise measures of patient-reported physical, mental and social wellbeing with high reliability (Cella et al., 2007, 2010). Various domains of well-being can be measured using validated item banks, or groupings of questionnaire items that reflect the construct of interest. PROMIS items have been validated among the general population, with recently recognized construct validity in the IBD population (Cella et al., 2010; Kappelman et al., 2014).

IBD Partners selected short form PROMIS item banks to measure individual constructs of health-related quality of life particularly relevant to IBD. Selected domains included anxiety, depression, fatigue, sleep disturbance, and satisfaction with social role. Each item bank consisted of 4 items. One item was also included to assess self-perceived general health. All PROMIS items included in the IBD Partners data set are included in Appendix H.

The majority of PROMIS items use a five-option response scale ranging in value from one to five (e.g., 1=Not at all, 2=A little bit, 3=Somewhat, 4=Quite a bit, 5=Very much) (Cella et al., 2010). Raw scores are summed when all questions have been answered. If a participant does not complete each item, a HealthMeasures Scoring Service provided through PROMIS is available to generate a reliable final score. The total raw score will range from 4 to 20 for each domain. Item scores are calibrated using a T-score metric which scales the raw score to a standardized score with a mean of 50 and a standard deviation of 10. A score of 50 is the average for the US general population for most PROMIS instruments. Score conversion tables to translate the total
raw score into a T-score for each participant are available through www.healthmeasures.net. Higher scores represent more of the measured domain. High scores for fatigue, anxiety, depression, and sleep disturbance represent poor health while high scores for social function and perceived general health represent good health (Kappelman et al., 2014).

2.4.2 Predictor Variables

Dietary Inflammatory Index (DII®) Score

IBD Partners administered a National Health and Nutrition Examination Survey (NHANES) Dietary Screener Questionnaire (DSQ) to e-cohort participants to collect data on average daily consumption in the prior month for various foods (Cohen et al., 2013; National Cancer Institute, 2021c). The DSQ collects data on intake frequency for fruits and vegetables, red meats and processed meats, cheese, milk, sweetened beverages, desserts, popcorn, beans, and rice, among others (see 2.6.1 NHANES DSQ).

The DSQ data was used as a basis to compute both a DII score and an Energy-Adjusted DII Score (E-DII™) for this study (Hébert et al., 2019; Shivappa et al., 2014a). The DII was developed based on an extensive literature search to quantify the effect of diet on inflammation using an algorithm that takes into account up to 45 food parameters identified in the search, including a combination of nutrients and food intake (Shivappa et al., 2014a). Due to unique differences observed in the relationship between total energy intake (a determinant of the DII) and nutrient intake, the energy-adjusted DII score (E-DII) was also developed. DII scores can range from a theoretically minimum -8.87, indicating a strongly anti-inflammatory intake, to a theoretically maximum +7.98, indicating a strongly pro-inflammatory intake (Shivappa et al., 2014a). At least 41
studies have demonstrated construct validity of the DII or E-DII against inflammatory biomarkers in different populations under varying conditions (Gialluisi et al., 2021; Li et al., 2021; Malcomson et al., 2021; Marx et al., 2021; Phillips et al., 2019; Saghafi-Asl et al., 2021; Skoczek-Rubińska et al., 2021; Zamora-Ros et al., 2015). Both the DII and E-DII scores were computed for each participant and analyzed against outcome variables (See 2.6 Converting DSQ Dietary Data to DII & E-DII Scores-Study 2).

Physical Activity

Physical Activity Data were collected using the Godin-Shephard Leisure Time Exercise Index (Godin, 2011; Godin & Shephard, 1985). This questionnaire was developed to measure leisure time physical activity and classify activity levels among healthy adults. The Leisure Time Activity Index has been validated to assess exercise behavior in different populations (Gionet & Godin, 1989). Concurrent validity was determined by assessing two main determinants of physical fitness, maximal aerobic capacity (VO$_2$max) and percentage of body fat, and their correlation with the scores from the leisure time physical activity questionnaire (Godin, 2011; Godin & Shephard, 1985). Significant correlation was found between the questionnaire and VO2max ($r=0.24$, $p<0.001$), as well as percentage of body fat ($r=0.13$, $p<0.01$) (Godin, 2011). Godin’s Leisure Time Exercise Index was also tested against a physical activity electronic motion sensor and confirmed to be a valid measure to assess physical activity (Miller et al., 1994).

The four-item questionnaire asks participants to indicate the number of times during a 7-day period that the participant engages in mild (minimal effort – e.g., easy walking, fishing), moderate (not exhausting – e.g., fast walking, tennis), and strenuous
(heart beats rapidly – e.g., running, basketball) physical activity for at least 15 minutes (Amireault & Godin, 2015; Godin, 2011; Godin & Shephard, 1985). (See Appendix I) Total Leisure-Time Activity scores are calculated by multiplying reported weekly frequencies of mild, moderate, and strenuous activities by corresponding Metabolic Equivalent of Task (MET) values, which indicate energy expenditure, of three, five and nine respectively, then summing the products of each intensity level (Godin, 2011; Godin & Shephard, 1985). In addition to Total Leisure Time Activity, frequency of engagement in PA at each intensity was assessed in this study as continuous variables of PA intensity-mild, moderate, and strenuous.

**Covariates**

Additional variables included age, sex, body mass index (BMI), race, education, smoking status, disease duration, medication class, and presence of conditions limiting participation in PA. Age was indicated by entering a numeric value. Sex was reported as either male or female. BMI (kg/m2) was calculated from participant-reported height and weight. Given that 84% of the participants indicated race as ‘White’, a dummy variable for race was created for this analysis as either ‘white’ White’ or ‘not White’. Education was indicated as ‘high school or less’ (combining survey response items of ‘12th grade’ and ‘less than 12th grade’), ‘some college’, ‘college’, and ‘graduate school’. Participants indicated smoking status as ‘never’, ‘ever’, or ‘current’. Disease duration was self-reported by entering a numeric value of years since first IBD diagnosis.

Participants reported on currently used medications by indicating ‘yes’ or ‘no’ to various listed medications and treatment methods. For this study, seven “medication classes” were grouped as follows: Corticosteroids included ‘oral corticosteroids’,
‘budesonide’, and ‘steroids, rectal’ questionnaire items; Aminosalicylates included ‘mesalamines oral’, ‘mesalamines rectal’, and ‘Azulfidine (sulfasalazine)’; Immunomodulators included ‘Azathioprine/6MP’ and ‘Oral MTX’ (methotrexate); Biologics included ‘infliximab’ and ‘adalimumab’; Antibiotics included ‘ciprofloxacin’, ‘metronidazole’, and ‘other antibiotics’, Complementary/Alternative included ‘probiotics’, ‘Other complementary or alternative therapy’, and ‘calcium’; Opioids included ‘opioids’. (Crohn’s & Colitis Foundation, 2021). Participants also reported the presence of other unrelated to IBD conditions that limit participation in physical activity, such as injury, by indicating ‘yes’ or ‘no’.

2.5 Data Analysis - Study 2

Data were analyzed using Stata 16 (StataCorp, College Station, TX). Descriptive statistics were generated for all variables of interest. Predictor variables were added individually as models were tested, watching for increases in R² to indicate the added variables are contributing to the explanatory power of model. All models were assessed for multicollinearity using a Variance Inflation Factor (VIF).

2.5.1 Hypothesis 1

To address hypothesis 1, associations between DII scores and health outcomes were tested with multivariable regression models using ordinary least squares. Disease activity, quality of life, and PROs were each predicted by a set of covariates and DII score. For all outcomes, control variables included: age, sex, BMI, race, education, smoking status, disease duration, medication class, and PA). Age, BMI, disease duration, and PA (Total Leisure Time Activity score) were included as continuous variables. Sex, race, education, smoking status, and medication class were included as categorical
variables. Dummy variables were created for race, education, and medication class (see categories used to create dummy variables in 2.4.2 Predictor Variables, Covariates). Missing responses were taken into account and included as a dummy variable (indicated by _9 in Stata variable names) for each categorical variable to ensure confidence in results.

Statistical models to address hypothesis 1 are as follows:

\[ Y(\text{disease activity}) = X_1(DII) + X_2(\text{physical activity}) + X_3(BMI) + \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{IBD-QOL}) = X_1(DII) + X_2(\text{physical activity}) + X_3(BMI) + \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{anxiety}) = X_1(DII) + X_2(\text{physical activity}) + X_3(BMI) + \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{depression}) = X_1(DII) + X_2(\text{physical activity}) + X_3(BMI) + \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{fatigue}) = X_1(DII) + X_2(\text{physical activity}) + X_3(BMI) + \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{satisfaction with social role}) = X_1(DII) + X_2(\text{physical activity}) + X_3(BMI) + \text{adjust for additional confounders} + \epsilon \]

An example of the Stata commands for analysis is as follows:

```
regress SCCAI_score DII LeisureActivityScore BMI age sex race_white race_9 ed_somecollege ed_college ed_gradschool ed_9 smokernever smokercurrent corticosteroids corticosteroids_9 aminosalicylates aminosalicylates_9 immunomodulator
```
To test for robustness with regards to explanatory power ($R^2$), models were run using the E-DII variable score in place of DII scores. The E-DII score was selected for final analysis given the variable’s greater explanatory ability, as well as lower skewness and other distributional characteristics in comparing among scores. DII and E-DII scores were analyzed as continuous variables. E-DII scores were subsequently analyzed as quartiles to test for linear trends across quartiles (Quartile 1= -4.13 to -1.46, Quartile 2= -1.46 to -0.35, Quartile 3= -0.35 to 0.96, Quartile 4= 0.96 to 4.47).

2.5.2 Hypothesis 2

To address hypothesis 2, associations between physical activity and health outcomes were tested with multivariable regression models using ordinary least squares. Physical activity was assessed as a Total Leisure Time Activity score, analyzed as a continuous variable. Disease activity, quality of life, and PROs were each predicted by a set of covariates and Total Leisure Time Activity scores. For all outcomes, control variables (with the use of dummy variables described previously) included: age, sex, BMI, race, education, smoking status, disease duration, medication class, E-DII score, and presence of conditions limiting participation in PA. Age, BMI, disease duration, and E-DII score were included as continuous variables. Sex, race, education, smoking status, medication class, and presence of conditions limiting participation in PA were included as categorical variables.

Statistical models to address hypothesis 2 are as follows:
\[ Y(\text{disease activity}) = X_1(\text{Leisure Time Physical Activity})+X_2(\text{E-DII})+X_3(\text{BMI})+ \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{IBD-QOL}) = X_1(\text{Leisure Time Physical Activity})+X_2(\text{E-DII})+X_3(\text{BMI})+ \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{anxiety}) = X_1(\text{Leisure Time Physical Activity})+X_2(\text{E-DII})+X_3(\text{BMI})+ \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{depression}) = X_1(\text{Leisure Time Physical Activity})+X_2(\text{E-DII})+X_3(\text{BMI})+ \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{fatigue}) = X_1(\text{Leisure Time Physical Activity})+X_2(\text{E-DII})+X_3(\text{BMI})+ \text{adjust for additional confounders} + \epsilon \]

\[ Y(\text{satisfaction with social role}) = X_1(\text{Leisure Time Physical Activity})+X_2(\text{E-DII})+X_3(\text{BMI})+ \text{adjust for additional confounders} + \epsilon \]

An example of the Stata commands for analysis is as follows:

```
regress SCCAI_score LeisureActivityScore EDII BMI age sex race_white race_9 ed_somecollege ed_college ed_gradschool ed_9 smokernever smokercurrent corticosteroids corticosteroids_9 aminosalicylates aminosalicylates_9 immunomodulator immunomodulator_9 biologics biologics_9 antibiotics antibiotics_9 complimentary_alt complimentary_alt_9 opioids opioid_9 other_conditionyes other_condition9 disease_duration if anysurgeries ==0
```

To address hypothesis 2a, physical activity was analyzed as total frequencies of engagement in PA at each level of intensity (mild, moderate, strenuous) to explore the differences in associations between differing exercise intensities and UC related health outcomes. Disease activity, quality of life, and PROs were each predicted by a set of
covariates, frequency of moderate intensity, and frequency of strenuous intensity. Frequency of mild intensity was excluded from the model as the reference comparator. Each intensity was assessed as a continuous variable.

Statistical models are as follows:

\[ Y(\text{disease activity}) = X_1(\text{moderate intensity}) + X_2(\text{strenuous intensity}) + X_3(E\text{-DII}) + X_4(\text{BMI}) + \text{adjust for additional confounders} + \varepsilon \]

\[ Y(\text{IBD-QOL}) = X_1(\text{moderate intensity}) + X_2(\text{strenuous intensity}) + X_3(E\text{-DII}) + X_4(\text{BMI}) + \text{adjust for additional confounders} + \varepsilon \]

\[ Y(\text{anxiety}) = X_1(\text{moderate intensity}) + X_2(\text{strenuous intensity}) + X_3(E\text{-DII}) + X_4(\text{BMI}) + \text{adjust for additional confounders} + \varepsilon \]

\[ Y(\text{depression}) = X_1(\text{moderate intensity}) + X_2(\text{strenuous intensity}) + X_3(E\text{-DII}) + X_4(\text{BMI}) + \text{adjust for additional confounders} + \varepsilon \]

\[ Y(\text{fatigue}) = X_1(\text{moderate intensity}) + X_2(\text{strenuous intensity}) + X_3(E\text{-DII}) + X_4(\text{BMI}) + \text{adjust for additional confounders} + \varepsilon \]

\[ Y(\text{satisfaction with social role}) = X_1(\text{moderate intensity}) + X_2(\text{strenuous intensity}) + X_3(E\text{-DII}) + X_4(\text{BMI}) + \text{adjust for additional confounders} + \varepsilon \]

An example of the Stata commands is as follows:

```
regress SCCAI_score PAs strenuous PAm moderate PAmild_9 age sex BMI race_white race_9 ed_somecollege ed_college ed_gradschool ed_9 smokernever smokercurrent corticosteroids corticosteroids_9 aminosalicylates aminosalicylates_9 immunomodulator immunomodulator_9 biologics biologics_9 antibiotics antibiotics_9 complimentary_alt complimentary_alt_9 opioids opioid_9 other_conditionyes other_condition9 disease_duration EDII if anysurgeries ==0
```
2.5.3 Hypothesis 3

This work’s third hypothesis explores the interaction effects between dietary inflammatory intake and physical activity on health outcomes in UC. To address hypothesis 3, data was analyzed with multivariate regression models using ordinary least squares including interaction terms. For all health outcomes, interactions were first tested between DII scores and Total Leisure Time Activity scores, and then tested again using E-DII in place of DII. For all outcomes, control variables (with the use of dummy variables described previously) included: age, sex, BMI, race, education, smoking status, disease duration, medication class, E-DII score, and presence of conditions limiting participation in PA.

Statistical models to address Hypothesis 3 are as follows:

\[ Y(\text{disease activity}) = X1(E-DII)+X2(\text{Total Leisure Time Activity})+ \]
\[ X1*X2(DII*PA)+X3(BMI)+\text{adjust for additional confounders}+\epsilon \]

\[ Y(\text{IBD-QOL}) = X1(E-DII)+X2(\text{Total Leisure Time Activity})+ X1*X2(\text{E-DII*PA})+X3(BMI)+\text{adjust for additional confounders}+\epsilon \]

\[ Y(\text{anxiety}) = X1(E-DII)+X2(\text{Total Leisure Time Activity})+ X1*X2(\text{E-DII*PA})+X3(BMI)+\text{adjust for additional confounders}+\epsilon \]

\[ Y(\text{depression}) = X1(E-DII)+X2(\text{Total Leisure Time Activity})+ X1*X2(\text{E-DII*PA})+X3(BMI)+\text{adjust for additional confounders}+\epsilon \]

\[ Y(\text{fatigue}) = X1(E-DII)+X2(\text{Total Leisure Time Activity})+ X1*X2(\text{E-DII*PA})+X3(BMI)+\text{adjust for additional confounders}+\epsilon \]

\[ Y(\text{satisfaction with social role}) = X1(E-DII)+X2(\text{Total Leisure Time Activity})+ X1*X2(\text{E-DII*PA})+X3(BMI)+\text{adjust for additional confounders}+\epsilon \]
Y(perceived general health) = X1(E-DII) + X2(Total Leisure Time Activity) + X1*X2(E-DII*PA) + X3(BMI) + adjust for additional confounders + ε

Additionally, interactions were also tested between frequency of exercise at each intensity and E-DII quartiles. Quartile 1 and mild intensity were excluded from the model as reference comparators. The statistical model used is as follows:

Y = X1(E-DII Quartile2) + X2(moderate intensity) + X1*X2(E-DII Quartile2*moderate intensity) + X3(E-DII Quartile3) + X3*X2(E-DII Quartile3*moderate intensity) + X4(E-DII Quartile4) + X4*X2(E-DII Quartile4*moderate intensity) + X5(strenuous intensity) + X1*X5(E-DII Quartile2* strenuous intensity) + X3*X5(E-DII Quartile3* strenuous intensity) + X4*X5(E-DII Quartile4* strenuous) (BMI) + adjust for additional confounders + ε

2.6 Converting DSQ Dietary Data to DII & E-DII Scores—Study 2

Data collected from an NHANES DSQ was used as a basis to compute both a DII score and an Energy-Adjusted DII Score (E-DII™) used as independent variables in this study (Hébert et al., 2019; Shivappa et al., 2014a).

2.6.1 NHANES DSQ


Participants responded to two DSQ questions for each Food Item: 1. During the past month, did you eat (or drink) any [food item]? Response options were ‘yes’ or ‘no’. 2a. During the past month, how often did you eat (or drink) [food item]? Response option was an open numerical entry (rate). 2b. Participants were also asked to indicate their reported frequency as per day, per week, or per month, or ‘don’t know’. In addition, participants were asked: What kind of cereal did you usually eat? Participants were able to select one cereal from a list of 328 cereal names, including ‘other’ as a selection option. Participants were then asked: During the past month, what second kind of cereal did you usually eat? Participants were again able to select a cereal from the list of 328 cereal names, including ‘other’ as a selection option. Participants we also asked: During the past month, what kind of milk did you usually drink? Response options included: 1. whole or regular 2. 2% fat or reduced-fat 3. 1%, ½%, or low-fat 4. Fat free, skim, or nonfat 5. Soy 6. Other.

2.6.2 Overview of Procedures
Using DSQ data, daily intake frequency for each food item was calculated in Excel. As portion-sizes of food intake was not included in the IBD Partners data set, data on average portion size or serving size was extracted from other sources (see 2.6.4 Identifying Average Portion Size or Serving Size). Daily intake frequency was multiplied
by the respective average portion size to calculate total intake equivalents for each of the 25 food items. Representative foods were identified for each of the 25 food items (See 2.6.6 Collecting Nutrient Data). Nutrient data for up to 19 food parameters were collected for each representative food and organized in Excel. Total nutrient profiles for each parameter were calculated for each participant and used to calculate a composite DII and E-DII score.

2.6.3 Calculating Daily Intake Frequency

Daily intake frequency for each food item was calculated in Excel. If a participant answered ‘yes’ to the DSQ question “During the past month, did you eat/drink any [food item]?” , daily frequency was calculated as the reported frequency rate divided by unit of time. When the unit of time was ‘day’, daily frequency was kept as reported. When the unit of time was ‘week’, daily frequency was calculated as reported frequency divided by 7. When the unit of time was ‘month’, daily frequency was calculated as reported frequency divided by 30 (National Cancer Institute, 2021a).

Missing frequency data:

In the instance participants indicated ‘yes’ to eating or drinking a food item, yet no frequency rate was reported and ‘don’t know’ was selected as the unit, daily frequency was calculated as zero. If a rate was reported, but ‘don’t know’ was selected as the unit of time, daily frequency was calculated using a ‘monthly’ unit of time. This assumption allowed for participant data to be included while calculating a frequency that most closely reflects a participant intake that leaned towards an lower assumed daily frequency in comparison to assuming a ‘weekly’ or ‘daily’ unit of time. This occurred 50 times.
among participants across all 25 food items, equaling an average of two participant frequency adjustments per each food item.

*Winsorized frequency data:*

Data was sorted in excel to identify extreme values of reported consumption rates. To reduce potential influence of extreme outlier frequency values, some data was winsorized as follows:

Coffee: Total daily frequency was winsorized at a maximum of 7 times per day. Only two participants reported a daily intake greater than 7. (Extreme values were 9 and 10 times per day.) A maximum of seven was selected, as a daily frequency of 7 was repeated within the data set multiple times.

Milk: Total daily frequency was winsorized at a maximum of 7 times per day. Only two participants reported a daily intake greater than seven. (Extreme values were 8 and 10 times a day.) A maximum of seven was selected, as a daily frequency of 7 was repeated within the data set multiple times.

Cereal: Total daily frequency was winsorized at a maximum total of four. Ten participants reported they ate cereal more than 4 times a day. (These ten participants reported eating cereal 5, 6, 7, or 30 times a day.) A maximum of four was selected to account for potentially eating cereal for three typical meals plus one snack.

Winsorizing coffee intake would decrease the inflammatory potential (improve the DII score) of their measured intake, as caffeine is a pro-inflammatory parameter. Winsorizing milk frequencies would potentially decrease the inflammatory potential (improve the DII score) as CHO and saturated fat are pro-inflammatory. The effect of winsorizing cereal on overall DII scores would be dependent on the type of cereal
indicated by each participant. Sugary cereals would act as pro-inflammatory, but fiber-rich fortified whole grain cereals may contribute to an anti-inflammatory effect.

2.6.4 Identifying Average Portion Size or Serving Size

Data on portion-sizes of food intake was not included in the reported DSQ data. Data indicating average portion sizes, which was needed for calculating participants’ total dietary intake, were collected as follows:

A NHANES DSQ scoring procedure uses mean sex-age specific portion size equivalents of food groups defined in the Dietary Guidelines for Americans, 2015 (National Cancer Institute, 2019, 2021b; Thompson et al., 2017; U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2010). Mean sex-age specific portion size equivalents for adults were obtained from the NHANES DSQ scoring procedures for the following food items: Fruit, 100% pure fruit juices, Refried beans, baked beans, beans in soup, cooked dried beans, whole grain bread, brown rice or other cooked whole grains, milk, cheese, green leafy or lettuce salad, fried potatoes, other kinds of potatoes, other vegetables, tomato sauces, salsa.

This study was unable to use the provided DSQ scoring sex-age specific portion size equivalents for the following food items: 1. Pizza, 2. Cookies, cake, pie, brownies 3. Doughnuts 4. Candy/chocolate 5. Fruit drinks/sports drinks 6. Soda 7. Frozen desserts 8. Coffee or tea 9. Popcorn 10. Cereals. Inability to use the provided mean portion sizes are due to the following: Mean portion size equivalents of pizza were presented to reflect fruit and vegetable equivalents verses mean portion size of the whole food. Mean portion size equivalents of popcorn and cereals were presented to reflect whole grain equivalents verses mean portion size of the whole food. Mean portion size equivalents of cereals,
cookies, doughnuts, chocolate/candy, sweetened fruit drinks/sports drinks, soda, ice cream or other frozen desserts, and coffee or tea were each presented to reflect teaspoon equivalents of added sugars verses the mean portion size of the whole food. (Multiple efforts to locate data on the initial 24-h NHANES dietary recall portion size data of whole foods used to calculate the portions sizes of added sugars or whole grains indicated by the DSQ scoring procedures proved unsuccessful.) For these food items, mean portion size estimates were obtained from the USDA as FDA Reference Amounts Customarily Consumed (U.S. Food & Drug Administration, 2022). Reference amounts of one serving size were presented as one value for all age groups and sex combined. Suggested portion sizes for cereals were based on cereal density. Suggested serving size for red meat and processed meat were obtained from American Heart Association. (See Appendix J)

2.6.5 Determining Total Daily Intake of Each Food Item

Daily intake frequency was multiplied by the respective average portion size, based on age and sex when applicable, to calculate total intake of each food item in cup, ounce, or gram equivalents for each participant.

2.6.6 Collecting Nutrient Data

Dietary nutrient profiles, consisting of at least 19 of nutrient parameters, are required to calculate a DII score. To obtain nutrient profiles to accompany the DSQ’s frequency of dietary intake data, representative foods were selected for each of the 25 food items (See Appendix K). Data for the following 25 available nutrient parameters, needed to calculate at DII/E-DII score for each participant, were collected for each representative food item using the USDA Food Data Central database: Energy (kcal),
Protein (g), Total Fat (g), Carbohydrate (g), Fiber (g), Iron (mg), Magnesium (mg), Zinc (mg), Selenium (ug), Vitamin C (mg), Thiamin (mg), Riboflavin (mg), Niacin (mg), Vitamin B6 (mg), Folic Acid+Folate (µg), Vitamin B12 (µg), Vitamin A (RAE) (µg), Beta-Carotene (µg), Vitamin E (mg), Vitamin D (D2+D3) (µg), Saturated Fat (g), Monounsaturated Fat (g), Polyunsaturated Fat (g), Cholesterol (mg), and Caffeine (mg).

Selecting Representative Foods

Representative foods were chosen to reflect the top consumed foods for each food item category of the DSQ. Representative foods selected for fruit, 100% pure fruit juices, beans, cheese, other vegetables were based on the 2019-2020 USDA data report for Loss-Adjusted per capita food availability, as “the data serve as proxies for actual consumption at the national level” (USDA Economic Research Service, 2021). The USDA notes that “Loss-adjusted food availability data (LAFA) are derived from food availability data by adjusting for food spoilage, plate waste, and other losses to more closely approximate actual consumption.” (USDA Economic Research Service, 2021). USDA data was reported in lbs/year, oz/day, and g/day, and organized by year dating from 1970 to 2018. For this study, data used to identify top consumed foods for each food item category was gathered from 2011 reports, given that the IBD Partners data was also collected in 2011.

The seven highest reported ‘consumed’ fruits, based on their 2011 per capita availability adjusted for loss data, were selected as representative foods for Fruit. Multiple fruits were selected for a representative fruit intake in efforts to generate a well-rounded, proportioned nutrient profile to best represent potential fruit intake among participants. The same approach was used to select representative vegetables for the ‘other vegetables’ food item. Potatoes, tomatoes, and lettuce were reported among the
top consumed vegetables, yet intake of these vegetables is reflected in other DSQ food items measured. The subsequent 5 highest reported consumed vegetables were selected for as representative foods for Other Vegetables. Per-capita food availability data for the two top fruit juices were reported at a noticeably higher consumption than all other juices, therefore the top two reported fruit juices were selected to represent consumption of 100% Pure Fruit Juices. In a similar fashion, the two top reported cheeses were selected to represent consumption of Cheese. The three top reported beans were selected in the same fashion as representative foods for the Refried Beans, Baked Beans, Beans in Soups, Cooked Dried Beans food item category. (See Appendix K)

Zeng et al. (2019), examined trends in red meat and processed meat consumption in the United States through 1999-2016, finding consistent consumption patterns of processed meat among adults over the 18 year trajectory. Zeng, et al (2019) identified the top five processed meats that accounted for 87% of total processed meat consumption: as luncheon meat (39.3%), sausage (24.4%), hot dog (9.4%), ham (9.4%), and bacon (4.6%). These five processed meats were used as representative foods for the Processed Meat Food Item.

For the Fruit, 100% Pure Fruit Juices, Beans, Cheese, Other Vegetables, and Processed Meat Food Items, multiple representative foods were selected to provide a well-balanced representative intake for each given food item. In cases where multiple representative foods were selected for one food item, intake of representative foods was proportioned based on reported consumption rates (See “Proportioning Combinations of Representative Foods for One Food Item” below).
Using words from the DSQ food item descriptions (National Cancer Institute, 2021c), the researcher searched USDA Data Central to select the representative food or foods that best matched the following remaining food item categories: Whole grain Bread, Brown Rice or Other Cooked Whole Grains, Red Meat, Pizza, Sweetened Fruit Drinks Sports Drinks or Energy Drinks, Soda, Coffee or Tea with Added Sugar, Chocolate or Other Types of Candy, Donuts, etc., Cookies Cakes Pie or Brownies, Ice Cream or other Frozen Desserts, Popcorn. (Selected representative foods for all 25 DSQ Food Items are shown in Appendix K.)

Two food items did not require use of representative foods. Participants indicated the type of milk they consumed by choosing from the following options: whole or regular; 2% fat or reduced-fat; 1%, ½%, or low-fat; fat-free, skim, or nonfat; soy; and other. If ‘other’ was selected, participants were able to specify their choice of alternative dairy by manual entry. Alternative entries included almond milk, lactose free milk, goat’s milk, rice milk, buttermilk, and cream/half & half. Cereal did not require representative foods, as participants were asked to select from a list of 328 specified cereals. 187 or the 328 specified cereals were indicated as consumed by participants (See Appendix L). For milk and cereal, DSQ response options were used in this study to obtain nutrient profiles for DII calculation.

Proportioning Combinations of Representative Foods for One Food Item

When multiple representative foods were used for one DSQ food item, nutrient data for representative foods were proportioned relative to most consumed, according to USDA data report for Loss-Adjusted per capita food availability (USDA Economic Research Service, 2021). (See Appendix K) Data used to identify top consumed foods for
each food item category was collected from 2011 reports, given that the IBD Partners
data was also collected in 2011. Proportions were determined by selecting the number of
representative foods (7 fruits), then totaling the per capita availability adjusted for loss in
g/day respective to each representative food. The per capita availability adjusted for loss
in g/day for each representative food was then divided by the totaled g/day to equate the
percentage of contribution each representative food would provide to the proportioned
nutrient profile.

When participants were asked to select the type of cereal they eat, they were
allowed to select up to two types of cereals. In cases where participants identified two
cereals, nutrient data for each cereal was proportioned at 50%.

**Gathering Nutrient Data for Representative Foods**

Nutrient data for each representative foods, as well as each of the 185 specified
cereals and reported milks were found using USDA Food Data Central. Cereals that
were unavailable on USDA Food Data Central were treated as a similar cereal that best
matched the participant’s initial reported selection (See Appendix L) and had typically
been discontinued from the market.

USDA Food Data Central provides nutrient data using information from five
distinct data types: Food and Nutrient Database for Dietary Studies 2017-2018 (FNDDS),
National Nutrient Database for Standard Reference Legacy Release (SR Legacy), USDA
Global Branded Food Products Database (Branded), Foundation Foods, and Experimental
Foods. This study gleaned nutrient data primarily from the FNDDS, as this database
typically provided a more comprehensive nutrient profile relative to the purposes of this
study. When FNDDS data was not available for a specific food, most often in the case
for cereals, SR Legacy or Branded data was collected. All nutrient data was organized and stored in Excel.

USDA Food Data Central databases provided nutrient data for a select number of portion sizes or measured amounts (e.g. grams, slices, cups, teaspoons). When possible, the measurement amount was selected to match the cup, gram, or ounce equivalent determined as the typical portion size for use in this study. (See 2.6.4 Identifying Average Portion Size or Serving Size). When an equivalent measurement amount was not available, nutrient data was recorded for the provided measurement amount and then multiplied by the appropriate percentage of the provided measured amount to result in nutrient values that reflected the portion sizes used for this study (See Appendix J and Appendix L).

Nutrient values for up to 25 parameters were gleaned for each food. These 25 parameters included: Energy (kcal), Protein (g), Total Fat (g), Carbohydrate (g), Fiber (g), Iron (mg), Magnesium (mg), Zinc (mg), Selenium (ug), Vitamin C (mg), Thiamin (mg), Riboflavin (mg), Niacin (mg), Vitamin B6 (mg), Folic Acid+Folate (µg), Vitamin B12 (µg), Vitamin A (RAE) (µg), Beta-Carotene (µg), Vitamin E (mg), Vitamin D (D2+D3) (µg), Saturated Fat (g), Monounsaturated Fat (g), Polyunsaturated Fat (g), Cholesterol (mg), and Caffeine (mg).

2.6.7 Calculating total nutrient profile for each participant

For every participant, a total nutrient profile was calculated. Values for each of the 25 nutrient parameters were totaled across all foods in order to obtain a single daily intake value per nutrient parameter for each participant. Nutrient profile calculations were performed in Excel.
Calculating Nutrient Parameter Values

For each of the 25 DSQ food items/categories, each participant’s total values for each of the 25 nutrient parameters were calculated. If a participant indicated ‘yes’ to eating a food item on the DSQ, the reported daily frequency of eating that item was multiplied by the representative food’s nutrient parameter value, with available age and sex specific portion sizes taken into account. For each participant, this was done for each of the individual 25 nutrient parameters, across all of the 25 DSQ food items and categories. Extensive if/then equations were written and applied in Excel to calculate all values (based on age and sex when age/sex specific portion sizes were applicable to the food item- see 2.6.4 Identifying Average Portion Size or Serving Size), described as follows:

When one representative food was used for a food item:

\[ \text{If ‘yes’ to eating food item, and (sex), within (a specified age group), then age/sex specific portion size (daily frequency*parameter value of representative food)} \]

When multiple representative foods were to be proportioned:

\[ \text{If ‘yes’ to eating food item, and (sex), within (a specified age group), then age/sex specific portion size * [daily frequency* \((\text{proportion % of representative food 1*parameter value of representative food 1 }) + (\text{proportion % of representative food 2*parameter value of representative food 2}) + (\text{proportion % of representative food 3*parameter value of representative food 3}) \)]} \]

An example of an excel command written to calculate each individual participant’s single parameter intake from three proportioned representative foods in one
food item category is as follows and includes commands that take into account sex, each age group, and each age/sex specific portion size:

\[
=IF(AND(D10=1,B10=1,C10>=18,C10<=25),(0.65*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8))))), IF(AND(D10=1,B10=2,C10>=18,C10<=25),(0.48*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=1,C10>=26,C10<=35),(0.56*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=2,C10>=26,C10<=35),(0.495*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=1,C10>=36,C10<=45),(0.72*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=2,C10>=36,C10<=45),(0.43*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=1,C10>=46,C10<=60),(0.63*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=2,C10>=46,C10<=60),(0.47*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=1,C10>=61,C10<=69),(0.655*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=2,C10>=61,C10<=69),(0.34*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=1,C10>=70),(0.635*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))), IF(AND(D10=1,B10=2,C10>=70),(0.37*(G10*((0.47*$I$6)+(0.29*$I$7)+(0.24*$I$8)))),0))))))))
\]

Similar equations were written for each of the 25 DSQ food items and individually adjusted for application to each of the 25 food parameters’ data.

**Calculating Nutrient Parameter Totals**

Total parameter values for each of the nutrient parameters across all representative foods were calculated for each participant. Using an excel spreadsheet, parameter values were summed for each participant, resulting in one total value for every nutrient parameter, which reflected the combined representative nutrient intake for that
particular parameter across all 25 DSQ food items and categories. Nutrient parameter values were organized by DSQ food items/categories using multiple Excel spreadsheets within one file. An example of one Excel equation used to calculate one parameter’s total value across all foods for one participant is as follows:


All nutrient parameter totals were calculated for each participant. Each participant’s total nutrient profile consisted of total parameter values for each of the 25 nutrient parameters.

2.6.8 Generating a Dietary Inflammatory Index Score

For this study, total nutrient profiles for each participant were submitted to James Hébert, PhD at the University of South Carolina, Department of Epidemiology, who calculated DII and E-DII scores from the provided representative nutrient data. A number of steps are taken to calculate a DII score. From a participant’s reported intake amount of a parameter (e.g., 6 g of fiber/day), an indexed ‘standard mean’ intake for that parameter is subtracted. The resulting value is divided by an indexed standard deviation. The value is then converted to a percentile. The percentage is doubled, from which 1 is then subtracted. This generates a centered percentile value, which is then multiplied by an overall food-parameter specific inflammatory effect score (Shivappa et al., 2014a). The resulting value is the food parameter-specific DII score (for one parameter). This
calculation is performed for each parameter and reported intakes separately for parameter-specific DII scores. DII scores for each parameter are then summed to calculate the participant’s total overall DII score.

**Summary**

This chapter outlined the mixed methods research design using two separate studies to address the specific aims guiding this dissertation. Chapter 4 presents the results of Study 1 and Study 2 in two separate manuscripts.
CHAPTER 4
RESULTS

4.1 Manuscript 1

“Preventing a flare would be to continue living as if you are in a flare even when you’re not, and I’m not good at that.”- The Use of Treatment and Self-Management Methods Among Patients with Ulcerative Colitis

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Abstract

Objective: This study examines how treatment and management methods are used by individuals with Ulcerative Colitis (UC) and how patients make decisions regarding the use of these methods throughout the disease course.

Methods: Qualitative data were collected using individual semi-structured interviews and analyzed using thematic analysis in Nvivo12.

Results: Decisions are shaped by a patient’s approach towards disease management, personal experiences, sources of information and individual motivating factors. Patients are willing to try new methods of management and overlook long-term implications in order to reduce suffering and be able to ‘function’ in the present day. Suffering may motivate long term behavior change, but the majority of participants tend to utilize most treatment and management methods as responses to flares and UC suffering instead of as preventative health behaviors.

Conclusion: This study offers added insight into how and why treatment and management methods are used to reduce the physical and psychosocial burden of illness associated with UC.

Practice Implications: Study findings can aid in framing patient education and behavioral interventions that assist patients with UC in adopting and sustaining self-management behaviors to reduce and prevent disease activity.
Introduction

Ulcerative Colitis (UC) is an inflammatory bowel disease (IBD) defined by inflammation and ulcerations of the mucosal lining of the colon and an unclear pathogenesis. Current frameworks suggest the development and progression of UC is a complex combination of environmental factors, abnormal immune response, gut microbiota, and genetic predisposition (Porter et al., 2020). The direct and indirect costs of IBD generate a substantial economic burden on patients and health care systems driven by factors such as medical therapies, hospitalizations, surgeries, lost work time with costs for UC totaling nearly $15 billion annually (Beard et al., 2020). UC is characterized by unpredictable fluctuations between periods of disease activity and remission. Periods of active disease, or flares, present exacerbations of disease symptoms and the greatest burden on daily functioning, yet disease activity often fluctuates in symptom severity over the disease course and much of the extraintestinal burden continues throughout periods of remission as well.

Patients with UC experience a range of gastrointestinal and extraintestinal symptoms that generate a significant burden on daily life. Prominent localized physical symptoms include rectal bleeding, bowel urgency, bowel frequency, diarrhea, and significant abdominal pain. Patients also report considerable physical and cognitive fatigue, isolation, reduced productivity, ‘brain fog’, diminished self-concept, anxiety, depression, strained relationships, as well as strained physical, emotional, and social functioning (Devlen et al., 2014; Fedosiejew et al., 2016; Fourie et al., 2018; López-Sanromán et al., 2017; Matini & Ogden, 2016; Yarlas et al., 2018). The most common approach for treatment and management of UC symptoms is physician-prescribed
pharmaceutical therapies. The primary goal of medical treatments for UC is to reduce symptoms and induce a state of remission by regulating the immune system with medication (Crohn’s and Colitis Foundation, 2022; Falvo & Holland, 2018). For many individuals with UC, pharmacotherapy is often reported as insufficient to maintain a ‘normal’ lifestyle. Moreover, the use of multiple concurrent medications is not uncommon in attempts to control symptoms (Falvo & Holland, 2018; Fourie et al., 2018; Matini & Ogden, 2016; McMullan et al., 2017).

Many of those diagnosed with UC seek out a combination of medical, lifestyle, and/or alternative treatment and management methods in efforts to mitigate disease symptoms, reduce dependence upon pharmaceuticals, and respond to the challenges of living with chronic illness. While existing research has indicated the use of various treatment and management methods among individuals with UC, current literature is lacking sufficient description of how individuals use treatment and management methods on a daily basis and over the disease course, as well as examination of the perspectives, resources, and motivations supporting utilization of various methods (Crooks et al., 2021).

Seeking out personal preference-based management options for treatment of UC has been associated with a high quality of life and successful self-management (Wickman et al., 2016). Greater understanding of patient perspectives and experiences influencing treatment and management decisions may inform evidence-based programs to promote self-management and contribute to improved patient care within the UC population. The purpose of this study is to examine how treatment and management methods are used by
individuals with UC and how patients make decisions regarding the use of these
treatment and management methods throughout the disease course.

Methods

Qualitative data were collected using individual semi-structured interviews (n=21) to obtain in-depth data reflecting the perspectives and experiences of individuals with UC. Eligibility criteria included: 1) diagnosis of UC; 2) duration of illness ≥5 years; 3) a minimum of one disease flare during the illness trajectory; and 4) English speaking.

Patients were recruited in collaboration with a large gastroenterology clinic in South Carolina (n=9), a support group for individuals experiencing Crohn’s and UC (n=2), an integrative medicine clinic in South Carolina, (n=1), and through posting study fliers in two UC-focused Facebook support groups (n=9). A purposive sampling strategy was used in recruitment collaborations with these entities for at least 20 participants. At the gastroenterology clinic, patients who met eligibility criteria were identified by clinic staff and mailed an invitation to participate in the study. Staff members of the support group and integrative medicine clinic identified qualifying individuals and shared study recruitment fliers. This study was approved by the University of South Carolina’s Institutional Review Board.

Interviews were conducted by KD in person (n=10), over a secure web-based platform (n=4), or over the phone (n=7) according to participant preference. Interviews lasted approximately one hour and addressed the participant’s retrospective illness trajectory, the impact of UC on daily life, experiences with medical and complementary or alternative treatment methods used to control disease activity, methods for self-managing the impact of UC on daily living, and processes of making decisions regarding
treatment and management of UC of the course of illness. (See Appendix E for full interview guide.) Participants shared their experiences using treatment and self-management methods and described factors that contributed to their decisions to use such methods.

Interviews were audio recorded, transcribed verbatim, and reviewed for accuracy. Thematic analysis was conducted using QSR International NVivo 12 software (QSR International, 2020). A primary coder (KD) led the analysis with input from a secondary coder (CB) throughout the process. Transcriptions were first read in whole to capture the overall context of passages (KD). An initial codebook was developed from analysis of the first five interviews using an emergent inductive approach, and guided the coding of subsequent transcripts, allowing for additional codes to be added as they emerged in the data (Creswell, 2007; Miles & Huberman, 2013; Patton, 2015). KD coded passages of text relevant to the study’s aim to reflect the content and meaning of each passage. Content and meaning of passages was discussed and clarified in biweekly meetings with KD and CB to verify the data analysis to ensure accurate representation of the data (Creswell, 2007; Miles & Huberman, 1994). Codes were organized into meaningful themes and sub-themes across all interviews to capture key elements of the participants’ experiences (Miles & Huberman, 1994, 2013). Themes on treatment and self-management methods used by participants were iteratively assessed and categorized as medical, lifestyle, or complementary/alternative methods.
Results

Study Participants

Of the 21 participants, 14 were female and 7 were male. The mean age was 46.9 years (range: 26-67 years). The mean number of years since diagnosis was 19.2 years (range: 5-47 years). A total of 3 participants had previously undergone bowel surgery to remove diseased portions of their colon. The vast majority of the sample (90%) were white. Eleven participants resided in South Carolina, two in North Carolina, and one in each of the following states: Wisconsin, Florida, New Jersey, Ohio, California, Connecticut, Georgia, and New York.

Treatment and Self-Management Methods Used Over the Disease Trajectory

Medical

Participants identified medication, surgery, and self-advocacy as predominant biomedical methods for treatment and management of UC. All participants reported involvement with a gastroenterologist for disease management and were advised by their physician to use medication as a primary treatment approach. Medications, primarily including aminosalicylates, biologics, immunomodulators, and corticosteroids, were used as the primary treatment approach to manage gastrointestinal symptoms of UC. Most participants used medication as continual maintenance therapy, while a few relied on medications only as a short-term response to observed increases in disease activity. The majority of participants reported declined responsiveness to medications over the course of their illness and reported needing new ‘stronger’ medications as their illness progressed. Prescription medication was used among some participants to manage
depression and anxiety post-diagnosis. A few also mentioned occasional use of medications to manage pain and sleep quality.

Three participants had undergone bowel surgery to remove diseased portions of their colon. Participants expressed that they had expected their UC trajectory to be eliminated after surgery, yet they continued to need self-management of GI symptoms, experience fatigue, and have other complications (e.g. J-pouch twists and blockages). These patients experienced bowel frequency, abdominal pain, stress of ostomy management, and psychosocial challenges that extended the burden of living with UC beyond surgery treatment. One woman who experienced blockages, pain, and extraintestinal manifestations of illness post-surgery explained:

“...it’s not a cure all...you had an auto immune [disease]...you’re never going to be normal” (8)

Some participants identified self-advocacy within the medical environment as a key method of self-management, emphasizing the value of being their own advocate and effectively communicating needs to their physician to “get the best treatment that you can” (17). One young woman described:

“...you really have to advocate for yourself...It’s like a job that, you have to pay attention” (16)

Some patients learned over time to be proactive in their medical treatment. Staying informed, advocating for treatment changes, and keeping ahead of their disease management was important for self-management. One man shared:

“...when I would go to the doctor early on, it was just like okay, a last resort type thing. I’m not getting any better, I need to schedule an appointment...over the
years I’ve learned…I need to stay ahead of my appointments, stay up with my lab work, get ahead of everything.” (17)

A handful of participants reported making significant efforts to research and study the disease and various treatment options to educate themselves and become an active participant in decision making over the course of their illness. A few participants also reported taking personal action to seek out support groups or professional therapy to help manage the emotional burden associated with UC.

*Lifestyle Choices*

Participants employed multiple lifestyle methods in efforts to mitigate the burden of UC in daily life. Manipulating dietary intake, reducing stress, engaging in physical activity, and obtaining sufficient rest each played a role in managing UC for the large majority of participants.

Most participants believed at some point, at least, during their disease trajectory that diet played a role in managing burden of UC. Among those participants, a spectrum of approaches and attitudes towards diet were evident. Most participants described an enduring effort to identify dietary triggers responsible for UC symptoms. A common management strategy among many participants was to skip or delay meals to avoid GI symptoms. One woman tried to avoid any potential public embarrassment by not eating before venturing out of her home, saying:

“If I want to go somewhere, what I have to do is by five o’clock I cut myself off from eatin’ if I want to do something the next day.” (6)
Reducing stress was frequently acknowledged as an essential method to self-manage and prevent flares. To cope with or reduce stress, many participants changed employment or reduced their daily workloads, including dropping out of school and seeking disability benefits. Additionally, participants limited their professional and social commitments, avoided stressful situations, engaged in exercise, spent time outdoors, found enjoyment in various hobbies, made conscious efforts to reframe thoughts and mindsets, enjoyed the companionship of a pet, and relied on faith and prayer. One participant enjoyed moments of heated relaxation to help her self-manage her UC:

“I have one of those blankets that you plug in...oh, that helps tremendously. I just lock the door, put the seat back, and curl up...heat helps...it relaxes me, and I think the fact that I’m relaxed relieves some of the UC.” (10)

Another woman described her efforts to alleviate stress, particularly when experiencing flares:

“I would not make plans with people at all because I knew every ounce of energy had to be given to doing my work, so I just wouldn’t plan things. It was horrible. ...Trying to get rid of things, not adding anything to your plate, saying no to people more, or not taking more things on that you could, just trying to simplify your life as much as possible.” (15)

Although GI symptoms often limited high levels of physical activity, many participants used exercise as a method to reduce stress, reduce joint pain, increase energy, improve sleep, and improve overall health. Spending time walking outside was reported by one man to help improve his health, reduce stress, and mentally re-frame the burden of UC on daily life. He explained:
“I walk and jog at times. As far as the stress and just on it’s own, I think it helps. I’ll go for a walk around the block, and I’ll look at the houses... just gets my mind to a different place...putting it in perspective of- I’m in my house having these digestive issues, I have colitis, but yet, outside of my world,...there’s a million other things going on... that have nothing to do with what my perceived huge troubles are.” (13)

Many participants reported sufficient sleep and rest as essential to prevent and recover from flares. Rest was a predominant method for managing daily life with UC as participants not only felt deeply fatigued during flares and periods of remission, but also as a method to reduce stress and inflammation in efforts to mitigate disease activity. One woman shared:

“I need to make sure I sleep. It sounds kind of lame, but I just lay around and try to heal... if you don’t get rest, it gets worse.” (16)

Complementary/Alternative Treatments

Participants reported little use of complementary or alternative methods to manage their UC symptoms. A few participants were taking or had tried taking probiotics as an effort to improve overall general health. A few participants reported taking Vitamin D supplements to offset deficiencies associated with UC. One woman followed a regimen of natural remedies suggested by her chiropractor and naturopathic primary care physician (ex. “high doses of fish oil and very specific probiotics...” (22)) but was unable to maintain such a regimen due primarily to cost. She also made her own aloe enemas and homemade suppositories with coconut oil and essential oils.
Participants mentioned short term experimentation with growing mint for tea, nicotine patches, psyllium seed husks, and peppermint oil. Although no participants reported use of non-prescription drug use, a few expressed curiosity towards trying such methods.

Massage therapy was occasionally used to reduce stress and manage pain, since, as one woman explained, “I felt it was more natural than taking pain medicine.” (9)

Table 4.1. Treatment and Management Categories with Predominant Methods Used

| Medical          | • Medication  
|                 | • Surgery  
|                 | • Self-Advocacy  
|                 | o Patient-provider communication  
|                 | o Stay informed  
|                 | o Keeping ahead of disease management  
|                 | o Seek out professional therapy  
| Lifestyle       | • Dietary Change  
|                 | o Identify trigger foods  
|                 | o Skip or delay meals  
|                 | • Stress Reduction  
|                 | o Change employment/Reduce Workload  
|                 | o Limit professional or social commitments  
|                 | o Exercise  
|                 | o Hobbies  
|                 | o Reframe mindsets  
|                 | o Faith/Prayer  
|                 | • Physical Activity  
|                 | • Sleep/Rest  
| Complementary/Alternative | • Probiotics  
|                 | • Vitamins  
|                 | • Naturopathic supplements  
|                 | • Massage Therapy  

Decision-making on Treatments and Self-management Methods

Sources of Information

Although all participants were under physician care to some degree, few participants reported that conversations with their physician provided a sufficient amount of information about treatment and management methods overall. Participants noted
personal research and reading about treatment methods as playing a strong role in self-advocacy. Many described doing research on the Internet, particularly for information about medication and diet. One man explained that the information online is simply more accessible than doctors, and added:

“The internet’s there 24/7. Your doctor isn’t.” (13)

While nearly all participants reported not personally knowing anyone else with UC, most participants gleaned information through word of mouth, as participants considered perspectives from their extended social circle or from individuals on social media sharing experiences with various methods. Shared information would sometimes inspire willingness to try new things, generate confusion after receiving mixed messages, or ignite fear and aversion towards various treatment methods, specifically surgery and certain medications. One woman described the value in learning from other UC patients through online support groups by saying:

“I utilize the Facebook pages a lot because it’s other people that actually have what I have...I know that even though doctors are there with all this information, they’re not experiencing it themselves, So, people that actually have what I have, I feel like they’re the best sources of information because they have personal experience.” (18)

A few participants read various books providing dietary guidance (e.g., blood type diets, gluten-free, night shade vegetables, eliminating toxins). Books were often recommended by a friend who was diagnosed with cancer or another autoimmune disease.
Decision Making Approach

Participants described various approaches to making decisions surrounding the use of treatment and management methods. Participants often relied on physician recommendations for medical therapies. Some participants described taking ownership of the illness experience by utilizing individual decision-making skills and an attitude of self-advocacy. A great deal of trial and error also directed the use of treatment and management methods, particularly prescription medications and dietary change.

A majority of participants resorted to following physician recommendations for UC treatment, trusting that their provider was more knowledgeable on best practices. A few of those participants described shared decision making based on physician’s analysis of blood and stool test data, some trusted physician recommendations “because they haven’t steered me wrong” (14), and many followed physician guidance blindly. For example, one woman described her treatment regimen by saying:

“Right now, [medication] and the [medication] pills too. I don’t even know if that does anything, really, but my doctor said to take it. So, I don’t know...but I’ll just keep taking it...My doctor just said ‘if it’s working don’t stop it’...like, don’t mess with it.” (16)

Despite potential side effects, long term repercussions, and even desire for more ‘natural’ treatment methods, most participants often resigned to “keep doing what I’m doing for now” (8) and maintain treatment options that seemed to be keeping disease activity at bay. One woman explained her willingness to receive treatment despite her fears of the future by saying:
“I’m scared that the infusions one day are going to cause another problem, which is really scary, cause it’s like a really serious strong drug that I’m taking...but I’m okay with it cause it helps me right now.” (5)

Another woman echoed:

“they say a lot of [specific medication] can cause liver cancer...I can’t worry about that later on. I have to be able to function today” (3)

There was difference between taking ownership for the health condition (i.e., attributing the disease and disease course to personal health behaviors) versus taking ownership of the illness experience (i.e., belief that individual choices and behaviors can modify the lived experience). Few participants felt that they were responsible for the course of illness, as UC is unpredictable, but some participants felt that they could control how they would handle their experiences with UC. Some participants described taking ownership of their illness experience and making their own decisions regarding how and when to use treatment and management methods. Some of these participants felt free to self-assess and make minor adjustments to their medication dosing. For example, one man described how he adjusted doses of his daily maintenance medication based on symptom activity, saying:

“I actually take one in the morning unless I have some sort of flaring going on, in which case I’ll take three.” (19)

Many of those who took ownership of their illness experience often worked through making changes in their own daily health behaviors in attempts to mitigate disease activity before reaching out for additional medical treatment. In response to a flare, many
participants described trying to reduce stress, adjust dietary intake, and/or rest. One woman shared:

“Despite the fact that I despise Prednisone with every fiber of my being, it does work. I only take it when I've done everything else on my own. I go through the process on my own first. I know when I need to ask for help.” (14)

Participants who took ownership of their illness experience used self-advocacy to manage their illness experience, often searching for greater satisfaction with treatment options and patient-provider communication. In regards to her experience with physicians who did not provide appropriate care, one woman emphasized:

“You need to find somebody else [physician] that listens to you...but you have to be informed and ask them the questions that...they're not a mind reader. You're wasting your time in there if you go in there and just go, ‘I don’t know, I just stopped feeling good.’” (3)

Most participants described extensive trial and error within treatment and self-management methods. As many insurance companies require a progressive treatment approach to the prescription of medications approved for UC, participants commonly experienced a pre-determined trial and error approach to finding a medication that could induce and maintain remission. Additionally, some participants preferred taking time to try all other available treatment options before resorting to certain medications or UC surgery. One woman felt overwhelmed by the impact the multi-step J-pouch surgery would have on her life and explained:

“And I decided at that point I just needed to take some time off and just try every possible approach that I could before I do surgery. (9)
Trial and error predominantly guided participant’s perspectives on diet as a self-management method. Some participants reported trying diet as a treatment method and observed no perceived success, and consequently disregarded diet as a treatment and management method. For example, one woman felt that the efforts she made to change her diet were ineffective, and concluded the following:

“I tried fixing my diet of going gluten free...that didn’t do anything...I started doing dairy free. That didn’t do anything. So for me, diet hasn’t made me any better.” (18)

Others identified dietary changes that seemed to alter their entire experience with UC, and therefore adopted new dietary behaviors long term. Many participants made associations between specific foods and disease activity based on immediate observed gastrointestinal symptoms. For example, one woman described how she identified packaged lunch meat as a food that ‘triggered’ UC symptoms using trial and error observations:

“As long as I buy deli meat, like, fresh sliced deli meat, it doesn’t bother me, but if I buy packaged, like off the shelf, yeah, it kicks my tail...packaged meat and I’m like ‘whew’, you know? Two or three times I’ll go to the bathroom after that. And for the longest time I couldn’t figure out what it was....I had a sandwich, why’d it bother me today? It’s a sandwich. But then I got putting two and two together that it was deli meat and that was, so, I don’t know.” (4)

Another man described his observations over time as he sought to identify patterns between diet intake and UC symptoms:
“You learn food that sort of will trigger things. The pepperoni pizza... four hours later I’ll be spending some time in the bathroom. You know, I mean, you avoid certain things. I won’t eat very spicy foods, they will just go through me. And there’s other times I can have chicken soup and I’ll be in the bathroom three or four times after that. So, it’s hard, you know, inflammatory bowel disease is a strange auto-immune type of disorder.” (21)

Motivating Factors for Treatment & Management Decisions

Overall, participants used treatment and management methods to reduce the physical and psychosocial burden of living with a chronic illness. Participants aimed to reduce gastrointestinal symptoms, overcome and recover from fatigue, cope with the fear and anxieties of an unpredictable illness, avoid embarrassment, cope with physical and emotional isolation, and avoid pain and suffering. Participants described various individual goals such as wanting to keep up with demands of daily life, raise a family, be productive, and have peace of mind.

Participants frequently reported that a strong motivator for change and method use across all treatment and management methods was the suffering associated with UC symptoms. Patients reported feeling ‘miserable.’ Suffering motivated a willingness to embrace new treatment recommendations and action towards adopting behavior change. Participants experienced flares and were subsequently willing to add additional or new prescriptions to their treatment regimen. One particular young woman felt hesitant to begin taking a biologic therapy, but explained how she weighed her decision:
“So, I can either not function, or lose my colon or whatever, or I can just bite the bullet and get this done.” (15)

Another participant avoided physician treatment until her suffering was too much to bear:

“I remember because I thought maybe it [flare] would just go away by itself. It would kind of ease off and it would get worse, and finally...I said, you guys got to do something. I’m going to die, this thing is killing me. And so they [physician’s office] gave me a month’s worth of Prednisone.” (20)

Ineffective treatment, and the associated suffering, often motivated participants to try new treatment modalities. One woman sought out homeopathic treatment when she felt other options were not working, saying “I just went to him kind of out of desperation” (22). Later, after a pregnancy and flare, she felt resigned to return to pharmaceutical therapies, explaining:

“what we were doing, just wasn’t...I was going downhill so fast that I ended up on, you know, Remicade” (22)

Suffering motivated a few participants to make significant lifestyle changes. For example, one young man explained how his initial experience with UC motivated him to increase his physical activity in order to live a healthy life:

“I used to like just sit around all day. Now I bike, I run, I walk everywhere.

...Probably like a month after I started getting symptoms,...like I was having symptoms and I was trying to be active...I wanted to be healthier in general. Just, I knew I had to change.” (11)
Another man reported making long term changes to his dietary patterns in addition to staying loyal to his maintenance medication to avoid living with active disease symptoms, saying:

“I’d eat a big bowl of bread pudding with a pint of ice cream…I cut that out and things improved. ...We used to eat a lot of red meat...switched over to fish and chicken. I pretty much quit eatin’ a lot of stuff too because I didn’t want to go to the bathroom so much.....I switched over to eating brown rice every day instead of French fries, and...deep fried Okra...if I bake them, they won’t irritate my tummy. ...I don’t want to go back to the old days again” (2).

Participants reported adopting the majority of treatment and management methods in reaction to flares with hopes to reduce UC symptoms and suffering. Outside of maintenance medications and efforts to reduce stress, participants rarely described the use of treatment and management methods as preventative measures against disease activity and disease progression. Preventative self-management was often perceived as challenging to maintain, given the common belief that:

“...preventing a flare would be to continue [living as if] you are in a flare even when you’re not, and I’m not good at that.” (15)

Discussion

Over the illness trajectory, patients with UC experience fluctuating levels of suffering associated with disease activity, with no clear or consistent patterns of treatment and management methods across patient experiences evident to yield optimal UC outcomes or justify disease flares. From the patient perspective, fluctuations in disease activity are attributed to stress, diminished medication effectiveness, or dietary triggers.
Decision making surrounding the use of various treatment and management methods is shaped by a patient’s approach towards disease management, personal experiences, sources of information and individual motivating factors.

In this study, the leading reported motivating factor for the use of treatment and management methods was personal suffering. Living with UC is accompanied by physical symptoms and psychosocial challenges that cause significant suffering and disruption in patients’ lives. Especially during times of active disease, patients are willing to try new methods of management and overlook long-term implications in order to reduce suffering and be able to ‘function’ in the present day. For a few patients, suffering has motivated long-term health behavior change. Although suffering motivates the use of treatment and management methods, this study found that the majority of participants tend to use treatment and management methods in reaction to suffering and disease activity.

Patients identify some medications and overall stress reduction as important methods to avoid UC flares, yet treatment and management methods are predominantly employed as efforts to recover from flares and reduce existing symptoms. Recent research is recognizing UC as a progressive illness with a growing need for preventative action against progressive damage and impairment (Cleveland et al., 2022). A need is evident for patients to shift away from reactive treatment and management approaches and adopt preventative behaviors. Work is needed to support and empower patients with UC to take action around disease activity, and to increase understanding on how behavioral management methods influence the disease course (Conley & Redeker, 2016; Rozich et al., 2020). Research is needed to design and evaluate methods to shift
treatment and management approaches away from reactive measures and promote preventative self-management behaviors.

Participants in this study typically rely on physician recommendations for the use of pharmaceutical therapies. At the same time, many patients reported that physicians did not provide sufficient information regarding treatment and management methods. A recent study interviewed 10 patients with UC about the drivers of decision-making regarding pharmaceutical treatments versus colorectal surgery, finding that patient-provider communication was a key driver of decision making, decision satisfaction, and adherence (Lai et al., 2019). Findings from this study suggest that many patients seek out and collect the majority of advice and information regarding forms of treatment and management methods from peers and the Internet. Additionally, the majority of treatment and management methods are adopted through a trial-and-error approach. Given that UC has no known cause or cure at this time, the use of medical therapies and lifestyle methods are guided by trial and assessment of effectiveness.

Findings from this study highlighted a difference between taking ownership for the health condition (i.e., attributing the disease and disease course to personal health behaviors) versus taking ownership of the illness experience (i.e., belief that individual choices and behaviors can modify the lived experience). Few participants feel that they are responsible for the unpredictable course of illness, but some believe that they can control, to varying degrees, how they manage their experiences with UC. A few patients in this study take an active approach to managing their illness experience through individual-based decision-making, health behavior change, and self-advocacy towards greater satisfaction with treatment options and patient-provider communication.
Overall, participants use an individualized mix of treatment and self-management methods to overcome the challenges of living with UC in daily life. Daily life with UC carries a significant physical, emotional, mental, professional, and social burden. Participants report unpredictable disease trajectories and adaptive approaches to treatment and disease management over time. Treatment and management effectiveness varies among participants, as does sustainability of method use. Medication, self-advocacy, dietary change, stress management, physical activity, and sleep improved participants’ individual experiences overall, yet are often utilized as responses to flares and UC suffering instead of as preventative health behaviors. Patients express reliance on physicians for pharmaceutical treatment, yet identified diet restrictions and stress management as a main approach for self-management of UC.

Diet is characterized in this study as a lifestyle method of treatment and management due to the context of participant responses describing dietary practices as a behavioral change to their normal or previous lifestyle. Individuals with UC have reported diet manipulation as a strategy for managing gastrointestinal symptoms for quite some time (Hall et al., 2005), yet research examining diet as a behavioral treatment and management method for mitigating disease activity is relatively new (Celiberto et al., 2018; Torres et al., 2019; Wark et al., 2021). This study found that dietary change as a management method often evolves over time through extensive trial and error, during which participants evaluate diet’s impact on disease activity based primarily on immediate GI symptoms. A study on dietary practices and beliefs among patients with UC also found that over 90% of patients’ beliefs regarding diet and disease activity were based on the patient’s personal experiences (Crooks et al., 2021).
Participants report strong beliefs regarding the negative impact of stress on disease activity. Reducing stress is widely reported as a key management method for preventing and recovering from flares. Prolonged stress can elicit numerous physiological reactions that contribute to immune dysfunction and increased inflammation (Glaser & Kiecolt-Glaser, 2005). Prolonged stress also contributes to imbalances in the microbiome and natural gut flora, shown to be associated with IBD (Aleksandrova et al., 2017; Lane et al., 2017). Living with UC is arguably, on its own, a chronic stressor. Patients experience fatigue and reduced productivity, strained relationships, marital disruption, reduced sexual activity, various misconceptions due to the social stigma that accompanies an ‘invisible’ illness (Larsson et al., 2017; Rapport et al., 2019; Taft et al., 2009). The burden of illness associated with UC contributes to the ongoing nature of the illness by adding prolonged stress and, therefore, systemic inflammation and a reduced immune system (Fedosiejew et al., 2016; Larsson et al., 2017).

The use of complementary and alternative methods is low among participants in this study. This may be due to the recruitment of a portion of the participant sample through a gastroenterology clinic. Some participants expressed openness to complementary and alternative methods, including supplements, chiropractic care, acupuncture, and massage therapy as potential treatments, but high costs and limited familiarity are strong barriers to use overall. Although various types of complementary and alternative methods exist, research examining their effect on UC is limited (Torres et al., 2019).
This study depended on volunteer participants who were willing to share their experiences with UC, which may skew the variability of the sample, yet the participant sample provided perspectives and experiences from patients under the care of many different health facilities. Although this study included recruitment through social media and integrative health care clinics, all participants reported treatment under physician care, which may have limited a broader collection of data on the use of alternative therapies. Findings from this study are limited to patient perspectives and do not assess the biopsychosocial effectiveness on reducing the burden of UC. At the same time, this qualitative study provides deeper understanding of the perspectives and lived experiences of patients with UC.

Recent research calls for an expanded view of self-management in IBD research; to expand beyond symptom management and explore methods for improving emotional, social, and psychological well-being among individuals with IBD (Peters & Brown, 2022). Most self-management interventions for people with UC target decision-making skills and partnering with healthcare providers, but lack focus on symptom management, employment, or other aspects of daily life affected by UC (Conley & Redeker, 2016). This study offers added insight into the use of treatment and management methods to manage the physical and psychosocial burden of illness on daily life.

Findings from this study can inform providers on factors that influence patient decision making and support improved patient-provider communication. Collaborative care between patients and providers helps patients feel a sense of control over their illness verses their illness controlling them, which, in turn, improves self-management overall (Plevinsky et al., 2016). Additionally, these findings can aid in framing patient education
and behavioral interventions that assist patients in adopting and sustaining self-management behaviors to reduce and prevent disease activity.
References


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4.2 Manuscript 2

Ulcerative Colitis is Associated with Diet-Related Inflammation and Physical Activity in the IBD Partners e-Cohort

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Abstract

*Background:* Individuals with Ulcerative Colitis (UC) seek complementary lifestyle methods, such as diet and physical activity (PA), to manage the challenges of living with chronic illness. The Energy Adjusted Dietary Inflammatory Index (E-DII™) measures the inflammatory potential of food intake and has never been studied among the UC population. This study tested the associations between E-DII scores, PA, and health outcomes.

*Methods:* Data obtained from IBD Partners e-cohort participants with UC (n=2,052) were analyzed using a cross-sectional, secondary data analysis. Dietary data were converted into an E-DII score. PA data were collected using the Godin-Shephard Leisure Time Activity Index. Outcome variables included the Simple Clinical Colitis Activity Index, Short Inflammatory Bowel Disease Questionnaire, and psychosocial PROMIS domains. Multivariable regression models controlled for age, sex, body mass index (BMI), race, education, diet, PA, smoking status, medication class, and disease duration.

*Findings:* Pro-inflammatory dietary intake, indicated by E-DII score, was associated with increased disease activity (β=0.166; p<0.001), anxiety (β=0.342; p=0.006), depression (β=0.408; p=0.004), fatigue (β=0.386; p=0.005), sleep disturbance (β=0.339; p=0.003), and decreased social satisfaction (β= -0.370; p=0.004) and QoL (β= -0.056; p<0.001). PA was inversely associated with disease activity (β= -0.108; p<0.001), anxiety (β= -0.025; p=0.001), depression (β= -0.025; p=0.001), fatigue (β= -0.058; p<0.001), and sleep disturbance (β= -0.019; p=0.008), while positively associated with social satisfaction (β=0.063; p<0.001), and QoL (β=0.005; p<0.001). The benefit across
outcomes, excluding depression, was greater for strenuous PA intensity than for moderate or mild. For all outcomes, interaction effects between E-DII and PA were not significant.

**Interpretation:** An anti-inflammatory diet and PA are associated with decreased disease activity, anxiety, depression, and fatigue, and improved QoL, sleep, and social satisfaction for patients with UC. Such modalities may aid in managing systemic and localized inflammation associated with UC and reduce the burden of UC on daily living.

**Funding:** Crohn’s and Colitis Foundation Young Investigator Award.

**Keywords:** inflammatory bowel diseases; disease severity; ulcerative colitis; diet; inflammation; dietary inflammatory index; physical activity
Introduction

Ulcerative Colitis (UC) is a chronic illness under the umbrella of Inflammatory Bowel Disease (IBD). UC is characterized by chronic inflammation and ulcerations in the colon’s mucosal lining due to abnormal inflammatory and immune system responses (Crohn’s and Colitis Foundation, 2022; Porter et al., 2020). The majority of cases are currently diagnosed in Western societies, reflecting to some extent reporting/diagnosis bias (Delgado-Rodríguez & Llorca, 2004; Jairath & Feagan, 2020; Solomon, 1992). Despite the complexity of the condition and irregularities in reporting and data collection (Mulder et al., 2014), IBD is becoming a global health issue as incidence rates are rising throughout the world (Jairath & Feagan, 2020; Windsor & Kaplan, 2019). For example, IBD is known to be grossly underreported in India (Amarapurkar et al., 2018; Banarjee et al., 2020; Jain & Venkataraman, 2021; Maroo et al., 1974; Olfatifar et al., 2021; Patel et al., 2013) where it has been determined to be a “sleeping giant” (Juyal et al., 2018). Some researchers parallel rapidly rising rates with the adoption of the Westernized diet and culture in Eastern countries (Kaplan & Windsor, 2021; Rizzello et al., 2019; Windsor & Kaplan, 2019).

Individuals with UC experience lifelong unpredictable fluctuations between periods of disease remission and exacerbations of disease activity (Falvo & Holland, 2018). Disease severity ranges from mild to moderate or severe (Peyrin-Biroulet et al., 2016). Disease activity generates physical symptoms such as abdominal pain, rectal bleeding, bowel urgency, bowel frequency, diarrhea, and fatigue, along with various extra-intestinal manifestations of disease, which interfere with maintaining normal daily activities (Fourie et al., 2018; Hall et al., 2005; Matini & Ogden, 2016; McMullan et al.,
Regardless of whether or not disease is active, the majority of individuals with UC report decreased work productivity, anxiety and depression, isolation, strained relationships, ‘brain fog’, poor sleep quality, and negative body image (Falvo & Holland, 2018; Fedosiejew et al., 2016; López-Sanromán et al., 2017; McMullan et al., 2017). UC has been found to influence individuals’ choices surrounding their employment status, career planning and development, family planning, and social engagement (Fourie et al., 2018; Hall et al., 2005; Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008).

Medical treatments for UC aim to reduce symptoms and induce a state of remission through reducing inflammation using pharmaceutical therapies. While certain drugs can lead to improvements in reducing disease activity, many patients report that pharmaceuticals, overall, provide insufficient treatment to induce or maintain remission and overcome the burden of UC in everyday life (Matini & Ogden, 2016; McMullan et al., 2017; Wickman et al., 2016; Wolfe & Sirois, 2008). Additionally, the cost of medication is a key driver of healthcare spending on UC (Beard et al., 2020), which has implications for patient affordability of and access to new medicines. Many individuals living with UC seek information on lifestyle methods (e.g., diet, physical activity) as complementary treatments to reduce symptoms, avoid medication side effects, achieve disease remission, reduce the burden of illness on the activities of every-day life and improve overall quality of life (Fourie et al., 2018; le Berre et al., 2020; McCormick et al., 2012; McMullan et al., 2017; Wolfe & Sirois, 2008).
Despite limited evidence to support consistent dietary recommendations for the management of UC, dietary change is a popular self-management method among UC patients (Rizzello et al., 2019). With varying success, many patients attempt to identify and avoid foods that seem to trigger gastrointestinal symptoms or adopt highly restrictive diets in response to a disease flare (Cohen et al., 2014; Jowett et al., 2004). Popular diets currently recommended for UC, such as the Specific Carbohydrate Diet (Cohen et al., 2014), Low-FODMAP diet (Carlson et al., 2015), and low-fiber diets, have received increasing attention among the IBD community and aim to reduce irritable bowel (note: irritable bowel vs inflammatory bowel) symptoms such as gassiness or diarrhea. These exclusion-focused diets can help ease the burden of UC to an extent, yet are often reported as difficult to maintain (Nazarenkov et al., 2019). Exclusionary diet practices can result in healthier dietary intake, but also can result in malnutrition, disengagement from social activities, excessive cognitive energy spent on food choices, frustration with the desire for excluded foods, and significant distress after straying from dietary exclusion goals (Nazarenkov et al., 2019). Low-fiber diets are often suggested to help ease the roughage passing through an inflamed colon during UC flares. Indeed, low-fiber and exclusion diets tend to be strongly pro-inflammatory (Khayyatzadeh et al., 2017; Krishnamurthy et al., 2012; Y. Ma et al., 2008). So, this prescription could tend to exacerbate the problem and amplify symptoms when adopted for an extended period of time. There is very limited evidence about the effectiveness of these recommended exclusion diets in healing the inflamed and ulcerated mucosal lining of the colon.

A successful approach to food choice among individuals with UC may be the adoption of an anti-inflammatory dietary lifestyle to manage the burden of living with
UC. Outside of the development of the IBD Anti-Inflammatory Diet (IBD-AID) protocol and subsequent examination of its interaction with the microbiome (Olendzki et al., 2022; Olendzki et al., 2014), the adoption of an anti-inflammatory dietary lifestyle has not been otherwise examined as a complementary treatment approach and self-management method for UC. An anti-inflammatory diet may play a significant role in self-managing the localized and systemic inflammation associated with UC and therefore may decrease disease activity and associated extraintestinal manifestations of illness. Among the general population, an anti-inflammatory dietary intake has been shown to decrease anxiety, depression, and risk of colon cancer, among other health outcomes (Shivappa et al., 2017; Shivappa, et al., 2016b). This method of dietary intake expands food choices by incorporating aromatic spices, blends of colorful foods, and plentiful intake of fruits, vegetables, and healthy fats.

Olendzki and colleagues developed the IBD-AID as a protocol built from the SCD diet that incorporates anti-inflammatory components to rebuild bacterial gut flora and mitigate disease activity (https://www.umassmed.edu/nutrition/ibd/ibdaid/) (Olendzki et al., 2014). An associated study screened medical records for 10 IBD patients who followed an IBD-Anti Inflammatory Diet and found improvements in gastrointestinal symptoms, yet the sample included only three cases of UC (Olendzki et al., 2014). Recent evidence indicates an association between the adoption of the IBD-AID and beneficial changes in the microbiome of IBD patients (Olendzki et al., 2022). Though there is abundant evidence on the relationship between diet-associated inflammation and diseases of the gastro-intestinal tract, and suggestive links from work using the Dietary Inflammatory Index (DII®) (Marx et al., 2021; Mirmiran et al., 2019; Phillips et al.,
2019; Shivappa et al., 2016a), additional carefully designed, ideally prospective, studies need to be conducted in order to provide sufficient scientific evidence to support clear dietary recommendations for the management of UC.

The DII is a literature-derived dietary index developed to measure the inflammatory potential of one’s food intake (Shivappa et al., 2014a). Outside of a study showing that a pro-inflammatory diet was a risk factor for developing UC (Shivappa, 2016a) and another one producing suggestive results (Mirmiran et al., 2019), the DII has never been studied among the UC population.

In addition to diet, physical activity (PA) is another behavioral method UC patients use for reduction and management of the physical and psychosocial burden of illness. PA is widely known to reduce stress and depression, regulate systemic inflammation, reduce the risk of co-morbidities, improve social relationships, and demonstrate quality of life benefits among the general population. Physical activity is highly likely to contribute to a reduced burden of illness among individuals with UC, yet few studies have examined PA among this population. Existing studies on PA and IBD suggest that although patients struggle with motivation to exercise during periods of active disease, engagement in PA or structured exercise is associated with improvements in quality of life, fatigue, and mental health (Eckert et al., 2019; Lamers et al., 2021; Raman et al., 2021; Wiestler et al., 2019). Additionally, evidence suggests that physical activity also may be an effective modifier in the disease course of UC (Eckert et al., 2019; Engles et al., 2018). However, recommendations for PA and maintenance of health among the UC population do not currently exist. Research is needed to determine the magnitude of effect physical activity has on decreasing the burden of illness.
associated with UC. Additionally, recent reviews call for data on the intensity and frequency of exercise that would generate the greatest benefit among individuals with UC in order to determine exercise recommendations for this population (Eckert et al., 2019; Engles et al., 2018; Nathan et al., 2013; Raman et al., 2021).

This research examines associations between diet-related inflammation, as indicated by the DII, physical activity at varying intensities, and both physical and psychosocial health outcomes associated with the burden of living with UC. To our knowledge, this is the first study to use the DII to examine dietary inflammatory potential and UC-related physical and psychosocial health outcomes. Results of this study may provide additional insights to physicians and patients regarding diet and PA as complimentary self-management methods to mitigate disease activity and manage the burden of UC. Such insights are needed to develop and provide evidence-based dietary and physical activity recommendations for the UC population.

Methods

The IBD Partners e-cohort provides the basis for analyses conducted to test the associations between diet-associated inflammation (using the DII), physical activity, and ulcerative colitis. IBD Partners, previously named the Crohn’s and Colitis Foundation of America (CCFA) Partners, is a longitudinal Internet-based cohort that aims to follow IBD patients and serve as a resource for education and research. Data obtained from participants in the IBD Partners e-cohort were analyzed using a cross-sectional, secondary data analysis design to examine associations between the inflammatory capacity of individuals’ diets, physical activity, and UC-related health outcomes.
Participants provided information on demographics, disease phenotype, disease activity, and medication use, among others, and completed self-report surveys regarding dietary patterns, physical activity, disease activity, IBD-specific quality of life, and various patient-reported outcomes (PROs) reflecting psychosocial elements relating to chronic illness. For this study, survey data were included from those participants over 18 years of age who self-reported a diagnosis of UC. Respondents who had undergone UC-related surgery were excluded.

Variables of Interest

The following variables were abstracted from validated measures administered within the IBD Partners survey. Dependent variables are the following:

**Disease Activity**

Disease activity was reported using the Simple Clinical Colitis Activity Index (SCCAI) (Long et al., 2012; Walmsley et al., 1998). The SCCAI is a validated self-report measure, with strong psychometric and performance validity for use among patients with UC (Higgins et al., 2007; Jowett et al., 2003). Patients are asked to rate bowel frequency during day and night, bowel urgency, rectal bleeding, general well-being, and extracolonic manifestations. Items are scored individually using Likert-scale type response options, then summed into a total disease activity score, with an additional point added per extracolonic manifestation. Scores range from 0-15+ points. Remission in UC is associated with a SCCAI score <2; clinical relapse is defined by a SCCAI score ≥5 (Jowett et al., 2003; Turner et al., 2009).
Disease-related Quality of Life

The Short Inflammatory Bowel Disease Questionnaire (SIBDQ) is a 10-item questionnaire used to assess disease-related quality of life among individuals with IBD (Irvine et al., 1996). The SIBDQ assesses four domains, including bowel, emotional, systemic, and social for a summed quality of life score relative to the two weeks prior to self-report. The SIBDQ is highly correlated with the full 32-item Inflammatory Bowel Disease Questionnaire (IBDQ), correlates to disease activity in patients with UC, and demonstrates good test-retest reliability (Irvine et al., 1996). Items are individually scored by a 7-point scale, totaled, and averaged for a total SIBDQ score, with 1 indicating poor HRQOL and 7 indicating optimum HRQOL.

Patient-Reported Outcome Domains

The National Institutes of Health Patient Reported Outcome Measurement Information System (PROMIS) is a system of precise measures of patient-reported physical, mental, and social wellbeing with high reliability (Cella et al., 2007, 2010). Various domains of well-being can be measured using validated item banks, or groupings of questionnaire items that reflect the construct of interest. PROMIS items have been validated among the general population, with recently recognized construct validity in the IBD population (Cella et al., 2010; Kappelman et al., 2014). IBD Partners administered short form PROMIS item banks to measure five individual constructs of health-related quality of life particularly relevant to IBD: anxiety, depression, fatigue, sleep disturbance, and satisfaction with social role. Each domain’s item bank consisted of 4 items, using a 5-option response scale ranging in value from 1 to 5. Item scores are calibrated using a T-score metric which scales the raw score to a standardized score with a mean of 50 and
a standard deviation of 10. A score of 50 is the mean for the United States general population for most PROMIS instruments. High scores for fatigue, anxiety, depression, and sleep disturbance represent poor health while high scores for social function represent good health (Kappelman et al., 2014).

The study’s independent variables are the following:

*Dietary Inflammatory Index (DII®) Score*

Dietary data were collected using a National Health and Nutrition Examination Survey (NHANES) Dietary Screener Questionnaire (National Cancer Institute, 2021c) that was used as a basis to compute both a DII score and an Energy-Adjusted DII Score (E-DII®) for this study (Hébert et al., 2019; Shivappa et al., 2014a). The DII was developed based on an extensive literature search to quantify the effect of diet on inflammation using an algorithm that takes into account up to 45 food parameters identified in the search, including a combination of nutrients and food intake (Shivappa et al., 2014a). Due to unique differences observed in the relationship between total energy intake (a determinant of the DII) and nutrient intake, the E-DII also was developed (Hébert et al., 2019). DII scores can range from a theoretically minimum -8.87, indicating a strongly anti-inflammatory intake, to a theoretically maximum +7.98, indicating a strongly pro-inflammatory intake (Shivappa et al., 2014a). At least 41 studies have demonstrated construct validity of the DII or E-DII against inflammatory biomarkers in different populations under varying conditions (Gialluisi et al., 2021; Li et al., 2021; Malcomson et al., 2021; Marx et al., 2021; Phillips et al., 2019; Saghafi-Asl et al., 2021; Skoczek-Rubińska et al., 2021; Zamora-Ros et al., 2015).
Physical Activity

Physical activity data were collected using the Godin-Shephard Leisure Time Physical Activity Questionnaire (Godin, 2011; Godin & Shephard, 1985). This questionnaire was developed to measure leisure-time physical activity among healthy adults and has been validated to assess exercise behavior in different (populations, with significant correlation to VO$_2$max, and percentage of body fat (Amireault & Godin, 2015; Gionet & Godin, 1989; Godin, 2011; Miller et al., 1994).

The 4-item questionnaire asks participants to indicate the number of times during a 7-day period that the participant engages in mild (minimal effort – e.g., easy walking, fishing), moderate (not exhausting- e.g., fast walking, tennis), and strenuous (heart beats rapidly- e.g. running, basketball) physical activity for at least 15 minutes (Amireault & Godin, 2015; Godin, 2011; Godin & Shephard, 1985). Total Leisure-Time Activity scores are calculated by multiplying reported weekly frequencies of mild, moderate, and strenuous activities by corresponding Metabolic Equivalent of Task (MET) values, which indicate energy expenditure, of three, five and nine respectively, then summing the products of each intensity level (Godin, 2011; Godin & Shephard, 1985). In addition to Total Leisure Time Activity, frequency of engagement in PA at each intensity was assessed in this study as continuous variables of PA intensity- mild, moderate, and strenuous.

Covariates

Additional variables included age, sex, body mass index (BMI), race, education, smoking status, disease duration, and medication class. Age was indicated by entering a numeric value. Sex was identified as either male or female. BMI (kg/m$^2$) was calculated
from participant-reported height and weight. Given that 84% of the participants indicated race as ‘White’, a dummy variable for race was created (‘White’ or ‘not White’).

Education was indicated as ‘high school or less’ (combining survey response items of ‘12th grade’ and ‘less than 12th grade’), ‘some college’, ‘college’, and ‘graduate school’.

Smoking status was denoted as ‘never’, ‘ever’, or ‘current’. Disease duration was self-reported by number of years since first IBD diagnosis. Participants reported on currently used medications by indicating ‘yes’ or ‘no’ to various listed medications and treatment methods. Seven “medication classes” were grouped as follows: Corticosteroids included ‘oral corticosteroids’, ‘budesonide’, and ‘steroids, rectal’ questionnaire items; Aminosalicylates included ‘mesalamines oral’, ‘mesalamines rectal’, and ‘Azulfidine (sulfasalazine)’; Immunomodulators included ‘Azathioprine/6MP’ and ‘Oral MTX’ (methotrexate); Biologics included ‘infliximab’ and ‘adalimumab’; Antibiotics included ‘ciprofloxacin’, ‘metronidazole’, and ‘other antibiotics’, Complementary/Alternative included ‘probiotics’, ‘Other complementary or alternative therapy’, and ‘calcium’; Opioids included ‘opioids’. (Crohn’s & Colitis Foundation, 2021) Participants also reported the presence of other conditions unrelated to IBD that limit participation in PA, such as injury, by indicating ‘yes’ or ‘no’.

Statistical Analysis

Associations between DII/E-DII scores and health outcomes were tested using multivariable regressions. Disease activity, quality of life, and PROs were each predicted by a vector of covariates (age, sex, BMI), race, education, smoking status, disease duration, medication class, and PA) and DII score. Models were assessed for multicollinearity using Variance Inflation Factors (VIF) and tested for explanatory power
robustness ($R^2$) when using the E-DII variable score versus DII scores. The E-DII score was selected for preferred specifications given the variable’s greater explanatory ability, as well as lower skewness and other distributional characteristics in comparing scores. E-DII scores were analyzed as a continuous variable, with subsequent analysis to test linear trends across quartiles.

Associations between physical activity and health outcomes also were tested using multivariable regressions. Again, disease activity, quality of life, and PROs were each predicted by a set of controls (age, sex, BMI, race, education, smoking status, medication class, disease duration, E-DII score, and presence of conditions limiting participation in PA), and physical activity. Physical activity was analyzed against each health outcome ($Y$). Physical activity modeled in two ways – First, as a Total Leisure-Time Activity Score ($X_2$), and second as intensity levels (where $X_2$ is moderate intensity, and $X_3$ is strenuous intensity). The full model appears as follows:

$$Y = B_0 + B_1 X_1 + B_2 X_2 + B_3 X_3 + \varepsilon,$$

where $X_1$ is a vector of controls and $\varepsilon$ is a random error term.

Interaction effects between E-DII scores expressed continuously and as quartiles with PA intensity were also tested.

**Results**

*Participant Characteristics*

A total of 2,368 patients with UC completed the surveys of interest to this study. After excluding patients who had undergone UC-related surgery, data from 2,052
respondents were included. Participant characteristics are described in Table 4.2, along with mean scores for each independent and dependent variable.

Dietary Inflammatory Intake

DII scores ranged from -2.94 to 4.48. E-DII scores ranged from -4.13 to 4.47 (mean=-0.25, median=-0.41). An increase of one point in E-DII score (indicating increased pro-inflammatory dietary intake potential) was significantly associated with increased SCCAI scores (p<0.001, t=4.71, [95%CI=0.97-0.24]), anxiety (p=0.006, t=2.73, [95%CI=0.096-0.59]), depression (p=0.001, t=3.32, [95%CI=0.17-0.65]), fatigue (p=0.005, t=2.82, [95%CI=0.12-0.66]) and sleep disturbance (p=0.003, t=2.99, [95%CI=0.12-0.56]), and decreased satisfaction with social role (p=0.004, t=-2.92, [95%CI=-0.62-0.12]) and SIBDQ scores (p<0.001, t=-3.87, [95%CI=-0.08-0.03]).

(See Table 4.3) Quartile analysis indicated a robust distribution and linear trends across quartiles. (See Table 4.4)

Physical Activity

Total leisure time activity was inversely associated with disease activity (p<0.001, t=-4.71, [95%CI=0.15-0.01]), anxiety (p=0.001, t=-3.29, [95%CI=0.04-0.01]), depression (p=0.001, t=-3.23, [95%CI=-0.04-0.01]), fatigue (p<0.001, t=-6.74, [95%CI=-0.08-0.04]), and sleep disturbance (p=0.008, t=-2.67, [95%CI=-0.03-0.01]), while positively associated with IBD-related quality of life (p<0.001, t=5.33, [95%CI=0.003-0.01]) and satisfaction with social role (p<0.001, t=7.94, [95%CI=0.07-0.08]). When comparing frequency of PA at mild, moderate, and strenuous intensity levels, the strongest associations existed between strenuous intensities of PA and each health outcome (though insignificant for depression). (See Table 4.5)
Interaction Effects

No significant interaction was observed between diet and physical activity across any of the outcomes. While diet and physical activity are understood to be correlated and have the potential to interact in their effect on health, the way they statistically impact UC-related health outcomes appears to be independent of each other in the context of this analysis.

Discussion

These findings suggest that an anti-inflammatory diet and increased physical activity is each likely to contribute to a lower burden of illness associated with UC. Significant associations were found between increases in E-DII scores (indicating pro-inflammatory dietary potential) and increases in disease activity, anxiety, depression, fatigue, and sleep disturbance, along with decreases in satisfaction with social role and health-related quality of life. As a corollary, these results suggest that an anti-inflammatory dietary intake may decrease disease activity, anxiety, depression, and fatigue, as well as improve disease-related quality of life, sleep, and satisfaction with social role.

For disease activity, a one point change in SCCAI score is considered clinically significant in the medial field. According to this study, where a one point E-DII score is significantly associated with a 0.17 point increase in SCCAI score, a patient with UC would need to change his or her E-DII score by about 6 points for a clinical difference in disease activity. DII scores range from a maximally pro-inflammatory diet score of +7.98 to a maximally anti-inflammatory diet score of -8.87, indicating a range of 16.85 points (Shivappa et al., 2014b). Within this range, a 6 point change in E-DII score would
require a legitimate, yet feasible change from a pro-inflammatory dietary intake to an anti-inflammatory dietary lifestyle.

Increases in total leisure time physical activity were associated with increases in IBD-related quality of life and satisfaction with social role, along with decreases in disease activity, anxiety, depression, fatigue, and sleep disturbance. Results suggest that increasing engagement in physical activity may reduce disease activity, anxiety, depression, fatigue, and sleep disturbance while improving IBD-related quality of life and satisfaction with social role. Increases in the frequency of strenuous activity indicated stronger associations with improved disease outcomes than increases in moderate or mild intensity activities. Findings suggest that increased engagement in physical activity at a strenuous intensity (i.e., heart beats rapidly) may yield greater improvements in disease outcomes in comparison to increases in moderate or mild PA. While each of these lifestyle-related factors appears to be associated with important UC outcomes, there was no indication of an interaction between these 2 important risk factors.

According to the results of this study, the adoption of an anti-inflammatory diet may be an effective approach to mitigating disease activity. This dietary approach differs from current recommended diets, which tend to focus solely on easing the GI symptoms associated with UC, such as diarrhea, bloating, and gassiness, and reducing roughage that passes through the colon by restricting various types of fruits, vegetables, and processed foods. Attention to the inflammatory potential of diet broadens the understood influence of diet beyond just the colonic symptoms, to improve immune system functioning and health of the whole body.
A common weakness of current diets suggested for UC is the lack of evidence that these diets decrease inflammation, which is essential for mucosal healing within the colon. The DII is a literature-derived index developed to measure the inflammatory potential of one’s food intake and found to be predictive of multiple inflammatory biomarkers, such as C-reactive protein, Interleukin-4,6,8, and 10, TNF-a, and calprotectin, among others (Gialluisi et al., 2021; Li et al., 2021; Malcomson et al., 2021; Saghafi-Asl et al., 2021; Shivappa et al., 2014a; Shivappa et al., 2014b; Skoczek-Rubińska et al., 2021; Wirth et al., 2014; Zamora-Ros et al., 2015). Given the established associations between the DII and inflammatory biomarkers (now in over 40 construct validation studies), along with the results of this study, there is suggestive evidence that an anti-inflammatory dietary intake may aid in managing systemic and localized, chronic “simmering” (Hofseth & Hebert JR, 2022) inflammation associated with UC and reduce the burden of UC on daily living. Results of this study support existing findings, which indicate that anti-inflammatory dietary intake is associated with decreased anxiety, depression, and risk of colon cancer, among other health outcomes (Marx et al., 2021; Phillips et al., 2019; Shivappa et al., 2017; Shivappa et al., 2016b). This research may advance the development of dietary recommendations for disease management and influence the food choices among UC patients seeking to manage the burden of illness associated with UC. Additional research is needed to examine the clinical impact of anti-inflammatory dietary intake on the course of UC.

Physical activity is known to regulate inflammation among healthy individuals. The medicinal benefits of PA are not fully understood among the IBD population, though existing studies tend to show improvements in gastrointestinal symptoms, quality of life,
and psychosocial outcomes, as well as a protective role in maintaining remission (Davis et al., 2022; Eckert et al., 2019; Raman et al., 2021). Our findings support the limited existing literature, indicating an association between increased engagement in PA and improved health outcomes among the UC population. Prior studies suggest that rates of exercise are inversely associated with disease activity (Eckert et al., 2019; Engles et al., 2018; Shephard, 2016). Although PA has not been shown to worsen symptoms and is recognized as safe among the majority of the IBD population (Engles et al., 2018; Nathan et al., 2013), motivation is low among patients with active disease due to fatigue, bowel urgency, and pain, among other symptoms (Davis et al., 2022; Lamers et al., 2021).

During periods of remission, patients with IBD are more receptive to engaging in PA and report improved health-related quality of life and self-image (Lamers et al., 2021; Taylor et al., 2018; Wiestler et al., 2019).

A significant gap in the literature calls for greater understanding of the frequency, intensity, and type of PA best suited for optimal health outcomes among the UC population. This study adds to the literature by examining the changes in association with UC health outcomes by intensities of PA. Our findings support results of existing studies. A recent Japanese study also examined total PA and PA intensities against clinical outcomes, finding that strenuous activity and increased total PA were each independently associated with improved mucosal healing in patients with UC (Watanabe et al., 2021). A study by Taylor et al., (2018), found health-related quality of life benefits (HRQoL) associated with all exercise intensities. Not only were high volumes of moderate and vigorous exercise associated with physical health-related quality of life, but high volumes of mild exercise (walking) also were associated with both physical and
mental HRQoL. Overall, studies argue that the employment of PA and structured exercise could potentially help mitigate and protect against active disease (Davis et al., 2022; Engles et al., 2018; Jones et al., 2015; Lamers et al., 2021). Additional research is needed to develop evidence-based physical activity recommendations for individuals with UC, with attention to exercise frequencies and intensities that may best reduce the daily burden of living with UC (Raman et al., 2021).

This study did not find interaction effects between dietary inflammatory intake and physical activity. Numerous studies have indicated the coupled benefits of diet and physical activity on health, energy, vitality, overall well-being among the general population (Stavsky & Maitra, 2019). Stavsky & Maitra (2019) examined the synergistic influence of diet and physical activity in the management of UC, outlining theoretical direct and indirect effects of diet and exercise on disease physiology, and proposed a decrease in pro-inflammatory diet and increase in aerobic exercise for protective influence against UC. While we did not see synergistic effect, it is also true that there was no antagonistic effect. Therefore, there is no indication that both improving diet and physical activity would result in a less favorable outcome than either one taken alone.

The cross-sectional design of this secondary data analysis limits causal inference. For example, the association between total physical activity, particularly higher frequency of strenuous physical activity, and decreased disease activity might be explained by a patient’s capacity to engage in exercise. Although patients with UC tend to recognize the benefits of physical activity on well-being, participation in exercise is often difficult given barriers associated with disease activity (Engles et al., 2018).
Research with longitudinal data is needed to better determine the mitigating influence of physical activity on the disease course and other related outcomes.

The sample in this study is largely female and white. Stratified analyses by sex were considered, yet given inconsistent findings on gender differences in UC outcomes (Greuter et al., 2020), this gender distribution was accounted for as a control variable in all models. While patients with UC often report feeling that their condition is not taken seriously by family, peers, and physicians (Fourie et al., 2018), this injustice is often compounded for African American women and other racial minorities in social communities and health care systems (Belgrave & Abrams, 2016). Overall, representation of racial minorities in research is a prominent limitation of health-related research (Ma et al., 2021). This analysis is limited by the predominantly white sample. Statistical models controlled for race as white and non-white to account for the skewed representation of racial difference in the population.

Findings from this study also are limited by the nature of computing DII scores from the NHANES DSQ. Additional studies using a comprehensive dietary assessment are needed to explore the relationships between the DII/E-DII and UC related health outcomes. As IBD Partners provides researchers with access to a large cohort of individuals with UC, this research highlights the need for administration of comprehensive dietary assessment measures among the IBD Partners cohort in order to best assess the role of diet in IBD management.

All data were collected through self-reported measures, subjecting all results to potential reporting bias. At the same time, no other study, to our knowledge, has examined diet and physical activity’s associations with UC-related outcomes among such
a large cohort. Very little research exists using the DII/E-DII among UC patients, and no other research associated with IBD Partners has examined and compared the associations between physical activity, particularly the frequencies of exercise intensities, and UC related health outcomes. This study’s findings are also accompanied by high $R^2$ values, indicating strong explanatory power of our statistical models.

Study findings will aid future research that may expand models of patient care and self-management programs to include anti-inflammatory dietary intake and PA as complementary lifestyle methods that may reduce disease symptoms, maintain remission, and improve psychosocial well-being among individuals with UC. More research in this area will contribute to creating evidence-based health promotion programs for PA and dietary change in UC.
Table 4.2 Characteristics of Participants* with Ulcerative Colitis and mean scores for independent and dependent variables from IBD Partner’s 2011 e-cohort data (n=2,052).

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD) or %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.82 (14.41)</td>
</tr>
<tr>
<td>sex - % female</td>
<td>71.39</td>
</tr>
<tr>
<td>Race - % White</td>
<td>84.35</td>
</tr>
<tr>
<td>Disease Duration (years)</td>
<td>11.75 (10.61)</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>25.56 (5.91)</td>
</tr>
<tr>
<td>Education %</td>
<td></td>
</tr>
<tr>
<td>HS or Less</td>
<td>7.4</td>
</tr>
<tr>
<td>Some College</td>
<td>18.17</td>
</tr>
<tr>
<td>College</td>
<td>40.74</td>
</tr>
<tr>
<td>Graduate School</td>
<td>29.09</td>
</tr>
<tr>
<td>Never smokers, %</td>
<td>63.59</td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>4.3</td>
</tr>
<tr>
<td>Prior smokers %</td>
<td>32.06</td>
</tr>
<tr>
<td>Conditions limiting PA %yes</td>
<td>9.9</td>
</tr>
<tr>
<td>Medication/Treatment Class**</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>17.1</td>
</tr>
<tr>
<td>Aminosalicylates</td>
<td>73.4</td>
</tr>
<tr>
<td>Immunomodulator</td>
<td>25.4</td>
</tr>
<tr>
<td>Biologics</td>
<td>17.3</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>2.2</td>
</tr>
<tr>
<td>Complimentary/Alternative</td>
<td>30.5</td>
</tr>
<tr>
<td>Opioids</td>
<td>4.68</td>
</tr>
<tr>
<td>DII score</td>
<td>2.279 (1.28)</td>
</tr>
<tr>
<td>E-DII score</td>
<td>-0.251 (1.68)</td>
</tr>
<tr>
<td>Leisure Time Physical Activity</td>
<td>33.16 (26.98)</td>
</tr>
<tr>
<td>Strenuous***</td>
<td>1.39 (1.91)</td>
</tr>
<tr>
<td>Moderate</td>
<td>2.36 (2.79)</td>
</tr>
<tr>
<td>Mild</td>
<td>3.02 (3.24)</td>
</tr>
<tr>
<td>SCCAI</td>
<td>3.34 (2.77)</td>
</tr>
<tr>
<td>SIBDQ</td>
<td>4.96 (1.14)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>53.39 (9.4)</td>
</tr>
<tr>
<td>Depression</td>
<td>51.37 (9.3)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>53.89 (10.53)</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>51.35 (8.29)</td>
</tr>
<tr>
<td>Satisfaction with Social Role</td>
<td>49.05 (9.5)</td>
</tr>
</tbody>
</table>

* Respondents who had undergone UC-related surgery were excluded.

** Respondents were allowed to report current use of any or all medications/treatments. Concurrent use of multiple medications is evident as total percent currently using medication/treatments is 170.58%.

*** Frequency scores indicate the number of times in the last 7 days an individual participated in at least 15 minutes of physical activity at the associated intensity.
Table 4.3 Comparison between Dietary Inflammatory Index and Energy-Adjusted Dietary Inflammatory Index scores’ associations with UC-Related Health Outcomes from IBD Partners 2011 e-cohort.

|                     | Coef. | Std Err. | t     | P>|t| | [95% CI] | R²         | Adj. R² |
|---------------------|-------|----------|-------|------|----------|-----------|---------|
| SCCAI               | 0.15  | 0.05     | 3.23  | 0.001| [.06, .24]| 0.195     | 0.183   |
| SIBDQ               | -0.05 | 0.02     | -2.67 | 0.008| [-.09, -.01]| 0.208     | 0.196   |
| Anxiety             | 0.14  | 0.16     | 0.85  | 0.40 | [-.18, .46]| 0.092     | 0.079   |
| Depression          | 0.16  | 0.16     | 0.97  | 0.33 | [-.16, .47]| 0.091     | 0.078   |
| Fatigue             | 0.32  | 0.18     | 1.78  | 0.08 | [-.03, .67]| 0.148     | 0.136   |
| Sleep Disturbance   | 0.35  | 0.15     | 2.36  | 0.02 | [.058, .63]| 0.082     | 0.068   |
| Satisfaction w/Social Role | -0.39 | 0.16 | -2.39 | 0.02 | [-.71, -.07]| 0.119     | 0.106   |

**Associations between Energy-Adjusted Dietary Inflammatory Index Scores and UC-Related Health Outcomes**

|                     | Coef. | Std Err. | t     | P>|t| | [95% CI] | R²         | Adj. R² |
|---------------------|-------|----------|-------|------|----------|-----------|---------|
| SCCAI               | 0.17  | 0.04     | 4.71  | p<0.001| [.097, .24]| 0.200     | 0.188   |
| SIBDQ               | -0.06 | 0.01     | -3.87 | p<0.001| [-.08, -.03]| 0.211     | 0.199   |
| Anxiety             | 0.34  | 0.13     | 2.73  | 0.006| [.096, .59]| 0.095     | 0.082   |
| Depression          | 0.41  | 0.12     | 3.32  | 0.001| [.17, .65]| 0.095     | 0.082   |
| Fatigue             | 0.39  | 0.14     | 2.82  | 0.005| [.12, .66]| 0.151     | 0.138   |
| Sleep Disturbance   | 0.34  | 0.11     | 2.99  | 0.003| [.12, .56]| 0.084     | 0.070   |
| Satisfaction w/Social Role | -0.37 | 0.13 | -2.92 | 0.004| [-.62, -.12]| 0.120     | 0.107   |

Note: Specifications include age, sex, BMI, race, education, smoking status, medication class, disease duration, and physical activity.
### Table 4.4 Associations between Energy-Adjusted Dietary Inflammatory Index (E-DII) Quartiles* and UC-Related Health Outcomes from IBD Partners 2011 e-cohort.

| Health Outcome       | Quartiles* | Coef. | Std Err. | t     | P>|t| | [95% CI] | R^2   | Adj. R^2 |
|----------------------|------------|-------|----------|-------|-----|---------|-------|----------|
|                       | E-DII Quart2 | 0.07  | 0.16     | 0.46  | 0.64 | [-.24, .39] | 0.201 | 0.189    |
| SCCAI                | E-DII Quart3 | 0.38  | 0.16     | 2.32  | 0.02 | [0.06, .70]  |       |          |
|                      | E-DII Quart4 | 0.73  | 0.17     | 4.35  | <0.001 | [.4, 1.06]  |       |          |
|                       | E-DII Quart2 | -0.02 | 0.07     | -0.35 | 0.73 | [-.15, .11]  | 0.211 | 0.199    |
| SIBDQ                | E-DII Quart3 | -0.10 | 0.07     | -1.49 | 0.14 | [-.23, .03]  |       |          |
|                      | E-DII Quart4 | -0.26 | 0.07     | -3.71 | <0.001 | [-.39, -.12] |       |          |
| Anxiety              | E-DII Quart2 | -0.01 | 0.57     | -0.02 | 0.99 | [-1.12, 1.1] | 0.096 | 0.082    |
|                      | E-DII Quart3 | 0.63  | 0.58     | 1.09  | 0.28 | [-.51, 1.8]  |       |          |
|                      | E-DII Quart4 | 1.56  | 0.59     | 2.63  | <0.01 | [.398, 2.73] |       |          |
| Depression           | E-DII Quart2 | 0.46  | 0.56     | 0.82  | 0.41 | [-.64, 1.55] | 0.095 | 0.081    |
|                      | E-DII Quart3 | 0.59  | 0.57     | 1.03  | 0.30 | [-.53, 1.71] |       |          |
|                      | E-DII Quart4 | 1.80  | 0.58     | 3.09  | <0.01 | [-11, -.05]  |       |          |
| Fatigue              | E-DII Quart2 | -0.22 | 0.62     | -0.04 | 0.72 | [-1.44, .996] | 0.151 | 0.137    |
|                      | E-DII Quart3 | 0.27  | 0.64     | 0.43  | 0.67 | [-.97, 1.52] |       |          |
|                      | E-DII Quart4 | 1.54  | 0.65     | 2.37  | 0.02 | [.26, 2.81]  |       |          |
| Sleep Disturbance    | E-DII Quart2 | -0.11 | 0.51     | -0.02 | 0.82 | [-1.12, .89] | 0.084 | 0.070    |
|                      | E-DII Quart3 | 0.20  | 0.52     | 0.39  | 0.70 | [-.82, 1.12] |       |          |
|                      | E-DII Quart4 | 1.40  | 0.54     | 2.61  | <0.01 | [.35, 2.46]  |       |          |
| Satisfaction with    | E-DII Quart2 | 1.09  | 0.57     | 1.91  | 0.06 | [-.030, 2.21] | 0.124 | 0.110    |
| Social Role          | E-DII Quart3 | 0.54  | 0.59     | 0.92  | 0.36 | [-.61, 1.69] |       |          |
|                      | E-DII Quart4 | -1.25 | 0.60     | -2.00 | 0.05 | [-2.38, -.25] |       |          |

Note: Specifications include age, sex, BMI, race, education, smoking status, medication class, disease duration, and physical activity.

*Energy-Adjusted Dietary Inflammatory Index Quartiles calculated from IBD Partners e-cohort 2011 dietary data. Values for E-DII across quartiles - Quartile 1=-4.13 to -1.46, Quartile 2= -1.46 to -0.35, Quartile 3= -0.35 to 0.96, Quartile 4= 0.96 to 4.47.
### Table 4.5 Associations between Total Leisure Time Exercise Activity, Frequencies of Intensity, and UC-Related Health Outcomes from IBD Partners 2011 e-cohort.

|                  | SCCAI | Std Err | t    | P>|t| | [95% CI] | R^2 | Adj R^2 |
|------------------|-------|---------|------|------|---------|------|---------|
| **Leisure Time Activity** |       |         |      |      |         |      |         |
| Leisure Time Activity | -0.01 | <0.01   | -4.71 | <0.001 | [-.15, -.01] | 0.208 | 0.195   |
| Strenuous         | -0.14 | 0.03    | -4.19 | <0.001 | [-.20, -.07] | 0.212 | 0.199   |
| Moderate          | -0.08 | 0.03    | -3.12 | <0.01  | [-.13, -.03] | 0.212 | 0.199   |
| **SIBDQ**         |       |         |      |      |         |      |         |
| Leisure Time Activity | 0.01 | <0.01   | 5.33  | <0.001 | [.003, .01] | 0.221 | 0.209   |
| Strenuous         | 0.06  | 0.01    | 4.3   | <0.001 | [.03, .08] | 0.227 | 0.213   |
| Moderate          | 0.04  | 0.01    | 3.75  | <0.001 | [.018, .06] | 0.227 | 0.213   |
| **Anxiety**       |       |         |      |      |         |      |         |
| Leisure Time Activity | -0.03 | 0.01   | -3.29 | <0.01  | [-.04, -.01] | 0.109 | 0.096   |
| Strenuous         | -0.39 | 0.12    | -3.37 | <0.01  | [-.62, -.16] | 0.112 | 0.097   |
| Moderate          | -0.09 | 0.07    | -1.25 | 0.21   | [.24, .05] | 0.112 | 0.097   |
| **Depression**    |       |         |      |      |         |      |         |
| Leisure Time Activity | -0.03 | 0.01   | -3.23 | <0.01  | [-.040, -.01] | 0.108 | 0.094   |
| Strenuous         | -0.20 | 0.11    | -1.77 | 0.08   | [-.43, -.02] | 0.109 | 0.095   |
| Moderate          | -0.16 | 0.07    | -2.17 | 0.03   | [-.30, -.02] | 0.109 | 0.095   |
| **Fatigue**       |       |         |      |      |         |      |         |
| Leisure Time Activity | -0.06 | 0.01   | -6.74 | <0.001 | [-.08, -.04] | 0.166 | 0.153   |
| Strenuous         | -0.82 | 0.13    | -6.48 | <0.001 | [-1.06, -.57] | 0.173 | 0.160   |
| Moderate          | -0.28 | 0.08    | -3.41 | <0.01  | [-.44, -.12] | 0.173 | 0.160   |
| **Sleep Disturbance** |       |         |      |      |         |      |         |
| Leisure Time Activity | -0.02 | 0.01   | -2.67 | <0.01  | [-.03, -.01] | 0.090 | 0.075   |
| Strenuous         | -0.32 | 0.10    | -3.02 | <0.01  | [-.52, -.11] | 0.094 | 0.079   |
| Moderate          | -0.06 | 0.08    | -0.75 | 0.45   | [.22, .097]  | 0.094 | 0.079   |
| **Satisfaction w/Social Role** |       |         |      |      |         |      |         |
| Leisure Time Activity | 0.06  | 0.01    | 7.94  | <0.001 | [.07, .08]  | 0.134 | 0.120   |
| Strenuous         | 0.73  | 0.12    | 6.29  | <0.001 | [.50, .96]  | 0.140 | 0.125   |
| Moderate          | 0.40  | 0.09    | 4.46  | <0.001 | [.23, .58]  | 0.140 | 0.125   |

Note: Specifications include: age, sex, BMI, race, education, smoking status, medication class, disease duration, E-DII score, and presence of conditions limiting participation in PA.
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CHAPTER 5

SUMMARY, IMPLICATIONS AND RECOMMENDATIONS

Summary of Major Findings

The purpose of this study was to understand the impact of treatment and management methods on the daily burden of Ulcerative Colitis using a mixed-methods design. Study one was a qualitative study involving semi-structured interviews with patients diagnosed with UC from across the US. The research questions and interview guide were guided by a literature review and conceptual framework. The specific aim of this study was to examine how treatment and management methods are used by individuals who have been living with UC for at least 5 years and how patients make decisions regarding the use of these treatment and management methods.

Study 1

Findings from study one indicate that over the illness trajectory, patients with UC experience fluctuating levels of suffering associated with disease activity, with no clear or consistent patterns of treatment and management methods evident across patient experiences to yield optimal UC outcomes or justify disease flares. From the patient perspective, fluctuations in disease activity are attributed to stress, diminished medication effectiveness, or dietary triggers. Decision making regarding the use of various treatment and management methods is shaped by a patient’s approach towards disease management, personal experiences, sources of information, and individual motivating factors.
In this study, the most predominant motivating factor for the use of treatment and management methods is personal suffering. Living with UC is accompanied by physical symptoms and psychosocial challenges that cause significant suffering and disruption in patients’ lives. Especially during times of active disease, patients are willing to try new methods of management and overlook long-term implications in order to reduce suffering and be able to ‘function’ in the present day. For a few patients, suffering has motivated long-term health behavior change. Although suffering motivates the use of treatment and management methods, this study found that the majority of participants tend to use treatment and management methods in reaction to suffering and disease activity. Patients identify some medications and overall stress reduction as important methods to avoid UC flares, yet treatment and management methods are predominantly employed as efforts to recover from flares and reduce existing symptoms. Recent research is recognizing UC as a progressive illness with a growing need for preventative action against progressive damage and impairment (Cleveland et al., 2022). A need is evident for patients to shift away from reactive treatment and management approaches and adopt preventative behaviors.

Participants in this study typically rely on physician recommendations for the use of pharmaceutical therapies. At the same time, many patients do not rely on physicians to provide sufficient information regarding treatment and management methods. A recent study interviewed 10 patients with UC about the drivers of decision-making regarding pharmaceutical treatments versus colorectal surgery, finding that patient-provider communication was a key driver of decision making, decision satisfaction, and adherence (Lai et al., 2019). Findings from this study suggest that many patients seek out
and collect the majority of advice and information regarding all forms of treatment and management methods from peers and the internet. Additionally, the majority of treatment and management methods are adopted through a trial-and-error approach. Given that UC has no known cause or cure at this time, the use of medical therapies and lifestyle methods are guided by trial and assessment of effectiveness.

Findings from this study highlighted a difference between taking ownership for the health condition (i.e., attributing the disease and disease course to personal health behaviors) verses taking ownership of the illness experience (i.e., belief that individual choices and behaviors can modify the lived experience). Few participants feel that they are responsible for the course of illness, as UC is unpredictable, but some believe that they can control, to varying degrees, how they manage their experiences with UC. A few patients in this study take an active approach to managing their illness experience through individual-based decision-making, health behavior change, and self-advocacy towards greater satisfaction with treatment options and patient-provider communication.

Overall, participants use an individualized mix of treatment and self-management methods to overcome the challenges of living with UC in daily life. Daily life with UC carries a significant physical, emotional, mental, professional, and social burden. Participants report unpredictable disease trajectories and adaptive approaches to treatment and disease management over time. Treatment and management effectiveness varies among participants, as does sustainability of method use. Medication, self-advocacy, dietary change, stress management, physical activity, and sleep improve participants’ individual experiences overall, yet are often utilized as responses to flares and UC suffering instead of as preventative health behaviors. Patients express reliance
on physicians for pharmaceutical treatment, yet identify diet restrictions and stress management as a main approach for self-management of UC.

Diet is characterized in this study as a lifestyle method of treatment and management due to the context of participant responses describing dietary practices as a behavioral change to their normal or previous lifestyle. Individuals with UC have reported diet manipulation as a strategy for managing gastrointestinal symptoms for quite some time (Hall et al., 2005), yet research examining diet as a behavioral treatment and management method for mitigating disease activity is relatively new (Celiberto et al., 2018; Torres et al., 2019; Wark et al., 2021). This study found that dietary change as a management method often evolves over time through extensive trial and error, during which participants associate diet’s impact on disease activity based primarily on their personally-observed immediate GI symptoms. A study on dietary practices and beliefs among patients with UC also found that over 90% of the leading information guiding patients’ beliefs regarding diet and disease activity were based on the patient’s personal experiences (Crooks et al., 2021).

Participants report strong beliefs regarding the negative impact of stress on disease activity. Reducing stress is widely reported as a key management method for preventing and recovering from flares. Prolonged stress can elicit numerous physiological reactions that contribute to immune dysfunction and increased inflammation (Glaser & Kiecolt-Glaser, 2005). Prolonged stress also contributes to imbalances in the microbiome and natural gut flora, shown to be associated with UC (Aleksandrova et al., 2017; Lane et al., 2017). Living with UC is arguably, on its own, a chronic stressor. Patients experience fatigue and reduced productivity, strained
relationships, marital disruption, reduced sexual activity, various misconceptions due to
the social stigma that accompanies an ‘invisible’ illness (Larsson et al., 2017; Rapport et
al., 2019; Taft et al., 2009). UC has been described as an ‘invisible’ illness, where many
patients feel that others, including health professionals, do not recognize, understand, or
validate the gravity of their illness experience (Fourie et al., 2018; Hall et al., 2005;
Wolfe & Sirois, 2008). The burden of illness associated with UC contributes to the
ongoing nature of the illness by adding prolonged stress and, therefore, systemic
inflammation and a reduced immune system (Fedosiejew et al., 2016; Larsson et al.,
2017).

The use of complementary and alternative methods is low among participants in
this study. This may be due to the recruitment of a portion of the participant sample
through a gastroenterology clinic. Some participants express openness to complementary
and alternative methods, including supplements, chiropractic care, acupuncture, and
massage therapy as potential treatments, but high costs and limited familiarity are strong
barriers to use overall. Although various types of complementary and alternative
methods exist, research examining their effect on UC is limited (Torres et al., 2019).

Study 2

Study two used a cross-sectional secondary data analysis design using data
obtained from participants in the IBD Partners e-cohort. The specific aim of this study
was to examine associations between dietary inflammatory potential, physical activity,
and health outcomes associated with the burden of living with UC. This research
examined associations between diet-related inflammation, as indicated by the DII,
physical activity at varying intensities, and both physical and psychosocial health outcomes associated with the burden of living with UC.

Findings from this quantitative study suggest, overall, that an anti-inflammatory diet and increased physical activity are each likely to contribute to a lower burden of illness associated with UC. Significant associations were found between increases in E-DII scores (indicating pro-inflammatory dietary potential) and increases in disease activity, anxiety, depression, fatigue, and sleep disturbance, along with decreases in satisfaction with social role and health-related quality of life. As a corollary, these results suggest that an anti-inflammatory diet may decrease disease activity, anxiety, depression, and fatigue, while improving disease-related quality of life, sleep, and satisfaction with social role.

Increases in total leisure time physical activity were associated with increases in IBD-related quality of life and satisfaction with social role, along with decreases in disease activity, anxiety, depression, fatigue, and sleep disturbance. Results suggest that increasing engagement in PA may reduce disease activity, anxiety, depression, fatigue, and sleep disturbance while improving IBD-related quality of life and satisfaction with social role.

Increases in the frequency of strenuous activity indicated stronger associations with improved disease outcomes than increases in moderate or mild intensity activities. These findings suggest that increased engagement in PA at a strenuous intensity (heart beats rapidly) may yield greater improvements in UC-related health outcomes in comparison to increases in moderate or mild PA.
While dietary inflammatory intake and PA are lifestyle-related factors that appear to be associated with important UC outcomes, there was no indication of an interaction between these 2 important risk factors. Numerous studies have indicated the coupled benefits of diet and physical activity on health, energy, vitality, overall well-being among the general population (Stavsky & Maitra, 2019). Stavsky & Maitra (2019) examined the synergistic influence of diet and physical activity in the management of UC, outlining theoretical direct and indirect effects of diet and exercise on disease physiology, and proposed a decrease in pro-inflammatory diet and increase in aerobic exercise for protective influence against UC. While we did not see synergistic effect in this analysis, it is also true that there was no antagonistic effect. Therefore, there is no indication that both improving diet and physical activity would result in a less favorable outcome than either one taken alone.

According to the results of this study, the adoption of an anti-inflammatory diet may be an effective approach to mitigating disease activity. This dietary approach differs from current recommended diets, which tend to focus solely on easing the GI symptoms associated with UC, such as diarrhea, bloating, and gassiness, and reducing roughage that passes through the colon by restricting various types of fruits, vegetables, and processed foods. Attention to the inflammatory potential of diet broadens the understood influence of diet beyond just the colonic symptoms, to improve immune system functioning and health of the whole body.

A common weakness of current diets suggested for UC is the lack of evidence that these diets decrease inflammation, which is essential for mucosal healing within the colon. The DII is a literature-derived index found to be predictive of multiple
inflammatory biomarkers, such as C-reactive protein, Interleukin-4,6,8, and 10, TNF-a, and calprotectin, among others (Gialluisi et al., 2021; Li et al., 2021; Malcomson et al., 2021; Saghafi-Asl et al., 2021; Shivappa et al., 2014a; Shivappa, et al., 2014b; Skoczek-Rubińska et al., 2021; Wirth et al., 2014; Zamora-Ros et al., 2015). Given the established associations between the DII and inflammatory biomarkers (now in over 40 construct validation studies), along with the results of this study, there is suggestive evidence that an anti-inflammatory dietary intake may aid in managing systemic and localized, chronic “simmering” inflammation associated with UC and reduce the burden of UC on daily living (Hofseth & Hebert, 2022). Results of this study support existing findings, which indicate that anti-inflammatory dietary intake is associated with decreased anxiety, depression, and risk of colon cancer, among other health outcomes (Marx et al., 2021; Phillips et al., 2019; Shivappa et al., 2017; Shivappa, et al., 2016b). This research may advance the development of dietary recommendations for disease management and influence the food choices among UC patients seeking to manage the burden of illness associated with UC. Additional research is needed to examine the clinical impact of anti-inflammatory dietary intake on the course of UC.

This study analyzed both DII and E-DII scores for robust consideration of nutrient density versus energy density. The E-DII score was selected for preferred specifications given the variable’s greater explanatory ability, as well as lower skewness and other distributional characteristics in comparing scores. Overall, the E-DII scores provided a better range of participant scores. The E-DII may have fit the data better due to the nature of the nature of the DSQ dietary data. The food groups assessed in the dietary measure captured a nutrient dense profile, with many energy dense food items also
represented. The E-DII may have fit the data better as this population tends to preferentially adjust their dietary intake as well as delay or restrict eating.

Physical activity is known to regulate inflammation among healthy individuals. The medicinal benefits of PA are not fully understood among the UC population, though existing studies tend to show improvements in gastrointestinal symptoms, quality of life, and psychosocial outcomes, as well as a protective role in maintaining remission (Davis et al., 2022; Eckert et al., 2019; Raman et al., 2021). Our findings support the limited existing literature, indicating an association between increased engagement in PA and improved health outcomes among the UC population. Prior studies suggest that rates of exercise are inversely associated with disease activity (Eckert et al., 2019; Engles et al., 2018; Shephard, 2016). Although PA has not been shown to worsen symptoms and is recognized as safe among the majority of the UC population (Engles et al., 2018; Nathan et al., 2013), motivation is low among patients with active disease due to fatigue, bowel urgency, and pain, among other symptoms (Davis et al., 2022; Lamers et al., 2021). During periods of remission, patients with UC are more receptive to engaging in PA and report improved health-related quality of life and self-image (Lamers et al., 2021; Taylor et al., 2018; Wiestler et al., 2019).

A significant gap in the literature calls for greater understanding of the frequency, intensity, and type of PA best suited for optimal health outcomes among the UC population. This study adds to the literature by examining the changes in association with UC health outcomes by intensities of PA. Our findings support results of existing studies. A recent Japanese study also examined total PA and PA intensities against clinical outcomes, finding that strenuous activity and increased total PA were each
independently inversely associated with mucosal healing in patients with UC (Watanabe et al., 2021). A study by Taylor et al., (2018), found HRQoL benefits associated with all exercise intensities. Not only were high volumes of moderate and vigorous exercise associated with physical HRQoL, but high volumes of mild exercise (walking) also were associated with both physical and mental HRQoL. Overall, studies argue that the employment of PA and structured exercise could potentially help mitigate and protect against active disease (Davis et al., 2022; Engles et al., 2018; Jones et al., 2015; Lamers et al., 2021). Additional research is needed to develop evidence-based physical activity recommendations for individuals with UC, with attention to exercise frequencies and intensities that may best reduce the daily burden of living with UC (Raman et al., 2021).

**Strengths and Limitations**

This research explored the impact of treatment and management methods on the daily burden of Ulcerative Colitis using a mixed-methods design. Study one was a qualitative study involving semi-structured interviews with patients diagnosed with UC from multiple states throughout the US. This study depended on volunteer participants who were willing to share their experiences with UC, which may skew the variability of the sample, yet the participant sample provided perspectives and experiences from patients under the care of many different health facilities. Although this study included recruitment through social media and integrative health care clinics, all participants reported treatment under physician care, which may have limited a broader collection of data on the use of alternative therapies. Findings from this study are limited to patient perspectives and do not assess the biopsychosocial effectiveness of treatment and management methods on reducing the burden of UC. At the same time, this qualitative
study provides deeper understanding of the perspectives and lived experiences of patients with UC.

Study two utilized quantitative methods to analyze relationships between dietary inflammatory intake, physical activity, and UC-related outcomes among over 2,000 patients with UC from the IBD Partners e-cohort. The cross-sectional design of this secondary data analysis limits causal inference within our findings. For example, the association between total physical activity, particularly higher frequency of strenuous physical activity, and decreased disease activity might be explained by a patient’s capacity to engage in exercise.

The sample in this study is largely female and white. Stratified analyses by sex were considered, yet given inconsistent findings on gender differences in UC outcomes (Greuter et al., 2020), this gender distribution was accounted for as a control variable in all models. Representation of racial minorities in research is a prominent limitation of health-related research (Ma et al., 2021). For this analysis, statistical models controlled for race as white and non-white participants to account for the skewed representation of racial difference in the study population.

All data were collected through self-reported measures, subjecting all results to potential reporting bias. At the same time, no other study, to our knowledge, has examined diet and physical activity’s associations with UC-related outcomes among such a large cohort. Very little research exists using the DII/E-DII among the UC population, and no other research associated with IBD Partners has examined and compared the associations between physical activity, particularly the frequencies of exercise intensities,
and UC related health outcomes. This study’s findings are also accompanied by high $R^2$ values, indicating strong explanatory power of our statistical models.

Findings from this study also are limited by the nature of computing DII scores from the NHANES DSQ. DSQ dietary data included frequency of consumption for 25 different food items. Data on portion sizes of food intake were not included, and nutrient profiles for participant intake were collected and computed using representative foods. For this study, DII scores are based on representative data and were not computed from true dietary recall data. Multiple representative foods were selected and proportioned within many DSQ food item categories to avoid inflated DII scores, account for participant intake preferences not indicated within the data, and to reflect a broad range of nutrient intake. Improved use of dietary assessment tools is needed among IBD Partners cohort in order to better assess the role of diet in IBD management.

**Conclusion and Implications for Future Research**

Patients with UC are striving for clear understanding and guidance on how to reduce the burden of living with UC and achieve increased ‘normalcy’ in daily life. From this dissertation study, we have gained insights on why patients use various treatment and management methods and how behavioral methods of diet and PA may impact the illness experience. This work supports a need for increased attention to the role and impact of health behaviors in managing disease activity and preventing disease progression.

From this research, we learned that an anti-inflammatory diet is likely to contribute to a lower burden of illness associated with UC. Anti-inflammatory dietary intake is associated with reduced disease activity, anxiety, depression, fatigue, and sleep disturbance, along with improved satisfaction with social functioning and IBD-related
quality of life. This research may advance the development of dietary and recommendations for disease management and influence the food choices among UC patients seeking to manage the burden of illness associated with UC. Though there is abundant evidence on the relationship between diet-associated inflammation and diseases of the gastro-intestinal tract, and suggestive links from work using the Dietary Inflammatory Index (DII®) (Marx et al., 2021; Mirmiran et al., 2019; Phillips et al., 2019; Shivappa, et al., 2016a), additional carefully designed, ideally prospective, studies need to be conducted in order to provide sufficient scientific evidence to support clear dietary recommendations for the management of UC.

This research used the DII to analyze diet in a large cohort of UC patients with a limited dietary assessment measure. Studies using a comprehensive dietary assessment are needed to explore the relationships between the DII/E-DII and UC related health outcomes. As IBD Partners provides researchers with access to a large cohort of individuals with UC, this research highlights the need for administration of comprehensive dietary assessment measures among the IBD Partners cohort in order to best assess the role of diet in IBD management.

The DII is a literature-derived index found to be predictive of multiple inflammatory biomarkers of significant interest to the etiology of UC, such as C-reactive protein, Interleukin-4,6,8, and 10, TNF-a, and calprotectin, among others (Gialluisi et al., 2021; Li et al., 2021; Malcomson et al., 2021; Saghafi-Asl et al., 2021; Shivappa, et al., 2014a; Shivappa, et al., 2014b; Skoczek-Rubińska et al., 2021; Wirth et al., 2014; Zamora-Ros et al., 2015). Future studies should aim to examine DII/E-DII scores and
inflammatory biomarkers among patients with UC to identify the clinical impact of an anti-inflammatory diet on UC.

We also learned that engagement in PA, is likely to contribute to a lower burden of illness. In particular, engagement in PA at higher levels of intensity have a stronger association with positive health outcomes. A significant gap in the literature calls for greater understanding of the frequency, intensity, and type of PA best suited for optimal health outcomes among the UC population. This study adds to the literature by examining the differences in association with UC health outcomes by intensities of PA. Additional research is needed to develop evidence-based PA recommendations for individuals with UC, with attention to exercise frequencies and intensities that may best reduce the daily burden of living with UC (Raman et al., 2021). Future research with longitudinal data is needed to better determine the mitigating influence of PA on the disease course and other related outcomes. Future studies should also aim to develop PA interventions among UC patients, tailored to account for the burden of illness experienced in daily life.

From patient perspectives and experiences, we gained greater understanding of the factors that play a role in the use of treatment and management methods. A driving factor in decision making is personal suffering. Especially during times of active disease, patients are willing to try new methods of management and overlook long-term implications in order to reduce suffering and be able to ‘function’ in the present day. Suffering may motivate long term change, but we learn from this study that the majority of participants tend to use treatment and management methods in reaction to suffering and disease activity. Patients identify some medications and overall stress reduction as
important methods to avoid UC flares, yet treatment and management methods are predominantly employed as efforts to recover from flares and reduce existing symptoms. Research is needed to design and evaluate methods and interventions to shift treatment and management approaches away from reactive measures and promote preventative self-management behaviors.

This research also observed a difference between taking ownership for one’s health condition and action to take ownership of one’s illness experience. Although UC follows an unpredictable disease course, we learn that self-advocacy for treatment satisfaction and patient-provider communication, individual-based decision making, and health behavior changes are evident among patients who take ownership of their experience living with UC. Findings from this study can inform providers on factors that influence patient decision making and support improved patient-provider communication. Collaborative care between patients and providers helps patients feel a sense of control over their illness verses their illness controlling them, which, in turn, improves self-management overall (Plevinsky et al., 2016). Additionally, these findings can aid in framing patient education and behavioral interventions that assist patients in adopting and sustaining self-management behaviors to reduce and prevent disease activity.

Integrated clinics are needed for IBD care to support treatment for patients with UC. Physicians typically lack the capacity to train patients on self-management during an office visit, as well as professional training in nutrition, health behavior change, psychology, and other interdisciplinary fields. Professional training of IBD-specific patient educators may benefit patients with UC needing support beyond physician care.
Insurance coverage of integrated care services is needed to increase patient access to self-management skill development.

Most self-management interventions for people with UC target decision-making skills and partnering with healthcare providers, but lack focus on symptom management, employment, or other aspects of daily life affected by UC (Conley & Redeker, 2016). This study offers added insight into the use of treatment and management methods to manage the physical and psychosocial burden of illness on daily life. Additional future studies are needed to explore beyond symptom management and examine methods for improving emotional, social, and psychological well-being over the course of illness (Conley & Redeker, 2016; Peters & Brown, 2022; Rozich et al., 2020). Study findings will support future research that may expand models of patient care and creating evidence-based health promotion programs to include anti-inflammatory dietary intake and PA as complementary lifestyle methods that may reduce disease symptoms, maintain remission, and improve psychosocial well-being among individuals with UC.

In summary, this research addresses gaps in the literature related to the impact of treatment and management methods on the daily burden associated with Ulcerative Colitis. This research provides patient perspectives on use of treatment and management methods and insights on patient decision making over the course of illness. This research identifies the potential impact of anti-inflammatory dietary intake and physical activity on the burden of illness, and contributes to the development of dietary and physical activity recommendations for the UC population. This work also identifies future lines of research to expand models of patient care and promote behavioral health methods for reducing the burden of UC in daily life.
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Dear Patient,

You are eligible to participate in an exciting new research study aiming to learn directly from patients about the impact of Ulcerative Colitis on everyday life. This letter is to inform you of the study and invite you participate. This research is associated with the Department of Health Promotion, Education, and Behavior at the University of South Carolina. You are invited to participate because you are older than the age of 18, diagnosed with Ulcerative Colitis, you have been living with Ulcerative Colitis for at least 5 years, and have experienced at least one flare.

Your valuable contribution to this research will guide the Ulcerative Colitis community, including patients and health care providers, towards a better understanding of the experiences faced while managing UC in everyday life.

Participation is voluntary and confidential. If you decide to take part in this study, you will participate in a private one-on-one interview with a trained researcher who has a personal history of living with Ulcerative Colitis. During this interview, you will be asked about your experiences during diagnosis, your challenges and successes managing your illness, and how UC has impacted your daily life. The interview will be scheduled to take place at a location and time that is convenient for you, and will last approximately one hour. Please know that your participation in the study is not connected in any way to your healthcare services, and no negative consequences can happen if you refuse to participate.

You will not be identified by name on the interview transcripts or in any final products that may result from the research. Risks associated with participation are minimal. You have the right to refuse to answer any questions or stop participation at any time. After the interview concludes, you will receive a $25.00 cash gift card in appreciation of your time and participation.

For more information, or to participate in this study please contact the researcher directly by phone or e-mail:

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806-206-5771
kdubois@email.sc.edu
If you have questions or concerns about your rights as a research participant, you may call the IRB manager at University of South Carolina at 803-777-6670.

Thank you for your consideration,
Dr. Anjani Jammula, M.D.
GHS Gastroenterology & Liver Center
890 W. Faris Road, Suite 100
Greenville, SC 29605
(864) 455-2888
APPENDIX B.

RECRUITMENT FLYER FOR INTERVIEWS- AIM 1

Living with Ulcerative Colitis?

Share your story!

Take part in a unique research study.

You will receive $25.00 in appreciation of your time.

Participant requirements:

✓ Age 18 or older
✓ Diagnosed with Ulcerative Colitis
✓ At least 5 years since initial diagnosis
✓ Experienced at least 1 flare

How does living with Ulcerative Colitis influence your daily life?

Volunteer for a confidential, one-on-one interview with a trained researcher, who has a personal history of Ulcerative Colitis.

The interview will take place at a location and time that is convenient for you, and will last no longer than one hour.

Interested? Please contact Kelli DuBois
806-206-5771 or kdubois@email.sc.edu

This study is associated with the University of South Carolina, Department of Health Promotion, Education, and Behavior
APPENDIX C.

PHONE SCRIPT FOR RECRUITING VOLUNTEER PARTICIPANTS- AIM 1

Hello,

I am so glad you are interested in sharing your story for this study. Did you hear about this study from a letter or a flyer?

If Letter: Okay, great. Thank you so much for contacting me. The purpose of this study is to learn about the daily experiences of those individuals living with Ulcerative Colitis. You were identified by your physician as eligible to participate. Just to confirm your eligibility, Are you over the age of 18? Have you been diagnosed with Ulcerative Colitis? Have you been living with UC for over 5 years? Have you experienced at least one flare?

If Flyer: Okay, great. Thank you so much for contacting me. The purpose of this study is to learn about the daily experiences of those individuals living with Ulcerative Colitis. The first step is to make sure you are eligible to participate. Are you over the age of 18? Have you been diagnosed with Ulcerative Colitis? Have you been living with UC for over 5 years? Have you experienced at least one flare?

If not eligible: Unfortunately, you are not eligible to participate in this particular study because (reason). I really appreciate your interest. Do you know anyone with Ulcerative Colitis who may be eligible to participate? Please share my contact information with them if they are interested. Thank you.

If eligible: You are eligible to be a part of this study. Let me tell you about your role if you choose to participate.

You would meet with me at a location convenient for you for a confidential, one on one interview that would last approximately one hour. I could come to your home, we could meet at your physician’s office, or meet somewhere else that has a quiet private space for us to talk. I’ll ask you questions about your experiences during diagnosis, your challenges and successes managing your illness, and how UC has impacted your daily life.

Participation is voluntary and anonymous and is not connected in any way to your health care services. Any identifying information will be excluded from the transcripts and final reports. You also have the right to refuse to answer any questions I may ask or stop the interview at any time. Everything you share will be kept confidential. I have had UC for 13 years myself, and I would be grateful for the opportunity to learn from your
experiences and interview you as a part of my research study. Plus, you’ll receive a cash gift card of $25.00 as an expression of gratitude for your time and participation.

I would enjoy meeting with you to learn about your experiences. Would you be willing to meet with me for an interview?

I’ll be in your area from ‘date’ to ‘date’. Which day would work best for you? I can meet with you at ‘time slots’, which would be best?

I can come talk with you in the comfort of your own home, but we can also meet in a room at Dr. Jammula’s office or any other preferred quiet and private space. Where would you prefer I visit with you?

Thank you. Just to confirm, I’ll be meeting you on (date, time, location). I look forward to meeting you.
APPENDIX D.

PRE-INTERVIEW ELIGIBILITY SCREENER-AIM 1

Name:
Phone Number:
Age:
Gender:
Race/Ethnicity:
Approximate years since diagnosis:
Experienced at least one flare in last 5 years: Yes No
Currently in remission: Yes No
Disease Severity: Mild Moderate Severe
Current use of medications:
   Surgery: Yes No
      If yes, Type:
Interview Date:
Interview Time:
Interview Location:
APPENDIX E.

IN-DEPTH INTERVIEW GUIDE - AIM 1

“Thank you for your time and consideration of the invitation to participate in this research study. I am a student from the University of South Carolina and I am here to learn from you about your experiences living with Ulcerative Colitis. I have lived with UC for 13 years myself, with struggles in managing my illness over the years. I know that I’m not alone, and I am excited about the opportunity to learn about your story and understand how Ulcerative Colitis influences your life.

You have been invited to participate in this study because you were identified as eligible by your physician. Just confirm, you over the age of 18 you have been diagnosed with Ulcerative Colitis, and you have been living with Ulcerative Colitis for at least 5 years. Is that correct?

Our conversation will take approximately 60 minutes. The conversation is voluntary and anonymous. You have the right to refuse to answer any question or stop the interview at any time. Everything you share will be kept confidential and reported anonymously. Information on names or any other piece that may reveal your identity will be excluded from any transcripts and reports. Nothing you say will be shared with your healthcare provider or any other individuals who provide care or services for you. If you have any questions after I leave today, you may contact Kelli DuBois at kdubois@email.sc.edu.

Remember, everything you say is confidential, so please feel comfortable in sharing your experiences. Don’t hold back. Do I have your permission to audio record this conversation so that I may review your story again after we finish? [Consent given/denied]” Okay, let’s get started.

Experience with Ulcerative Colitis

To begin, tell me about how long you’ve been living with Ulcerative Colitis.

Probes: Has your UC changed in any way over the years?
How often would you say that you experience flares?
For how long does a flare last?

Do you feel that you’re in control of your UC or that your UC is in control of you?

Probes: What has been the biggest difficulty living with UC?
Have you ever experienced remission?
Describe a flare, what does a flare look like for you?
Follow up: How do you know when you’re having a flare?
What do you do next?
Management Methods

How do you manage your UC?
- Probes: What medication, if any, are you taking now?
  - What medications, if any, have you taken in the past?
  - How do you feel about taking medication?

When you experience a flare, what are the steps you take to reduce your symptoms?
- Follow up: How would you describe how *step* helps you manage a flare?
  - Probes: For how long does this help?
  - Duration/Dose
  - How did you know to do *step*?
  - Where did you learn about that?
- Follow up: What else do you do to recover from a flare?

Have you found any kinds of things you can do to help avoid a flare?
- Probes: Tell me more about how that helps you avoid a flare.
  - Duration, dose, Type
  - Where did you learn to do that?

What role does food play in your UC?
- Probe: How do you choose what to eat?

Have you tried other treatment methods outside of medication for UC in the past?
- If none of the following are mentioned:
  - Sometimes people participate in other health practices such as acupuncture, aroma therapy, herbal therapies, massage, or yoga to help manage their UC.
  - What are your experiences with alternative treatments to manage the challenges associated with your UC?
- When complementary/alternative treatments are mentioned:
  - Probes: Type, Duration, Dose
  - Tell me about how you use that to manage your UC.
  - Are there any other methods you have tried?

What other things do you do to help manage the impact of UC on your daily life? Even the things your doctor doesn’t know about, and even if you think it’s crazy, how do you manage the impact of UC on your life?
- Follow up: Over the years, in what ways have you made changes, if any, to your lifestyle as a result of your UC?
  - Probes: What led to that change?
  - What were you expecting that change to do for you?
  - How has that change impacted your life with UC?

Are there other treatments or methods to manage living with UC that you’ve heard of or been interested in, but haven’t tried?
- Probes: For what reasons have you not used this?
Do you know others who do things differently than you?
What have you learned about their experiences?
How do the things you do that you’ve told me about (eg. acupuncture, etc) fit with treatments from your doctor?

What else were you expecting me to ask about today that you haven’t been able to share yet?

Demographics

Age:
Gender:
Race/Ethnicity:
Age of Diagnosis/Years with UC:
Surgery: Yes No
Level of Education:
APPENDIX F.

SIMPLE CLINICAL COLITIS ACTIVITY INDEX (SCCAI) - AIM 2

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bowel frequency (day)</strong></td>
<td></td>
</tr>
<tr>
<td>1–3</td>
<td>0</td>
</tr>
<tr>
<td>4–6</td>
<td>1</td>
</tr>
<tr>
<td>7–9</td>
<td>2</td>
</tr>
<tr>
<td>&gt;9</td>
<td>3</td>
</tr>
<tr>
<td><strong>Bowel frequency (night)</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1–3</td>
<td>1</td>
</tr>
<tr>
<td>4–6</td>
<td>2</td>
</tr>
<tr>
<td><strong>Urgency of defecation</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Hurry</td>
<td>1</td>
</tr>
<tr>
<td>Immediately</td>
<td>2</td>
</tr>
<tr>
<td>Incontinence</td>
<td>3</td>
</tr>
<tr>
<td><strong>Blood in stool</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Trace</td>
<td>1</td>
</tr>
<tr>
<td>Occasionally frank</td>
<td>2</td>
</tr>
<tr>
<td>Usually frank</td>
<td>3</td>
</tr>
<tr>
<td><strong>General well-being</strong></td>
<td></td>
</tr>
<tr>
<td>Very well</td>
<td>0</td>
</tr>
<tr>
<td>Slightly below par</td>
<td>1</td>
</tr>
<tr>
<td>Poor</td>
<td>2</td>
</tr>
<tr>
<td>Very poor</td>
<td>3</td>
</tr>
<tr>
<td>Terrible</td>
<td>4</td>
</tr>
<tr>
<td><strong>Extracolonic manifestations</strong></td>
<td></td>
</tr>
<tr>
<td>(Uveitis, pyoderma gangrenosum,</td>
<td></td>
</tr>
<tr>
<td>erythema nodosum, arthropathy)</td>
<td>1 per</td>
</tr>
<tr>
<td><strong>manifestation</strong></td>
<td></td>
</tr>
</tbody>
</table>

Figure F.1 Simple Clinical Colitis Activity Index (S. L. Jowett et al., 2003)
APPENDIX G.

SHORT INFLAMMATORY BOWEL DISEASE QUESTIONNAIRE (SIBDQ)- AIM 2

1. How often has the feeling of fatigue, or of being tired and worn out, been a problem for you during the last 2 weeks?
   1 = All of the time
   2 = Most of the time
   3 = A good bit of the time
   4 = Some of the time
   5 = A little of the time
   6 = Hardly any of the time
   7 = None of the time

2. How often during the last 2 weeks have you had to delay or cancel a social engagement because of your bowel problem?
   1 = All of the time
   2 = Most of the time
   3 = A good bit of the time
   4 = Some of the time
   5 = A little of the time
   6 = Hardly any of the time
   7 = None of the time

3. How much difficulty have you had, as a result of your bowel problems, doing leisure or sports activities you would have liked to have done during the last 2 weeks?
   1 = A great deal of difficulty, activities made impossible
   2 = A lot of difficulty
   3 = A fair bit of difficulty
   4 = Some difficulty
   5 = A little difficulty
   6 = Hardly any difficulty
   7 = No difficulty; the bowel problems did not limit sports or leisure activities

4. How often during the last 2 weeks have you been troubled by pain in the abdomen?
   1 = All of the time
   2 = Most of the time
   3 = A good bit of the time
   4 = Some of the time
   5 = A little of the time
   6 = Hardly any of the time
   7 = None of the time

5. How often during the last 2 weeks have you felt depressed or discouraged?
   1 = All of the time
   2 = Most of the time
   3 = A good bit of the time
4 = Some of the time  
5 = A little of the time  
6 = Hardly any of the time  
7 = None of the time

6. Overall, *in the last 2 weeks*, how much of a problem have you had with passing large amounts of gas?  
   1 = A major problem  
   2 = A big problem  
   3 = A significant problem  
   4 = Some trouble  
   5 = A little trouble  
   6 = Hardly any trouble  
   7 = No trouble

7. Overall, *in the last 2 weeks*, how much of a problem have you had maintaining or getting to the weight you would like to be?  
   1 = A major problem  
   2 = A big problem  
   3 = A significant problem  
   4 = Some trouble  
   5 = A little trouble  
   6 = Hardly any trouble  
   7 = No trouble

8. How often *during the last 2 weeks* have you felt relaxed and free of tension?  
   1 = None of the time  
   2 = A little of the time  
   3 = Some of the time  
   4 = A good bit of the time  
   5 = Most of the time  
   6 = Almost all of the time  
   7 = All of the time

9. How much of the time *during the last 2 weeks* have you been troubled by a feeling of having to go to the bathroom even though your bowels were empty?  
   1 = All of the time  
   2 = Most of the time  
   3 = A good bit of the time  
   4 = Some of the time  
   5 = A little of the time  
   6 = Hardly any of the time  
   7 = None of the time
10. How much of the time *during the last 2 weeks* have you felt angry as a result of your bowel problem?

1 = All of the time  
2 = Most of the time  
3 = A good bit of the time  
4 = Some of the time  
5 = A little of the time  
6 = Hardly any of the time  
7 = None of the time
APPENDIX H.

PROMIS MEASURES USED IN IBD PARTNERS COHORT STUDY - AIM 2

<table>
<thead>
<tr>
<th>PROMIS domain</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I felt fearful</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I found it hard to focus on anything other than my anxiety</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>My worries overwhelmed me</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I felt uneasy</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I felt worthless</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I felt helpless</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I felt depressed</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I felt hopeless</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Fatigue</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I feel fatigued</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I have trouble starting things because I am tired</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>How run-down did you feel on average</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>How fatigued were you on average</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>My sleep quality was</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>My sleep was refreshing</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I had a problem with my sleep</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I had difficulty falling asleep</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Satisfaction with social role</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I am satisfied with my ability to do things for fun with others</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I am satisfied with my ability to do things for my family</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I am satisfied with my ability to meet the needs of my friends</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>I am satisfied with my ability to do the work that is really important to me (include work at home)</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Pain interference</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>How much did pain interfere with your day-to-day activities?</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>How much did pain interfere with work around this home?</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>How much did pain interfere with your ability to participate in social activities?</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>How much did pain interfere with your household chores?</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

General Health Question: In general, my health is...

○ Excellent
○ Very good
○ Good
○ Fair
○ Poor

Figure H.1. PROMIS Measures used in IBD Partners Cohort Study (Kappelman et al., 2014)
APPENDIX I.

GODIN-SHEPHARD LEISURE-TIME PHYSICAL ACTIVITY QUESTIONNAIRE

THE GODIN-SHEPHARD LEISURE-TIME PHYSICAL ACTIVITY QUESTIONNAIRE

**Figure 1: THE GODIN AND SHEPHARD LEISURE-TIME PHYSICAL ACTIVITY QUESTIONNAIRE**

During a typical **7-day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

<table>
<thead>
<tr>
<th><strong>Exercise</strong></th>
<th><strong>Times per week</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STRENuous EXERCISE</strong>&lt;br&gt;(HEART BEATS RAPIDLY)&lt;br&gt;(e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)</td>
<td>______</td>
</tr>
<tr>
<td><strong>MODerate EXERCISE</strong>&lt;br&gt;(NOT EXHAUSTING)&lt;br&gt;(e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)</td>
<td>______</td>
</tr>
<tr>
<td><strong>MILD EXERCISE</strong>&lt;br&gt;(MINIMAL EFFORT)&lt;br&gt;(e.g., yoga, archery, fishing from river bank, bowling, horseshoeing, golf without using a cart, snow-mobiling, easy walking)</td>
<td>______</td>
</tr>
</tbody>
</table>

Adapted from Godin, G. (1983). Psychosocial factors influencing intentions to exercise in young students. Graduate Department of Community Health, University of Toronto, Toronto.

Figure I.1. Godin-Shephard Leisure-Time Physical Activity Questionnaire (Godin, 2011)
# APPENDIX J.

## AVERAGE PORTION SIZE OR SERVING SIZE FOR REPRESENTATIVE FOODS NEEDED

TO CALCULATE NUTRIENT PROFILES

Table J.1. Average Portion or Serving Size Used to Calculate Nutrient Profiles

<table>
<thead>
<tr>
<th>Food Items</th>
<th>Proportion Rate</th>
<th>Representative Foods</th>
<th>Average Portion/Serving Size</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>WOMEN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18-25 26-35 36-45 46-60 61-69 &gt;69</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MEN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18-25 26-35 36-45 46-60 61-69 &gt;69</td>
<td></td>
</tr>
<tr>
<td>Fruit (including fresh, frozen or canned)</td>
<td>31%</td>
<td>banana</td>
<td>0.76 0.733333 0.71 0.71 0.59875 0.99 0.76 0.721667 0.94 0.764 0.63</td>
<td>NHANES DSQ, Median Portion size equivalents for age groups (IN CUP EQUIVALENTS)</td>
</tr>
<tr>
<td></td>
<td>21%</td>
<td>apple</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>pineapple</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>grapes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>watermelon</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9%</td>
<td>oranges</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9%</td>
<td>strawberries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100% pure fruit juices</td>
<td>68%</td>
<td>orange juice</td>
<td>0.99 0.94 0.826667 0.78375 0.62 0.62 1.305 1.305 1.06 1 0.981667 0.74</td>
<td>NHANES DSQ, Median Portion size equivalents for age groups (IN CUP EQUIVALENTS)</td>
</tr>
<tr>
<td></td>
<td>32%</td>
<td>apple juice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refried beans, baked bean, beans in soups, cooked dried beans</td>
<td>47%</td>
<td>dry pinto</td>
<td>0.48 0.495 0.43 0.47 0.34 0.37 0.65 0.56 0.73 0.63 0.655 0.635</td>
<td>NHANES DSQ, Median Portion size equivalents for age groups (IN CUP EQUIVALENTS)</td>
</tr>
<tr>
<td></td>
<td>29%</td>
<td>dry peas &amp; lentils</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24%</td>
<td>black beans</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole grain bread, not white bread</td>
<td></td>
<td></td>
<td>1.83425 1.83425 1.7637 1.69315 1.51678 1.384503 2.08704 2.02596 1.97534 1.97534 1.83425 1.7637</td>
<td>NHANES DSQ, Median Portion size equivalents for age groups (IN CUP EQUIVALENTS)</td>
</tr>
<tr>
<td>Brown rice or other cooked whole grains</td>
<td></td>
<td></td>
<td>1.47 1.4262B3 1.364575 1.338867 1.195 1.2075 1.7653 1.975 1.723 1.64 1.581033 1.579375</td>
<td>NHANES DSQ, Median Portion size equivalents for age groups (IN CUP EQUIVALENTS)</td>
</tr>
<tr>
<td>Milk (specified)</td>
<td></td>
<td></td>
<td>1 1 1 0.855 0.75 0.69 1.150833 1.0625 1.25 1 0.94 0.75</td>
<td>NHANES DSQ, Median Portion size equivalents for age groups (IN CUP EQUIVALENTS)</td>
</tr>
</tbody>
</table>

---

1 cup equivalent = 1 cup of fruit juice
1 cup equivalent = 1 cup cooked dry beans or peas
1 ounce equivalent = 1 ounce dry rice (approximately 1/2 cup cooked rice; 1 medium [1 ounce] slice of whole grain bread)
1 cup equivalent = 1 cup milk, yogurt, or fortified soymilk
(Table J.1 Continued)

<table>
<thead>
<tr>
<th>Food Items</th>
<th>Reference Food Categories</th>
<th>1 cup equivalent= 1.5 ounces natural cheese or 2 ounces processed cheese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheese</td>
<td>NHANES DSQ see Median Portion size equivalents for age groups</td>
<td>0.67 0.67 0.6625 0.67 0.625 0.65 0.89 0.76 0.74 0.72875 0.74 0.67</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 cup equivalent=1 cup cut-up raw or cooked vegetables; 1/2 cup dried vegetables; 1 cup juice; 2 cups raw leafy greens</td>
</tr>
<tr>
<td>Green leafy or lettuce salad with or without other vegetables</td>
<td>fresh head lettuce / fresh leaf lettuce</td>
<td>0.28 0.28 0.4025 0.44 0.396667 0.38 0.25 0.3 0.265 0.38 0.33 0.38</td>
</tr>
<tr>
<td>Fried potatoes</td>
<td>Potatoes/Frozen potatoes</td>
<td>0.535 0.535 0.435 0.4175 0.445 0.53 0.55 0.56 0.64 0.55 0.53 0.515</td>
</tr>
<tr>
<td>Other kinds of potatoes</td>
<td>white potato fresh</td>
<td>0.57 0.54 0.59 0.54 0.53 0.61 0.845 0.85 0.88875 0.77 0.81 0.815</td>
</tr>
<tr>
<td>Other vegetables than salad or potatoes</td>
<td>15% canned sweet corn</td>
<td>0.4925 0.4775 0.5 0.5 0.51 0.48 0.525 0.545 0.555 0.56 0.57 0.515</td>
</tr>
<tr>
<td></td>
<td>35% onions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17% canned chile peppers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17% fresh bell peppers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16% fresh carrots</td>
<td></td>
</tr>
<tr>
<td>Tomato sauces, not including pizza sauce</td>
<td>Canned tomatoes/ Fresh tomatoes</td>
<td>0.47 0.505 0.47 0.4425 0.4875 0.425 0.56 0.605 0.68 0.496667 0.47 0.5675</td>
</tr>
<tr>
<td>Mexican type salsa made with tomato</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red Meat</td>
<td>American Heart Association</td>
<td></td>
</tr>
<tr>
<td>Processed Meat</td>
<td>American Heart Association</td>
<td>3 oz = suggested serving size for all adults</td>
</tr>
<tr>
<td>45% lunch meat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28% hot dog</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11% sausage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11% ham</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5% bacon</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 cup equivalent= 1.5 ounces natural cheese or 2 ounces processed cheese
(Table J.1 Continued)

<table>
<thead>
<tr>
<th>Food Items</th>
<th>Reference Food Categories</th>
<th>Reference Amount of One Serving Size (for all age groups and sex combined)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pizza (including frozen, fast food pizza, or homemade)</td>
<td>Mixed Dishes- Not measurable with cup, e.g. pizza...</td>
<td>140 g</td>
</tr>
<tr>
<td>Sweetened fruit drinks, sports drinks, or energy drinks</td>
<td>juices, nectars, fruit drinks</td>
<td>240 mL (8 fl oz)</td>
</tr>
<tr>
<td>Soda, non diet</td>
<td>carbonated and noncarbonated beverages</td>
<td>360 mL (12 fl oz)</td>
</tr>
<tr>
<td>Coffee or Tea with added sugar or honey</td>
<td>coffee or tea, flavored and sweetened</td>
<td>360 mL (12 fl oz)</td>
</tr>
<tr>
<td>Chocolate or other types of candy</td>
<td>all other candies</td>
<td>30 g</td>
</tr>
<tr>
<td>Donuts, sweet rolls, Danish, muffins, or pop-tarts</td>
<td>...donuts, danish, sweet rolls...muffins, toaster pastries</td>
<td>55 grams</td>
</tr>
<tr>
<td>Cookies, cake, pie, or brownies</td>
<td>25% each</td>
<td></td>
</tr>
<tr>
<td>Ice cream or other frozen desserts</td>
<td>ice cream, frozen yogurt, sherbet, frozen flavored and sweetened ice and pops...all types...</td>
<td>FDA Reference Amounts Customarily Consumed</td>
</tr>
<tr>
<td>Popcorn</td>
<td>Snacks- ‘all varieties, chips, pretzels, popcorns...</td>
<td>2/3 cup</td>
</tr>
<tr>
<td>Cereal (specified cereal type)</td>
<td>Breakfast cereals- (hot cereal type)</td>
<td>1 cup prepared; 40 g plain dry cereal; 55 g flavored, sweetened dry cereal</td>
</tr>
<tr>
<td></td>
<td>Breakfast cereals, ready-to-eat, weighing &lt;20 g per cup, e.g. Plain puffed cereal grains</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Breakfast cereals, ready-to-eat weighing 20g &lt; &gt;43g per cup; high fiber cereals containing 28g or more of fiber per 100g</td>
<td>15 grams</td>
</tr>
<tr>
<td></td>
<td>Breakfast cereals, ready-to-eat, weighing &gt;43g or more per cup</td>
<td>40 grams</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60 grams</td>
</tr>
</tbody>
</table>
## APPENDIX K.

**REPRESENTATIVE FOOD SELECTED TO COMPUTE NUTRIENT PROFILES**

Table K.1 Representative Foods Selected to Compute Nutrient Profiles

<table>
<thead>
<tr>
<th>Food Items</th>
<th>Top Consumed Foods</th>
<th>Representative Foods</th>
<th>Data Type</th>
<th>Food Code</th>
<th>Measure for nutrient count</th>
<th>mathematical adjustment to parameter amounts in order to equal cup &amp; oz equivalents or serving/portion size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruit (including fresh, frozen or canned)</td>
<td></td>
<td>banana</td>
<td>FNDDS</td>
<td>63107010</td>
<td>1 cup, NFS (150 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>apple</td>
<td>FNDDS</td>
<td>63101000</td>
<td>1 cup, NFS (125 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>pineapple</td>
<td>FNDDS</td>
<td>63141010</td>
<td>1 cup, chunks, (165 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>grapes</td>
<td>FNDDS</td>
<td>63123000</td>
<td>1 cup, NFS (151 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>watermelon</td>
<td>FNDDS</td>
<td>63149010</td>
<td>1 cup, NFS (152 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>oranges</td>
<td>FNDDS</td>
<td>61119010</td>
<td>1 cup, sections (180 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>strawberries</td>
<td>FNDDS</td>
<td>63223020</td>
<td>1 cup, NFS, (152 g)</td>
<td></td>
</tr>
<tr>
<td>100% pure fruit juices</td>
<td></td>
<td>orange juice</td>
<td>FNDDS</td>
<td>61210000</td>
<td>Quantity not specified</td>
<td>(248 g =1 fl oz (aka 31 g) x 8=1 cup)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>apple juice</td>
<td>FNDDS</td>
<td>64104010</td>
<td>Quantity not specified</td>
<td>(248 g =1 fl oz (aka 31 g) x 8=1 cup)</td>
</tr>
<tr>
<td>Refried beans, baked bean, beans in soups, cooked dried beans</td>
<td></td>
<td>dry pinto</td>
<td>FNDDS</td>
<td>41104000</td>
<td>1 cup (180 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dry peas &amp; lentils</td>
<td>FNDDS</td>
<td>41304980</td>
<td>1 cup (180 g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>black beans</td>
<td>FNDDS</td>
<td>41102000</td>
<td>1 cup (180 g)</td>
<td></td>
</tr>
<tr>
<td>Whole grain bread, not white bread</td>
<td></td>
<td>Bread, whole wheat</td>
<td>FNDDS</td>
<td>51300110</td>
<td>100g</td>
<td>multiplied by 0.2835=1 ounce(or 28.35 g)</td>
</tr>
<tr>
<td>Brown rice or other cooked whole grains</td>
<td></td>
<td>Rice, brown, cooked, NS as to fat added in cooking</td>
<td>FNDDS</td>
<td>56205011</td>
<td>1 cup, cooked (196 g)</td>
<td>divided by 2 to = 1/2 cup cooked</td>
</tr>
</tbody>
</table>
(Table K.1 Continued)

<table>
<thead>
<tr>
<th>Food Items</th>
<th>Food Code</th>
<th>Measure for nutrient count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (specified)</td>
<td>Milk, whole</td>
<td>FNDOS 11110000</td>
</tr>
<tr>
<td></td>
<td>Milk, reduced fat (2%)</td>
<td>FNDOS 11112110</td>
</tr>
<tr>
<td></td>
<td>Milk, low fat (1%)</td>
<td>FNDOS 11112210</td>
</tr>
<tr>
<td></td>
<td>Milk, fat free (skim)</td>
<td>FNDOS 11133000</td>
</tr>
<tr>
<td></td>
<td>Soy milk</td>
<td>FNDOS 11320000</td>
</tr>
<tr>
<td></td>
<td>Almond milk, sweetened</td>
<td>FNDOS 11350000</td>
</tr>
<tr>
<td></td>
<td>Milk, lactose free, fat free (skim)</td>
<td>FNDOS 1114320</td>
</tr>
<tr>
<td></td>
<td>Goat's milk, whole</td>
<td>FNDOS 11116000</td>
</tr>
<tr>
<td></td>
<td>Rice milk</td>
<td>FNDOS 11360000</td>
</tr>
<tr>
<td></td>
<td>Buttermilk, low fat (1%)</td>
<td>FNDOS 11115010</td>
</tr>
<tr>
<td></td>
<td>Cream, half</td>
<td>FNDOS 12120100</td>
</tr>
<tr>
<td>Cheese</td>
<td>cheddar cheese</td>
<td>FNDOS 14104000</td>
</tr>
<tr>
<td></td>
<td>mozzarella</td>
<td>FNDOS 14107010</td>
</tr>
<tr>
<td>(Total Vegetables)</td>
<td>Green leafy or lettuce salad with or without other vegetables</td>
<td>mixed salad greens, raw</td>
</tr>
<tr>
<td>Fried potatoes</td>
<td>Potatoes/frozen potatoes</td>
<td>potato, french fries, NFS</td>
</tr>
<tr>
<td></td>
<td>white potato fresh</td>
<td>potato, NFS (cat: white, baked or boiled)</td>
</tr>
<tr>
<td>Other vegetables than salad or potatoes</td>
<td>canned sweet corn</td>
<td>corn, canned, cooked, no added fat</td>
</tr>
<tr>
<td></td>
<td>onions</td>
<td>onions, cooked, from fresh, fat not added in cooking</td>
</tr>
<tr>
<td></td>
<td>canned chile peppers</td>
<td>Pepper, chili, green, canned</td>
</tr>
<tr>
<td></td>
<td>fresh bell peppers</td>
<td>peppers, green, cooked, NS as to fat added in cooking</td>
</tr>
<tr>
<td></td>
<td>fresh carrots</td>
<td>Carrots, raw</td>
</tr>
<tr>
<td>Tomato sauces, not including pizza sauce</td>
<td>Canned tomatoes/ Fresh tomatoes</td>
<td>spaghetti sauce (cat: pasta sauces, tomato-based)</td>
</tr>
<tr>
<td>Mexican type salsa made with tomato</td>
<td>Salsa, NFS</td>
<td>FNDOS 74402100</td>
</tr>
<tr>
<td>Red Meat</td>
<td>ground beef, cooked</td>
<td>FNDOS 21500100</td>
</tr>
</tbody>
</table>

1 oz = 28.35 g. Multiplied by 2 for recommended serving size. 85.5% to =3 oz equivalent.
### Table K.1 Continued

<table>
<thead>
<tr>
<th>Food Item selected from USDA</th>
<th>Food Code</th>
<th>Measure for nutrient count</th>
<th>FDA Reference Food Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Processed Meat</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lunch meat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ham, prepackaged or deli,</td>
<td>FNDDS</td>
<td>1 slice, NFS (28 g)</td>
<td></td>
</tr>
<tr>
<td>luncheon meat</td>
<td>25230210</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hot dog</td>
<td>FNDDS</td>
<td>100 g</td>
<td></td>
</tr>
<tr>
<td>Frankfurter or hot dog, NFS</td>
<td>25210110</td>
<td>1 oz, 28.35 g</td>
<td></td>
</tr>
<tr>
<td>sausage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sausage, NFS</td>
<td>FNDDS</td>
<td>1 oz, cooked (28.35 g)</td>
<td></td>
</tr>
<tr>
<td>25221400</td>
<td>1 oz, cooked (28.35 g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ham</td>
<td>FNDDS</td>
<td>1 oz, boneless, cooked</td>
<td></td>
</tr>
<tr>
<td>Ham, smoked or cured, cooked, NS as to fat eaten</td>
<td>22311000</td>
<td>1 oz, boneless, cooked (28.35 g)</td>
<td></td>
</tr>
<tr>
<td>bacon</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacon, NS as to type of meat, cooked</td>
<td>22600100</td>
<td>1 oz, cooked (28.35 g)</td>
<td></td>
</tr>
</tbody>
</table>

### Pizza (including frozen, fast food pizza, or homemade)

- Mixed Dishes: ‘Not measurable with cup, eg. ...pizza...
- Pizza with pepperoni, from restaurant or fast food, NS as to type of crust

**Sweetened fruit drinks, sports drinks, or energy drinks**

- Juices, nectars, fruit drinks
- Sports drink (Gatorade G)
- Soft drink, NFS (same as soft drink, cola)

**Soda, non diet**

- Carbonated and noncarbonated beverages...

**Coffee or Tea with added sugar or honey**

- Coffee or tea, flavored and sweetened
- Coffee, NS as to type

**Chocolate or other types of candy**

- All other candies
- Chocolate, sweet or dark

**Donuts, sweet rolls, Danish, muffins, or pop-tarts**

- Donuts, danish, sweet rolls...muffins, toaster pastries
- Doughnut, NFS (Cat: doughnuts, sweet rolls, pastries)

**Cookies, cake, pie, or brownies**

- Cookies
- Cake or cupcake, NFS as to type
- Cookie, brownie, NS as to icing
- Pie, NFS

**Ice cream or other frozen desserts**

- Ice cream, frozen yogurt, sherbet, frozen flavored and sweetend ice and pops...all types...
- Ice cream, NFS

**Popcorn**

- Snacks: ‘all varieties, chips, pretzels, popcorn,...
- Popcorn, NFS
### APPENDIX L.

**DSQ CEREAL LISTINGS, CEREAL SELECTED FROM USDA FOOD DATA CENTRAL, AND MEASURE FOR CALCULATING NUTRIENT PROFILES- AIM 2**

Table L.1 DSQ cereal listings, cereal match selected from USDA Food Data Central, and measure for calculating nutrient profiles

<table>
<thead>
<tr>
<th># of times selected by participants</th>
<th>weight per cup (g) (cooked)</th>
<th>DSQ Cereal Listing</th>
<th>Food Item selected from USDA Food Data Central</th>
<th>Data Type</th>
<th>Food Code (FNDDS) NBD # (SR Legacy) FDC ID (branded)</th>
<th>Measure for nutrient count (based on Cereal density and FDA Reference Amounts Customarily Consumed)</th>
<th>Calculated adjustment to parameter amounts to equal FDA Reference Amount of One Serving based on cereal density</th>
</tr>
</thead>
<tbody>
<tr>
<td>417</td>
<td>240 g</td>
<td>229 = Oatmeal</td>
<td>Oatmeal, NS as to regular, quick, or instant, NS as to fat added</td>
<td>FNDDS</td>
<td>56202960</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>240 g</td>
<td>94 = Cream of Wheat</td>
<td>Cream of wheat, NS as to regular, quick, or instant, NS as to fat</td>
<td>FNDDS</td>
<td>56206990</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>240 g</td>
<td>253 = Quaker Multigrain Oatmeal</td>
<td>Oatmeal, multigrain, NS as to fat</td>
<td>FNDDS</td>
<td>56203600</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>35 g dry</td>
<td>251 = Quaker Fruit and Cream Oatmeal</td>
<td>Cereals, Quaker, Instant Oatmeal, fruit and cream variety, dry</td>
<td>SR Legacy</td>
<td>8225</td>
<td>1 packet dry (35 g)</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>43 g dry</td>
<td>254 = Quaker Oatmeal Express</td>
<td>Oatmeal, multigrain, NS as to fat</td>
<td>FNDDS</td>
<td>56203600</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>240 g</td>
<td>211 = Multi Grain Oatmeal</td>
<td>Grits, NS as to regular, quick, or instant, NS as to fat (cooked)</td>
<td>FNDDS</td>
<td>56200990</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>240g</td>
<td>50 = Cheese Grits</td>
<td>Grits, with cheese, NS as to fat</td>
<td>FNDDS</td>
<td>56201090</td>
<td>1 cup, cooked (240g)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>240 g</td>
<td>252 = Quaker Instant Grits, all flavors</td>
<td>Grits, instant, made with water, NS as to fat</td>
<td>FNDDS</td>
<td>56201230</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>240 g</td>
<td>225 = Oat Bran cereal</td>
<td>Rice, cream of, cooked, NS as to fat</td>
<td>FNDDS</td>
<td>56205092</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>240 g</td>
<td>223 = Oat Bran Cereal, Quaker</td>
<td>Whole wheat cereal, cooked, NS as to fat</td>
<td>FNDDS</td>
<td>56207190</td>
<td>1 cup, cooked (240 g)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>90 = Cracklin' Oat Bran</td>
<td></td>
<td></td>
<td></td>
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<td>11</td>
<td>240 g</td>
<td>92 = Cream of Rice</td>
<td>Rice, cream of, cooked, NS as to fat</td>
<td>FNDDS</td>
<td>56205092</td>
<td>1 cup, cooked (240 g)</td>
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<td>3</td>
<td>240 g</td>
<td>325 = Whole wheat cereal</td>
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<td>FNDDS</td>
<td>56207190</td>
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<td>316 = Wheat cereal</td>
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<td>2</td>
<td>268 g</td>
<td>194 = Malt-O-Meal</td>
<td>Cereals, Malt-O-Meal, original, plain, prepared with water without salt</td>
<td>SR Legacy</td>
<td>8511</td>
<td>1 serving (3T dry cereal plus 1 cup water (268 g)</td>
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<td>1</td>
<td>240 g</td>
<td>195 = Malt-O-Meal, chocolate</td>
<td>Wheat cereal, chocolate flavored, cooked</td>
<td>FNDDS</td>
<td>56207370</td>
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<td>233 g</td>
<td>108 = Farina</td>
<td>Cereals, farina, enriched, cooked with water, with salt</td>
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<td>8173</td>
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<td>170g</td>
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<td>56200490</td>
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<td>170 g</td>
<td>201 = Millet</td>
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<td>140 g</td>
<td>31 = Bulgur</td>
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<td>FNDDS</td>
<td>56207130</td>
<td>1 cup, cooked (140g)</td>
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<td>111 g 6 = 100% Natural Granola, Oats &amp; Honey</td>
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<td>42</td>
<td>60 g</td>
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<td>Cereal (Uncle Sam)</td>
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<td>59 g</td>
<td>18 = Banana Nut Crunch Cereal</td>
<td>Cereal (Post Great Grains Banana Nut Crunch)</td>
<td>FNDDS</td>
<td>57106050</td>
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<td>260 = Raisin Bran, Post</td>
<td>Cereal (Post Raisin Bran)</td>
<td>FNDDS</td>
<td>57331000</td>
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<td>58 g</td>
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<td>Wheat bran, unprocessed</td>
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<td>57601100</td>
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<td>57 g</td>
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<td>Cereals ready-to-eat, WEETABIX whole grain cereal</td>
<td>SR Legacy</td>
<td>42237</td>
<td>1 cup (57 g)</td>
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<td>57 g</td>
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<td>57 g google</td>
<td>307 = Total Raisin Bran</td>
<td>Total Raisin Bran Cereal (General Mills Sales Inc)</td>
<td>Branded</td>
<td>758010</td>
<td>100g</td>
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<td>34</td>
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<td>Cereal, raisin bran</td>
<td>FNDDS</td>
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<td>Branded</td>
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<td>Cereal (Kellogg's Raisin Bran Crunch)</td>
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<td>53 g</td>
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<td>Cereal (Kellogg's Frosted Mini-Wheats)</td>
<td>FNDDS</td>
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<td>53 g</td>
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<td>SR Legacy</td>
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<td>8191</td>
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<td>Cereals ready-to-eat, POST, Shredded Wheat, lightly frosted, spoon-size</td>
<td>SR Legacy</td>
<td>8191</td>
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<td>43495</td>
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<td>1101802</td>
<td>100g</td>
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<td>50 g</td>
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<td>Cereal (Post Shredded Wheat) (1 cup spoon size biscuits)</td>
<td>FNDDS</td>
<td>57417000</td>
<td>1 cup, crushed (58 g)</td>
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<td>1 cup, crushed (58 g)</td>
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<td>279 = Shredded Wheat, Original</td>
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<td>57417000</td>
<td>1 cup, crushed (58 g)</td>
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<td>278 = Shredded Wheat, 100%</td>
<td>Cereal (Post Shredded Wheat) (1 cup spoon size biscuits)</td>
<td>FNDDS</td>
<td>57417000</td>
<td>1 cup, crushed (58 g)</td>
<td></td>
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<tr>
<td>5</td>
<td></td>
<td>203 = Mini-Wheats</td>
<td>Cereals ready-to-eat, Post, Shredded Wheat n' Bran, spoon size</td>
<td>SR Legacy</td>
<td>43393</td>
<td>100 g</td>
<td>multiplied by 0.60 for 60 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>47.2 g</td>
<td>276 = Shredded Wheat 'N Bran</td>
<td>Cereals ready-to-eat, Post, Shredded Wheat n' Bran, spoon size</td>
<td>SR Legacy</td>
<td>43393</td>
<td>100 g</td>
<td>multiplied by 0.60 for 60 g</td>
<td></td>
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<tr>
<td>4</td>
<td>44 g</td>
<td>22 = Blueberry Morning</td>
<td>Cereals ready-to-eat, Post Selects Blueberry Morning</td>
<td>SR Legacy</td>
<td>8192</td>
<td>100 g</td>
<td>multiplied by 0.60 for 60 g</td>
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<tr>
<td>37</td>
<td>44 g</td>
<td>179 = Kashi Heart to Heart Cereal</td>
<td>Cereal (Kashi Heart to Heart Honey Toasted Oat)</td>
<td>FNDDS</td>
<td>57301530</td>
<td>100 g</td>
<td>multiplied by 0.60 for 60 g</td>
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<tr>
<td>51</td>
<td>43 g</td>
<td>189 = Life (plain and cinnamon)</td>
<td>Cereal (Quaker Life)</td>
<td>FNDDS</td>
<td>57304100</td>
<td>1 cup (43 g)</td>
<td></td>
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</tr>
<tr>
<td>32</td>
<td>43 g</td>
<td>158 = Honey Bunches of Oats with Almonds</td>
<td>Cereal (Post Honey Bunches of Oats with Almonds)</td>
<td>FNDDS</td>
<td>57237300</td>
<td>1 cup (43 g)</td>
<td></td>
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<tr>
<td>15</td>
<td>43 g</td>
<td>284 = Special K Fruit &amp; Yogurt</td>
<td>Cereal (Kellogg’s Special K Fruit &amp; Yogurt)</td>
<td>FNDDS</td>
<td>57344015</td>
<td>1 cup (43 g)</td>
<td></td>
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<tr>
<td>6</td>
<td>42.6 g</td>
<td>285 = Special K Low Carb Lifestyle Protein Plus</td>
<td>Kellogg's Special K Cereal Low Carb Protein Plus</td>
<td>Branded</td>
<td>752152</td>
<td>100 g</td>
<td>multiplied by 0.40 for 40 g</td>
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(Table L.1 Continue)

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<th>41.3 g</th>
<th>156 = Honey Bunches of Oat with Strawberry Cereal ready-to-eat, Post, Honey Bunches of Oats with real strawberries</th>
<th>SR Legacy</th>
<th>57349000</th>
<th>100 g</th>
<th>multiplied by 0.40 for 40 g</th>
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<tr>
<td>51</td>
<td>41 g</td>
<td>114 = Frosted Flakes, Kellogg's Cereal (Kellogg's Frosted Flakes)</td>
<td>FNDDS</td>
<td>57237100</td>
<td>1 cup</td>
<td>40 g</td>
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<td>9</td>
<td>123 g</td>
<td>123 = Frosted flakes Cereal (Post Honey Bunches of Oats Honey Roasted)</td>
<td>FNDDS</td>
<td>57237100</td>
<td>1 cup</td>
<td>40 g</td>
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<td>8</td>
<td>41 g</td>
<td>73 = Cocoa Krispies Cereal (General Mills Golden Grains)</td>
<td>FNDDS</td>
<td>57224000</td>
<td>1 cup</td>
<td>40 g</td>
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<td>18</td>
<td>40 g</td>
<td>155 = Honey Bunches of Oat Honey Roasted Cereal (General Mills Cheerios Apple Cinnamon)</td>
<td>FNDDS</td>
<td>57103100</td>
<td>1 cup</td>
<td>40 g</td>
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<td>29</td>
<td>40 g</td>
<td>157 = Honey Bunches of Oats Cereal (General Mills Cinnamon Toast Crunch)</td>
<td>FNDDS</td>
<td>57125000</td>
<td>1 cup</td>
<td>40 g</td>
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<td>21</td>
<td>40 g</td>
<td>58 = Chex, Honey Nut Cereal (General Mills Chex Honey Nut)</td>
<td>FNDDS</td>
<td>57240100</td>
<td>1 cup</td>
<td>40 g</td>
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<td>17</td>
<td>40 g</td>
<td>287 = Special K Vanilla Almond Cereal (General Mills Cinnamon Toast Crunch)</td>
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<td>57344020</td>
<td>1 cup</td>
<td>40 g</td>
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<td>15</td>
<td>40 g</td>
<td>26 = Bran flakes Cereal (Post Bran Flakes)</td>
<td>FNDDS</td>
<td>57209000</td>
<td>1 cup</td>
<td>40 g</td>
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<td>9</td>
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<td>137 = Fruity Pebbles Cereal (Post Fruity Pebbles)</td>
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<td>57223000</td>
<td>1 cup</td>
<td>40 g</td>
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<tr>
<td>8</td>
<td>40 g</td>
<td>122 = Frosted corn flakes Cereal, frosted corn flakes</td>
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<td>1 cup</td>
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<td>2</td>
<td>40 g</td>
<td>97 = Crispy Brown Rice Cereal Cereal (Post Cinnamon Toast Crunch)</td>
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<td>740026</td>
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<td>40 g</td>
<td>62 = Chocolate frosted cereal Cereal (Kellogg's Chocolate Frosted)</td>
<td>Branded</td>
<td>651996</td>
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<td>1</td>
<td>40 g</td>
<td>115 = Frosted Flakes, Multi-O-Meal Cereal (Malt-O-Meal)</td>
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<td>57305210</td>
<td>40 g</td>
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<td>1</td>
<td>40 g</td>
<td>266 = Rice Krispies, Treats Cereal</td>
<td>Cereal (General Mills Cinnamon Toast Crunch)</td>
<td>FNDDS</td>
<td>57124050</td>
<td>1 cup</td>
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<tr>
<td>3</td>
<td>39 g</td>
<td>53 = Chex Morning Mix Cinnamon Cereal (Post Cinnamon Toast Crunch)</td>
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<td>57348000</td>
<td>1 cup</td>
<td>39 g</td>
</tr>
<tr>
<td>6</td>
<td>39 g</td>
<td>74 = Cocoa Pebbles Cereal (Post Cinnamon Toast Crunch)</td>
<td>FNDDS</td>
<td>57348000</td>
<td>1 cup</td>
<td>39 g</td>
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<td>3</td>
<td>38.6 g</td>
<td>148 = Grape-Nuts Flakes Cereal ready-to-eat, Post, Grape-Nuts Flakes</td>
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<td>8093</td>
<td>100 g</td>
<td>multiplied by 0.40 for 40 g</td>
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<td>1</td>
<td>x</td>
<td>146 = Grape Nut O's discontinued</td>
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<td>57113850</td>
<td>1 cup</td>
<td>37 g</td>
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<tr>
<td>1</td>
<td>38 g</td>
<td>320 = Wheat, puffed, presweetened with sugar Cereal, puffed wheat, sweetened</td>
<td>FNDDS</td>
<td>57416010</td>
<td>1 cup</td>
<td>38 g</td>
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<td>165</td>
<td>37 g</td>
<td>45 = Cheerios, Honey Nut Cereal (General Mills Cheerios Honey Nut)</td>
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<td>57241000</td>
<td>1 cup</td>
<td>37 g</td>
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<td>7</td>
<td>37 g</td>
<td>44 = Cheerios, Frosted Cereal (General Mills Cheerios Frosted)</td>
<td>FNDDS</td>
<td>57213850</td>
<td>1 cup</td>
<td>37 g</td>
</tr>
<tr>
<td>1</td>
<td>36 g</td>
<td>39 = Cheerios, Berry Burst Cereal (General Mills Cheerios Berry Burst)</td>
<td>FNDDS</td>
<td>57106260</td>
<td>100 g</td>
<td>multiplied by 0.40 for 40 g</td>
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<tr>
<td>2</td>
<td>x</td>
<td>43 = Cheerios, Berry Burst, Strawberry Banana Cereal (General Mills Cheerios Berry Burst)</td>
<td>FNDDS</td>
<td>57106260</td>
<td>100 g</td>
<td>multiplied by 0.40 for 40 g</td>
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<tr>
<td>1</td>
<td>x</td>
<td>41 = Cheerios, Berry Burst Triple Berry Cereal (General Mills Cheerios Berry Burst)</td>
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<tr>
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<td>x</td>
<td>40 = Cheerios, Berry Burst Strawberry Cereal (General Mills Cheerios Berry Burst)</td>
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<td>x</td>
<td>48 = Cheerios, Yogurt Burst, Strawberry Cereal (General Mills Cheerios Berry Burst)</td>
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<td>multiplied by 0.40 for 40 g</td>
</tr>
<tr>
<td>2</td>
<td>x</td>
<td>47 = Cheerios, Team Discontinued</td>
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<td>1</td>
<td>36 g</td>
<td>280 = Smacks Cereal (Kellogg's Honey Smacks)</td>
<td>FNDDS</td>
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<td>100 g</td>
<td>multiplied by 0.40 for 40 g</td>
</tr>
<tr>
<td>1</td>
<td>36 g</td>
<td>166 = Honey Smacks Cereal (Kellogg's Honey Smacks)</td>
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<td>g</td>
<td>Name</td>
<td>Manufacturer</td>
<td>FDC ID</td>
<td>weight (g)</td>
<td>CRM</td>
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<td>------------</td>
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<tr>
<td>29</td>
<td>36 g</td>
<td>190 = Lucky Charms</td>
<td>Cereal (General Mills Lucky Charms)</td>
<td>FNDDS</td>
<td>57305100</td>
<td>100 g</td>
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<td>17</td>
<td>36 g</td>
<td>32 = Cap’o Crunch</td>
<td>Cereal (Quaker Cap’o Crunch)</td>
<td>FNDDS</td>
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<td>100 g</td>
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<td>12</td>
<td>36 g</td>
<td>322 = Wheaties</td>
<td>Cereal (General Mills Wheaties)</td>
<td>FNDDS</td>
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<td>100 g</td>
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<td>36 g</td>
<td>75 = Cocoa Puffs</td>
<td>Cereal (General Mills Cocoa Puffs)</td>
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<td>7</td>
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<td>100 g</td>
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<td>3</td>
<td>36 g</td>
<td>237 = Oh’s</td>
<td>Cereal (Quaker Honey Graham Oh’s)</td>
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<td>57316710</td>
<td>100 g</td>
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<td>35 g</td>
<td>240 = Oh’s, Honey Graham</td>
<td>Cereal (Quaker Honey Graham Oh’s)</td>
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<td>3</td>
<td>35 g</td>
<td>81 = Cookie-Crisp (all flavors)</td>
<td>Cereal (General Mills Cookie Crisp)</td>
<td>FNDDS</td>
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<td>100 g</td>
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<tr>
<td>12</td>
<td>35 g</td>
<td>34 = Cap’o Crunch’s Crunch Berries</td>
<td>Cereal (Quaker Cap’o Crunch’s Crunchberries)</td>
<td>FNDDS</td>
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<td>100 g</td>
</tr>
<tr>
<td>1</td>
<td>34.6 g goog</td>
<td>188 = Kix, Berry Berry</td>
<td>Berry Berry Kix Cereal</td>
<td>Branded</td>
<td>1146799</td>
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<td>1</td>
<td>34g</td>
<td>14 = Amaranth Flakes</td>
<td>ARROWHEAD MILLS, ORGANIC AMARANTH FLAKES</td>
<td>Branded</td>
<td>364068</td>
<td>100 g</td>
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<td>227 = Oat cereal</td>
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<td>32 g</td>
<td>308 = Trix</td>
<td>Cereal (General Mills Trix)</td>
<td>FNDDS</td>
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<td>32g</td>
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<td>80</td>
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<td>46</td>
<td>31 g</td>
<td>286 = Special K Red Berries</td>
<td>Cereal (Kellogg’s Special K Red Berries)</td>
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<td>57344010</td>
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<td>31 g</td>
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<td>Cereal (General Mills Chex Corn)</td>
<td>FNDDS</td>
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<td>30 g</td>
<td>46 = Cheerios, Multi Grain</td>
<td>Cereal (General Mills Cheerios Multigrain)</td>
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<td>30 g</td>
<td>247 = Product 19</td>
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<td>751930</td>
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<td>16</td>
<td>29 g</td>
<td>84 = Corn Pops</td>
<td>Cereal (Kellogg’s Corn Pops)</td>
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<td>64 = Cinnamon Crunch Crispix</td>
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<td>Cereal (Kellogg’s Fruit Loops)</td>
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<td>257</td>
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<td>37 = Cheerios</td>
<td>Cereal (General Mills Cheerios)</td>
<td>FNDDS</td>
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<td>38</td>
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<td>83 = Corn Flakes, Kellogg’s</td>
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<td>FNDDS</td>
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<td>FNDDS</td>
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<td>51 g</td>
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<td>100 g</td>
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<tr>
<td>13</td>
<td>27 g</td>
<td>268 = Rice cereal</td>
<td>Cereal, rice flakes</td>
<td>FNDDS</td>
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<td>100 g</td>
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<td>3</td>
<td>26 g</td>
<td>269 =rice flakes</td>
<td>Cereal, rice flakes</td>
<td>FNDDS</td>
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<td>100 g</td>
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<td>27 g</td>
<td>138 = Golden Crisp</td>
<td>Cereal (Post Golden Crisp)</td>
<td>FNDDS</td>
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<td>100 g</td>
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<tr>
<td>68</td>
<td>26 g</td>
<td>264 = Rice Krispies</td>
<td>Cereal (Kellogg’s Rice Krispies</td>
<td>FNDDS</td>
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<td>100 g</td>
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<tr>
<td>8</td>
<td>26 g</td>
<td>98 = Crispy Rice</td>
<td>Cereal, crispy rice</td>
<td>FNDDS</td>
<td>57151000</td>
<td>100 g</td>
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(Table L.1 Continued)

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<td>25 g</td>
<td>86 = Corn flakes</td>
<td>Cereal, corn flakes</td>
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<td>25 g</td>
<td>305 = Total Corn Flakes</td>
<td>FNDDS 57134000</td>
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<td>87 g</td>
<td>Corn flakes, low sodium</td>
<td>multiplied by 0.40 for 40 g</td>
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<td>9</td>
<td>24 g</td>
<td>187 = Kix</td>
<td>Cereal (General Mills Kix)</td>
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<td>22 g</td>
<td>167 = Honeycomb</td>
<td>Cereal (Post Honeycomb)</td>
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<td>19 g</td>
<td>175 = Kashi</td>
<td>Cereal (Kashi 7 Whole Grain Puffs)</td>
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<td>19 g</td>
<td>186 = Kashi, Puffed</td>
<td>FNDDS 57301500</td>
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<td>19 g</td>
<td>85 = Corn Puffs</td>
<td>multiplied by 0.15 for 15 g</td>
</tr>
<tr>
<td>1</td>
<td>15 g</td>
<td>319 = Wheat, puffed</td>
<td>Cereal, puffed wheat, plain</td>
</tr>
<tr>
<td>4</td>
<td>14 g</td>
<td>271 = Rice, puffed</td>
<td>FNDDS 57416000</td>
</tr>
<tr>
<td>2</td>
<td>14 g</td>
<td>248 = Puffed Rice, Malt-O-Meal</td>
<td>Cereal, puffed rice</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>FNDDS 57340000</td>
</tr>
</tbody>
</table>

Table L.1 Continued: Cereals ready-to-eat, POST, Shredded Wheat, lightly Oatmeal, NS as to fat

- 1 cup, cooked (170 g)
- 1 cup, cooked (240 g)
- 1 cup, cooked (140 g)
- 1 cup, cooked (240 g)
- 1 cup, cooked (170 g)
- 1 cup, cooked (240 g)
- 1 cup, cooked (170 g)
- 1 cup, cooked (240 g)

Table L.1 Continued: Cereals ready-to-eat, Kellogg's Granola, lowfat, Kellogg's

- 1 cup, cooked (170 g)
- 1 cup, cooked (240 g)
- 1 cup, cooked (170 g)
- 1 cup, cooked (240 g)
- 1 cup, cooked (170 g)
- 1 cup, cooked (240 g)
- 1 cup, cooked (170 g)
- 1 cup, cooked (240 g)