UNIVERSITY OF MANITOBA

The Relationship between Adverse Childhood Experiences and Healthcare Use in the Manitoba IBD Cohort Study

by

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ABSTRACT

Background: Adverse childhood experiences (ACEs) include child maltreatment and household dysfunction experiences. ACEs are risk factors for poor health outcomes. Inflammatory bowel disease (IBD) is a chronic inflammatory condition that also is associated with adverse health outcomes. We hypothesized that persons diagnosed with IBD and exposed to an ACE would exhibit greater healthcare use than persons with IBD never exposed to an ACE.
Research Objectives: The objectives were to estimate the prevalence of ACEs in individuals diagnosed with IBD, test the association between the number and type of ACEs and healthcare use, and test the association between perceived level of trauma from ACEs and healthcare use.
Methods: The cohort included 345 participants from the population-based Manitoba IBD Cohort Study. Self-reports of ACEs were linked to provincial administrative health data. IBD and non-IBD-related healthcare use measures included general and specialist physician visits, hospitalizations, length of hospital stay, and prescription drug use. Mean annual estimates of healthcare use measures were produced for the 60-month period following ACE report. Generalized linear models (GLMs) were used to test the association between healthcare use and ACEs. All models were adjusted for confounding covariates of demographics, IBD disease characteristics, behavioral risk factors, comorbid conditions, and perceived psychological stress.
Results: The prevalence of at least one ACE in the study cohort was 74.2%. Mean annual estimates for non-IBD-related GP visits were significantly increased for cohort members exposed to physical and sexual abuse relative to those not exposed. The GLMs revealed significant decreases in IBD-related healthcare use for cohort members exposed to an upheaval between parents and who report high perceived trauma from ACEs.
Conclusions: The estimated prevalence of at least one self-reported ACE in persons with diagnosed IBD was higher than estimates from other comparable sources, which may reflect the different types of ACEs included in this study. The long period of time between ACE exposure and healthcare use measurement may have contributed to the limited impact of ACEs on estimated healthcare use. Future research could further explore the associations amongst ACE exposure, perceived psychological stress, and other health outcomes.

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I. Introduction

Background

Adverse childhood experiences (ACEs) are typically categorized into child maltreatment and household challenges. The former includes (1) physical abuse, (2) sexual abuse, (3) emotional abuse, (4) physical neglect, and (5) emotional neglect and the latter includes (6) exposure to domestic violence, (7) household substance abuse, (8) household mental illness, (9) parental separation or divorce, and (10) incarceration of a household member (Anda, Butchart, Felitti, & Brown, 2010). ACEs can be predictive of future physical and mental health outcomes (Anda et al., 2010; Felitti et al., 1998). This relationship has been studied across individuals with a variety of chronic health conditions, including cardiovascular disease, chronic lung disease, chronic liver disease, cancer, depression, anxiety and several other mental health disorders (Felitti et al., 1998; Gilbert et al., 2015). Although there is an association between ACEs and the onset of some chronic diseases, the literature indicates that a more consistent relationship exists between ACEs and risk factors for chronic disease than between ACEs and the development of chronic disease (Campbell, Walker, & Egede, 2016; Felitti et al., 1998). These risk factors include alcohol and drug abuse, smoking, obesity, and depression, suicide, and psychological stress (Anda et al., 1999; Campbell et al., 2016; Chapman et al., 2004; Danese et al., 2009; Dube et al., 2001; Dube et al., 2003; Shonkoff et al., 2012). The relationships between ACEs and risk factors for chronic disease have led researchers to believe that underlying mechanisms help predict an individual's transition from childhood adversity to chronic disease, which is the most common cause of increased healthcare use, disability, and early death (Chung & Chen, 2017; Huh, Kim, Lee, & Chae, 2017; Rose, Xie, & Stineman, 2014).

While the relationships amongst ACEs, risk factors, health outcomes, and healthcare use have been explored among a variety of disease cohorts, no studies have, to our knowledge, been conducted among individuals with inflammatory bowel disease (IBD). IBD includes Crohn's disease and ulcerative colitis; complex, chronic conditions manifested by inflammation and ulceration in the gastrointestinal (GI) tract. While IBD is accompanied by a diverse set of physical symptoms including, increased frequency and urgency of bowel movements, abdominal discomfort, and fatigue, it also exhibits a bi-directional association with mental health outcomes including, stress, anxiety, and depression (Bernstein, 2016). Likewise, these types of mental health outcomes are also commonly associated with ACEs (Chapman et al., 2004). Therefore, it is possible that ACEs could greatly impact persons with IBD including their disease activity and overall healthcare use.

IBD symptoms relapse and remit in an unpredictable pattern. It is a costly disease in terms of direct medical costs which include, general practitioner (GP) and specialist care, emergency care, and inpatient visits ("Direct Costs," 2008). These costs tend to increase during periods of severe disease (Bassi, Dodd, Williamson, & Bodger, 2004; Cohen et al., 2010). The unpredictability of individuals' disease activity has prompted research into the various symptom "triggers" including, the effects of psychological stress (Bernstein et al., 2010; Singh, Graff, & Bernstein, 2009). Researchers have observed that perceived psychological stress is associated with IBD symptom exacerbations (Bernstein et al., 2010; Mawdsley & Rampton, 2005; Singh et al., 2009). Given that ACEs also exhibit a causal connection with maladaptive stress, it is likely that these experiences will impact persons with IBD; including, their overall disease activity and disease-related healthcare use (Danese et al., 2009; Shonkoff et al., 2012). ACES have a positive association with overall GI symptom activity in persons with irritable bowel syndrome (IBS);

there may be a likelihood of a similar trend in persons with IBD (Drossman et al., 1990; Park et al., 2016). Thus, we hypothesized that persons diagnosed with IBD who were exposed to at least one ACE would exhibit greater healthcare use than persons with IBD who were never exposed to an ACE. Furthermore, we predicted that this relationship would be influenced by the effects of demographic/behavioral risk factors, comorbid conditions, psychological stress and IBD disease characteristics.

Purpose and Objectives

The purpose of this research was to test the association between ACEs, perceived trauma, and healthcare use amongst individuals diagnosed with IBD. The objectives were:

1. To estimate the prevalence of ACEs in individuals diagnosed with IBD;
2. To test the association between ACEs, which included number and type, and non-IBD and IBD-related healthcare use amongst individuals with a confirmed IBD diagnosis; and
3. To test the association between perceived level of trauma of ACEs and non-IBD and IBD-related healthcare use amongst individuals with a confirmed IBD diagnosis.

Thesis Outline

Chapter Two of this thesis includes a review of relevant research literature that informed the study hypotheses and objectives. The review describes in more detail, the relationship between ACEs and psychological stress and between IBD and psychological stress. This chapter also outlines the potential confounding factors that affect IBD disease activity and an individual's overall healthcare use, including demographic and behavioral risk factors, comorbid

conditions, and IBD disease characteristics. Chapter Three outlines the research methods including the study design and data sources. This study used a retrospective cohort design; data from the Manitoba IBD Cohort Study was linked to provincial administrative health data to achieve the objectives. The strengths and limitations of study methods are also acknowledged within this chapter. Chapter Four details the results of the analyses. We report on individuals with an IBD diagnosis who were exposed to at least one ACE as well as individuals with an IBD diagnosis who were never exposed to an ACE. Descriptive statistics for each group were compared. Individuals in six ACE categories were also described in detail. Healthcare use measures were compared for cohort members exposed to at least one ACE with those who were never exposed to an ACE. Additionally, healthcare use measures were compared for cohort exposed to different numbers and types of ACEs, as well as, different levels of perceived trauma of ACEs. Chapter Five provides a summary of the final study results, further discussion about the strengths and limitations of these findings, recommendations for research and action, and overall conclusions.

II. Review of Literature

Outline

This chapter begins by introducing the Andersen and Newman Framework for Health Services Utilization; a framework that conceptualizes the types of characteristics predicting individual-level healthcare use. This chapter examines the clinical impact of IBD including common disease characteristics and the psychological and social aspects of IBD. It also introduces ACEs as a chronic, environmental stressor with the potential to influence an individual's health profile including health outcomes and healthcare utilization.

The Andersen and Newman Framework for Health Services Utilization

In 1960, Ronald Andersen and John Newman developed a framework of the contextual and individual-level factors that either facilitate or impede healthcare utilization (Aday & Andersen, 1974; Andersen & Newman, 1973). Over time, this framework has been updated to include a wide range of factors related to overall health and healthcare use (Andersen, Davidson, & Baumeister, 2015). The Andersen-Newman framework identifies healthcare utilization as a function of an individual's predisposing, enabling, and need characteristics (Figure 2.1) (Aday & Andersen, 1974; Andersen & Newman, 1973; Andersen et al., 2015). Predisposing characteristics include socio-cultural and demographic (e.g., age, sex) characteristics; these characteristics are not under an individual's control and may indirectly predispose one to utilize healthcare. Enabling characteristics include the facilitators and barriers that affect individuals' access to healthcare. For example, income may deter persons from accessing expensive healthcare resources. Need characteristics are defined as the most direct causes of individual healthcare utilization. This category also includes perceived need; whether or not an individual

views their problem(s) as requiring professional help. Need characteristics include comorbid conditions and various disease characteristics that result in an increased need for healthcare resources (Leukefeld, Logan, Martin, Purvis, & Farabee, 1998). Modified versions of the Andersen-Newman framework exist; in the past, behaviors such as smoking, alcohol-use, and Body Mass Index (BMI) have been categorized as both predisposing and need characteristics. More recent versions of the Andersen-Newman framework incorporate health behaviors as a separate category that includes factors such as smoking, alcohol use, and BMI (Andersen et al., 2015).

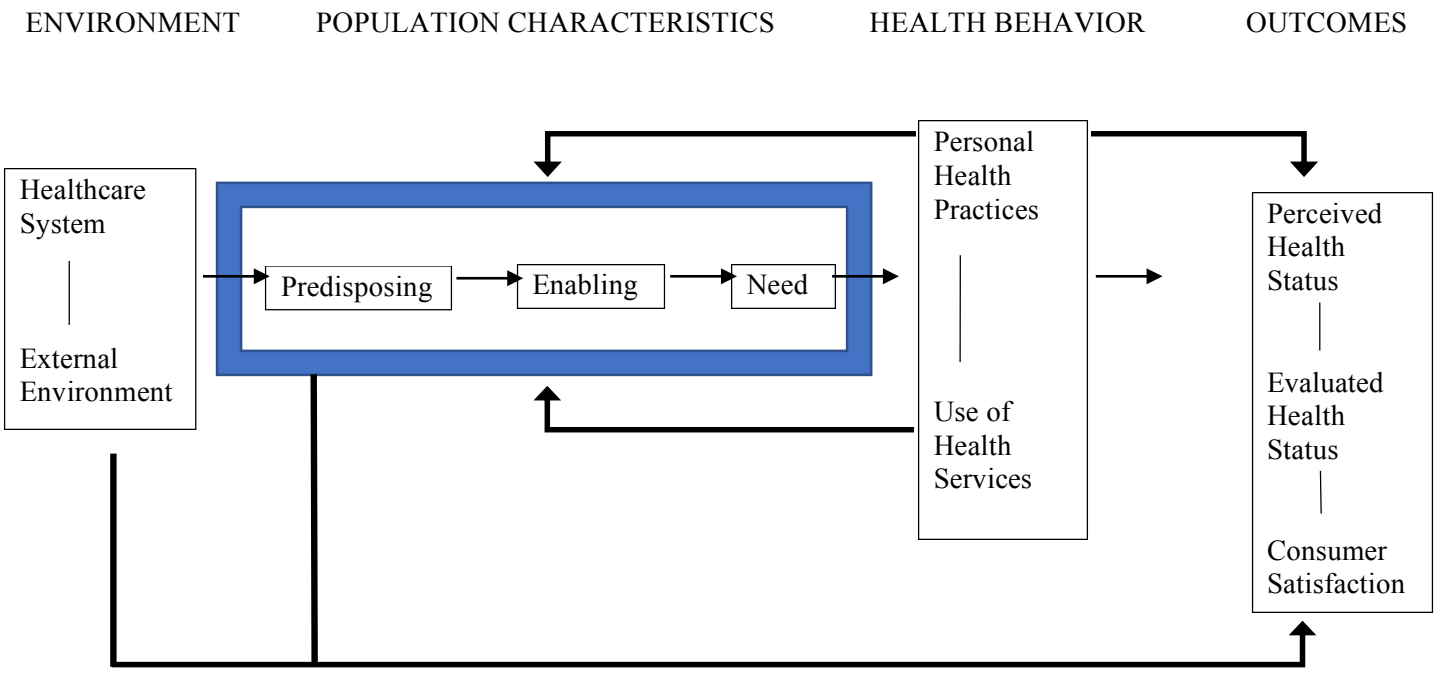

Figure 2.1: The Andersen-Newman Framework for Health Services Utilization

Studies have identified need characteristics as the strongest predictors of an individual's healthcare use relative to predisposing and enabling characteristics (Leaf et al., 1988; Padgett, Struening, & Andrews, 1990). According to the Andersen-Newman framework, healthcare use

has three different components including: (1) type of service (e.g., physician, hospital, laboratory, diagnostics, medication, etc.), (2) purpose of service (e.g., primary, secondary, tertiary, or custodial care), and (3) unit of analyses (e.g., contacts in a given period) (Leukefeld et al., 1998). The multiple components of the Andersen-Newman definition for healthcare use allows for variation in how healthcare use is defined in research and for different disease cohorts.

The diagnostics and clinical/pharmacological treatments associated with IBD symptoms and complications are comprehensive and expensive, especially during periods of increased disease activity/severity (Bernstein et al., 2009; Rocchi et al., 2012). Previous research relating IBD and healthcare utilization has used administrative data to methodologically quantify office-based visits, inpatient hospitalizations, and drug dispensations (Kappelman et al., 2011; Melesse et al., 2017). Few studies have made a clear distinction between healthcare used in relation to the IBD diagnosis and healthcare used for non-IBD-related reasons (Kappelman et al., 2011).

The Clinical Impact of Inflammatory Bowel Disease including Psycho-Social Factors

Individuals with IBD present with symptoms mostly referred to the gastrointestinal tract, including: abdominal pain, diarrhea, and rectal bleeding. They may also experience fatigue, or other extraintestinal manifestations of disease such as arthralgias (Singh et al., 2011). As with many chronic illnesses, the overall clinical impact of IBD cannot be fully accounted for by degree of inflammatory activity (Drossman, 1996; Rocchi et al., 2012) or by symptomatology. Increasingly, psychological stress and other psycho-social factors have been identified as important contributing factors to disease activity, quality of life (QoL), and other patient-related outcomes, including the amount of healthcare services utilized (Bernstein et al., 2010; Graff, Walker, & Bernstein, 2011; Lix et al., 2008; Walker et al., 2008). These findings are further

supported by evidence of increased healthcare use at a tertiary IBD center among patients affected by psychological health outcomes and severe disease activity (Click et al., 2016).

While IBD itself may exist as a psychological stress, anything that actually disrupts or that is perceived to disrupt homeostatic functioning can be classified as a "stressor"; a stressor can be physiological (e.g., pain, injury or anxious perceptions), but it may also be environmental (e.g., the death of a loved one) (Selye, 1956). A stressor can be acute, chronic, and/or recurrent. While more than one study has identified a bi-directional relationship between perceived psychological stress and IBD disease characteristics, recent studies are beginning to pinpoint other important sources of stress (Bernstein et al., 2016). Stress related to other common issues such as work, family, and finances are often considerably higher among persons with IBD reporting active IBD symptoms relative to persons reporting inactive IBD symptoms (Bernstein et al., 2016). Thus, for persons with IBD, the source of stress that is assessed should not be limited to disease characteristics.

Adverse Childhood Experiences: A Chronic, Environmental Stressor

Over time, a variety of retrospective, self-report tools have been designed to collect information about ACEs (Roy & Perry, 2004). While no universal classification system for ACEs exists across research domains, it is common to assess exposure to ten types of ACEs categorized broadly as child maltreatment (5 ACEs) and household challenges (5 ACEs) (Anda et al., 2010). Child maltreatment includes: (1) physical abuse, (2) sexual abuse, and (3) emotional abuse; acts of commission (overt actions or words) that can result in serious short or long-term harm to a child's health, survival, development, or dignity (Butchart, 2006; Herrenkohl, 2005). Child maltreatment also includes: (4) physical neglect and (5) emotional

neglect; acts of omission or failure to provide a child with basic physical, emotional, or educational needs (Herrenkohl, 2005). Household challenges include exposure to: (6) domestic violence, (7) household substance abuse, (8) household mental illness, (9) parental separation or divorce, and (10) incarceration of household member.

Population-based data from the ACE Study in the United States (US) indicates that approximately 60 percent of the general population report exposure to at least one ACE (Centers for Disease Control and Prevention, 2016; Metzler, Merrick, Klevens, Ports, & Ford, 2017). Similar results (55.8%) were reported for one Canadian province (McDonald, Kingston, Bayrampour, & Tough, 2015). Current Canadian population-based data indicates approximately 26 percent of persons report exposure to physical abuse and 10 percent to sexual abuse during childhood (Afifi et al., 2014). The Alberta ACE Study (McDonald et al., 2015) found that significantly less people reported childhood physical abuse (11.0%) and slightly more reported childhood sexual abuse (14.9%). The Canadian population data indicates that significantly more women reported childhood sexual abuse than men, and significantly more men report childhood physical abuse than women (Afifi et al., 2014). Population data from the US also indicated that 23.3% of persons report exposure to an upheaval between parents including, separation or divorce (Centers for Disease Control and Prevention, 2016).

ACEs are often cumulative, displaying a dose-response relationship with risk factors for chronic disease and negative health outcomes (Felitti et al., 1998; Merrick et al., 2017). Thus, an ACE score is commonly calculated in ACE research; an ACE score refers to the number of different ACEs experienced by an individual (score from 0 to 10). Data from ten US states in the Behavioral Risk Factor Surveillance System (BRFSS) displays ACE prevalence broken down by ACE scores: 1 ACE (23.3%), 2 ACEs (13.0%), 3 ACEs (7.8%), 4 or more ACEs (15.1%)

(Metzler et al., 2017). Similar ACE counts have been reported for one Canadian province: 1 ACE (24.0%), 2 ACEs (12.0%), 3 ACE (8.0%), 4 or more ACEs (12.0%) (McDonald et al., 2015). This study also displayed evidence for a graded relationship between number of ACEs and health outcomes with an inflammatory or mental health component (i.e. IBS, pain, chronic fatigue, depression, anxiety, and substance dependence).

For persons who have been exposed to ACEs, increased levels of inflammatory proteins in adulthood are suggestive of a neurological system dysregulation previously caused by disruption to the developing brain (disrupted neurodevelopment) (Levine, Cole, Weir, & Crimmins, 2015; Nurius, Green, Logan-Greene, & Borja, 2015). This type of disruption is associated with maladaptive emotion regulation techniques, social functioning, and heightened reactivity to future stressors (Chung & Chen, 2017; Cristobal-Narvaez et al., 2016; Huh et al., 2017). The ability to regulate emotions and function within a social setting is developed in the early stages of life through emotional exchanges between caregivers and children (Huh et al., 2017). ACEs, especially repeated interpersonal trauma between caregivers and children which includes both physical and sexual abuse, can severely disrupt neurodevelopment and ultimately effect emotion regulation and social functioning (Huh et al., 2017). Persons who have been exposed to ACEs use more maladaptive emotion regulation techniques such as self-blame, rumination, catastrophizing, and blaming others, all of which influence health-related beliefs and behaviors (Chung & Chen, 2017; Cristobal-Narvaez et al., 2016; Huh et al., 2017).

ACEs are associated with high levels of perceived stress, smoking, substance abuse, risky sexual behaviors, and overeating (Dube et al., 2003; Ford et al., 2011; Monnat & Chandler, 2015; Nurius et al., 2015). Moreover, maladaptive emotion regulation and heightened reactivity to stress thought to be caused by ACEs are also associated with worse functional impairment.

This impairment includes poor at-work and at-home management, decreased engagement in social and leisure activities, and interpersonal relationships (Karatzias et al., 2017). These factors can contribute to an individual's poor health, increased risk of morbidity/co-morbidity, and overall socioeconomic status (Adler, Epel, Castellazzo, & Ickovics, 2000; Chartier, Walker, & Naimark, 2010; Karatzias et al., 2017; Matthews, Gallo, & Taylor, 2010), factors which in turn can impact healthcare use (Chartier et al., 2010).

Healthcare use in relation to ACEs has been investigated in a number of studies. A recent study that investigated general practice (GP) visits, emergency department (ED) attendance, and nights spent in hospital, observed significantly higher odds of healthcare use with increasing numbers of ACEs (i.e., higher ACE score) (Bellis et al., 2017). A study that included women with a history of both physical and/or sexual abuse during childhood revealed that participants exhibited increased relative rates of mental health, physician, hospital, and pharmacy service use relative to women never exposed to physical and/or sexual abuse (Bonomi et al., 2008). Additional studies reveal similar relationships between ACE exposure and prescription drug dispensations including psychotropic drug dispensations (Anda, Brown, Felitti, Dube, & Giles, 2008; Koskenvuo & Koskenvuo, 2015).

Summary

Stress from trauma in childhood damages the developing brain. Disruption to neurodevelopment can influence the stress response and coping mechanisms that lead to health and social problems in adulthood. These mechanisms by which ACEs influence health and well-being throughout the lifespan are conceptually represented by the ACE pyramid (Figure 2.2) (Felitti et al., 1998).

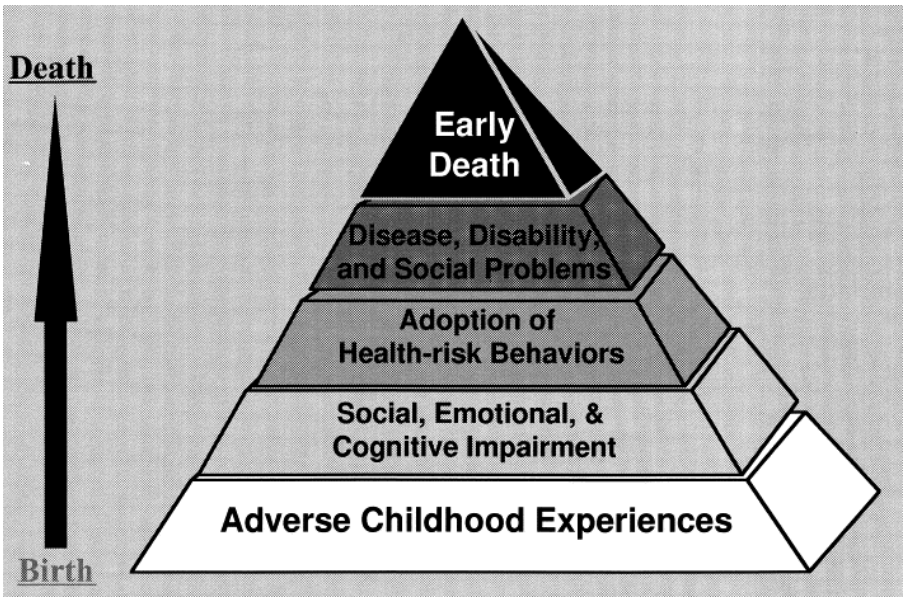

Figure 2.2: The ACE Pyramid

ACEs display significant relationships with health outcomes involving both inflammatory and/or mental health components. As IBD is a chronic inflammatory condition that is strongly associated with psychological stress, ACEs may greatly impact IBD disease activity and healthcare utilization.

III. Methods

Study Design and Data Source

The current research used a retrospective cohort design. Data from the Manitoba IBD Cohort Study were linked to administrative health data of Manitoba Health, Active Living, and Seniors to achieve the research objectives. Linkage was possible for a total of 362 respondents to the Manitoba IBD Cohort Study. Individuals were excluded from the study if they did not complete a Childhood Traumatic Events Scale (CTES) at the 12-month survey (n=17).

The Manitoba IBD Cohort Study is a longitudinal, population-based study of multiple determinants of health outcomes in persons with IBD who were diagnosed within seven years prior to study enrolment. The IBD Cohort Study drew on individuals in the University of Manitoba IBD Research Registry, a population-based registry that encompassed about 50% of all individuals in Manitoba diagnosed with IBD. The IBD Cohort Study was initiated in 2002 with funding from the Canadian Institutes of Health Research (CIHR). Semi-annual follow-up, which relied on a combination of surveys and interviews, occurred for a twelve-year period. The IBD Cohort Study enrolled individuals 18 years and older living in Manitoba with a confirmed IBD diagnosis. The median duration of time between diagnosis and cohort entry was 4.3 years and 60% of individuals who participated in the study were female.

Information about ACEs and perceived level of trauma from these experiences was captured by the CTES (Appendix A). The CTES asks about exposure to three commonly defined ACEs: (1) physical abuse, (2) sexual abuse, (3) an upheaval between parents (including, divorce or separation) and three additional traumatic experiences: (4) death of a very close friend or family member, (5) severe illness or injury, and (6) any other upheaval thought to significantly shape one's life or personality. It was administered along with the 12-month survey to all

respondents and was intended to provide a better understanding of the effect that ACEs may have on an individual's experience of IBD. Participants had the option to decline answering any of the questions. Semi-annual surveys (45-60 minutes) and annual interviews (45-60 minutes) were used to collect information about demographics, IBD disease characteristics, other medical problems, general well-being, and emotional status.

Administrative health data were linked with the survey data to capture objective measures of healthcare use as well as diagnoses of comorbid conditions. Individuals who consented to participate in the Manitoba IBD Cohort Study gave permission for researchers to access provincial administrative databases. The administrative databases that were used in this study included: (1) the Manitoba Health Registry, which captures individual-level demographics and health insurance coverage, (2) medical claims (i.e., physician billings), which consist of physician visits in offices, hospitals, and outpatient departments; information about physicians' specialties and diagnoses is also provided, (3) hospital separation abstracts, which are completed upon hospital discharge; they capture clinical information about inpatient hospitalization (i.e. diagnoses and procedure codes), and (4) prescription drug dispensation records from the Drug Program Information Network (DPIN), which provide information about medication use. Numerous studies have documented the completeness and accuracy of Manitoba's administrative health data for research about health and healthcare use of Manitoba's population (Bernstein, Blanchard, Leslie, Wajda, & Yu, 2000; Bernstein, Blanchard, Rawsthorne, & Wajda, 1999; Garland et al., 2012; Roos et al., 1993; Roos & Nicol, 1999).

Study Measures

Independent Variable: ACEs & Perceived Trauma. Self-reported ACEs experienced at age 16 years and younger were collected at the 12-month survey by the CTES (Appendix A). The CTES has been shown to have good reliability and validity, it has demonstrated sensitivity to clinical symptoms including post-traumatic stress disorder (PTSD) (Pennebaker & Susman, 1988; Scheller-Gilkey, Moynes, Cooper, Kant, & Miller, 2004). Information collected with the CTES was used to construct binary (i.e., yes/no) measures for cohort members who experienced one or more ACEs. In this study, individuals could report up to six types of ACEs including three commonly defined ACEs: (1) physical abuse, (2) sexual abuse, and (3) an upheaval between parents (such as divorce or separation), and three other traumatic experiences: (4) a death of a very close friend or family member, (5) experience of an extreme illness or injury, and (6) any other major upheaval that was thought to shape one's life or personality significantly. Binary (i.e., yes/no) measures for each type of ACE were analyzed. ACEs were not mutually exclusive, therefore a count ranging from none to six, represented the number of types of ACEs that individuals experienced (ACE Count). Using this count, we constructed categories: no ACEs, 1 ACE, 2 ACEs, and 3 or more ACEs. Perceived level of trauma for each category of ACEs was also collected (i.e., if yes, how traumatic was this?). Perceived level of trauma was captured using a Likert-type scale, where one represented not at all traumatic and seven represented extremely traumatic. If an individual experienced more than one type of ACE, the highest perceived level of trauma reported was used. Perceived level of trauma from ACEs was modelled as a categorical variable based on the frequency of responses (median: 5); low perceived trauma (≤5), and high perceived trauma (>5).

Outcome Variables: Healthcare Use. Twelve measures of healthcare use were defined. These included: (1) number of non-IBD-related general physician (GP) visits, (2) number of IBD-related GP visits, (3) number of non-IBD-related specialist (SP) visits, (4) number of IBD-related SP visits, (5) Non-IBD-related inpatient hospital admission (yes/no), (6) IBD-related inpatient hospital admission (yes/no), (7) number of non-IBD-related inpatient hospital days, (8) number of IBD-related inpatient hospital days, (9) number of IBD prescription drug dispensations, (10) number of psychotropic prescription drug dispensations, (11) number of antibiotic prescription drug dispensations, and (12) number of other prescription drug dispensations. IBD-related GP and SP visits had an International Classification of Disease 9th revision, clinical modification (ICD-9-CM) code of 555 (Crohn's disease) or 556 (ulcerative colitis) in administrative data. IBD-related complications were also included in IBD-related general and specialist physician visits: 537 (other disorder of the stomach or duodenum), 558 (other non-infectious gastroenteritis and colitis), 560 (intestinal obstruction without hernia), 565 (anal fissure and fistula), 566 (abscess of anal and rectal region), 567 (peritonitis), 569 (other disorders of the intestine, ex: rectal bleed), 578 (GI bleed), 579 (intestinal malabsorption), 789 (symptoms involving the abdomen and pelvis), 787 (symptoms involving digestive system). In addition to ICD-9-CM codes, an International Classification of Diseases 10th revision, Canada (ICD-10-CA) code of K50 (Crohn's disease), K51 (ulcerative colitis), or K52 (other and unspecified non-infective gastroenteritis and colitis) were used to define IBD-related hospitalizations. ICD-10 codes were used for all inpatient visits from 2004 and onward. Otherwise all prior inpatient stays and all outpatient visits were coded by ICD-9 codes. ATC codes and drug identification numbers (DINs) were used to identify IBD-related medications, psychotropic medications, and antibiotic medications (Appendix B). See Appendix C for

exclusions associated with pregnancy and childbirth. All healthcare use measures were defined for the 60-month (i.e., 5-year) period following completion of the CTES collected at the 12-month cohort survey. We used this duration of time to ensure that even rare events (e.g., hospitalizations) could be analyzed.

Covariates: Demographic and Behavioral Risk Factors. Sex (male/female), age group at 12-month survey completion (18-44 years, 45+ years; this categorization was based on previous research using Manitoba IBD Cohort Study data), income quintile for which approximately 20% of cohort members fall into each quintile of Q1 (lowest income), Q2, Q3, Q4, and Q5 (highest income), smoking status (never/not daily, daily), alcohol use (never/less than once a week, 1 to 3 times a week, greater than 3 times a week), BMI category (18.5-24.9 (healthy weight), <18.5 or ≥25 (underweight/overweight/obese), and social functioning (SF) (measured as a continuous variable using the Short Form 36 item Health Survey (Hays, Sherbourne, & Mazel, 1993). A maximum of eleven SF scores were collected for each cohort member between cohort entry (0-month survey completion) and 60-month survey completion. If a cohort member was missing any SF data points across the 60-month period, their mean score calculation was based on the appropriate denominator (i.e., total number of SF scales completed).

Covariate: Comorbidity. Comorbidity was measured using the Charlson Comorbidity Index (CCI). The CCI was defined from all ICD-9-CM and ICD-10-CA diagnoses in hospital separation abstracts and physician claims for the 365-day period prior to (and including) the 12-month survey completion date. Each comorbidity has an associated weight (ranging from one to six) based on the adjusted risk of mortality and resource use. Weights for comorbid conditions were summed, the higher the score, the higher an individual's level of comorbidity.

Covariate: Perceived Psychological Stress (PSS). A self-report, 14-item, validated measure of an individual's level of perceived psychological stress was collected at the 12-month survey using a perceived psychological stress scale (PSS-14) (Cohen, Kamarck, & Mermelstein, 1983). The PSS-14 is the most widely used scale measuring perceived psychological stress and it has acceptable reliability and validity. Overall PSS-14 scores were obtained by first reversing the scores of the seven positive items (items: 4, 5, 6, 7, 9, 10, and 13; e.g., 0=4; 1=3; 2=2; 3=1; 4=0), and summing the scores for the 14 items. Normative data taken from a North American sample have a mean score of 19.6 +/- 7.5 (Sheldon Cohen & Janicki-Deverts, 2012). Perceived stress has shown to be quite stable over time therefore, mean perceived stress scores across the 60-month time period following cohort entry was reported. A maximum of eleven PSS-14 scores were collected for each cohort member. If an individual was missing any PSS-14 data points across the 60-month period, their mean score calculation was corrected by using the appropriate denominator (i.e., total number of PSS scales completed).

Covariates: IBD Disease Characteristics. Disease type was categorized as: (1) Crohn's disease (CD), or (2) ulcerative colitis/indeterminate colitis (UC) by research staff following physician chart review. Disease activity for the 60-month period following the CTES completion was measured using the Manitoba IBD Index (MIBDI) (Clara et al., 2009). The MIBDI, developed and validated as part of the Manitoba IBD Cohort Study, uses a single item to describe symptom persistence. Every six months, cohort members answered, "In the past six months my disease has been (1) constantly active, giving me symptoms every day; (2) often active, giving me symptoms most days; (3) sometimes active, giving me symptoms on some days (for instance 1-2 days/week); (4) occasionally active, giving me symptoms 1-2 days/month; (5) rarely active, giving me symptoms on a few days in the past six months; or (6) I was well in the

past 6 months, what I consider a remission or absence of symptoms." Active disease can be defined as experiencing symptoms constantly to occasionally (responses 1 to 4).

A maximum of eleven MIBDI scores were collected for each cohort member over the 60-month observation period. The percentage of active MIBDI scores determined which mutually exclusive category an individual was assigned to: less than 39% active scores indicated (1) minimally or inactive disease, 39% to 81% active scores indicated (2) moderately active disease, and greater than 81% active scores indicated (3) very active disease. If an individual was missing MIBDI scores over time, the correct denominator (total number of MIBDI scores completed) were used to calculate appropriate percentage estimates. Cohort members who completed less than three MIBDI scores were excluded from this analysis. Previous IBD-related surgeries (yes/no) and the duration of time between IBD diagnosis date and 12-month survey completion (measured in years) were also included.

Data Analysis

For the first objective, to estimate the prevalence of ACEs in individuals with IBD, we used frequencies and percentages to describe the number of individuals who were (1) exposed to one or more ACE and (2) never exposed to an ACE. Frequencies, percentages, and means (standard deviations) were used to describe the demographic and behavioral risk factors, comorbid conditions, perceived psychological stress, and IBD disease characteristics for persons who were exposed and never exposed to an ACE. Differences between the two groups were tested using χ^2 tests of independence for categorical variables and t-tests for continuous variables.

We estimated the prevalence (%) of individuals with an IBD diagnosis who experienced no ACEs, one ACE, two ACEs, and three or more ACEs. Using frequencies, percentages, and

means as appropriate, we compared the demographic and behavioral risk factors, comorbid conditions, perceived stress, and IBD disease characteristics for persons exposed to the different ACE count categories. Differences among the four groups were tested using χ^2 tests of independence for categorical variables and analysis of variance (ANOVA) for continuous variables.

For the second objective, to test the association of ACEs, including specific types of ACEs with IBD- and non-IBD-related healthcare use in individuals diagnosed with IBD, we counted the number of outcome events in annual increments for the 60-month period following CTES completion at the 12-month survey. The count measures included: non-IBD-related GP visits, IBD-related GP visits, non-IBD-related specialist visits, IBD-related specialist visits, non-IBD-related hospital days, non-IBD-related hospital days, IBD-related prescription drug dispensations, psychotropic prescription drug dispensations, antibiotic prescription drug dispensations, and other prescription drug dispensations. Furthermore, individuals were categorized as yes/no for IBD- and non-IBD-related hospital admissions over the 60-month period following the CTES completion (i.e., a binary variable was created).

The mean of the annual average estimates, standard errors, and the median of annual average estimates were calculated for discrete count outcome healthcare use measures (e.g., IBD-related GP visits) for: (a) cohort members exposed to at least one ACE and persons never exposed to an ACE, (b) cohort members belonging to different ACE count categories (no ACEs, one ACE, two ACEs, and three or more ACEs), (c) cohort members exposed to physical abuse and cohort members never exposed to physical abuse, (d) cohort members exposed to sexual abuse and cohort members never exposed to sexual abuse, (e) cohort members exposed to the death of a very close friend or family member and cohort members never exposed to the death of

a very close friend or family member, (f) cohort members exposed to a severe illness/injury and cohort members never exposed to a severe illness/injury, and (g) cohort members exposed to an upheaval between parents and cohort members never exposed to an upheaval between parents. Similarly, percentages were reported for binary healthcare use measures (e.g., IBD-related hospitalizations). Differences between groups (i.e., exposed/not exposed) were tested using χ^2 tests of independence for categorical variables, t-tests and ANOVA for continuous variables.

Generalized liner models (GLMs) with generalized estimating equations (GEEs) and negative binomial distributions were used to test for differences in the rate of outcome measures (e.g., IBD-related GP visits) for: (a) persons exposed to at least one ACE and persons never exposed to an ACE, (b) cohort members belonging to different ACE count categories (no ACEs, one ACE, two ACEs, and three or more ACEs), (c) cohort members exposed to physical abuse and cohort members never exposed to physical abuse, (d) cohort members exposed to sexual abuse and cohort members never exposed to sexual abuse, (e) cohort members exposed to the death of a very close friend or family member and cohort members never exposed to the death of a very close friend or family member, (f) cohort members exposed to a severe illness/injury and cohort members never exposed to a severe illness/injury, and (g) cohort members exposed to an upheaval between parents and cohort members never exposed to an upheaval between parents. The negative binomial distribution is a reasonable choice for modeling dispersed data (Gardner, Mulvey, & Shaw, 1995). For binary outcome measures (e.g., IBD-related hospital admission) we used GLMs with GEEs and a logit link function. GEEs were used to account for clustering of visits within individuals over time. An autoregressive correlation structure was assumed for the repeated measurements; it allows for correlations to be highest between measurements that are closest together in time and lowest for measurements that are further apart in time.

Crude rates of healthcare use measures were compared using unadjusted GLMs. The adjusted GLMs, which were used to test the factors associated with healthcare use, included the following covariates: sex, age group, income quintile, smoking status, alcohol use, BMI category, social functioning sub-score, CCI score category, PSS score, IBD disease type, proportion of positive MIBDI scores, previous-IBD related surgeries, and time (in years) between diagnosis and 12-month survey completion.

Relative rates (RRs) for discrete counts and odd ratios (ORs) for binary measures along with 95% confidence intervals (95% CIs) were estimated for all models. Model fit was assessed using the quasi-likelihood under the independence model criterion (QIC). When compared across models, lower QIC values indicated better fit.

For the third objective, to test the association between perceived level of trauma of ACEs and IBD- and non-IBD-related healthcare use in individuals diagnosed with IBD, we produced frequencies/percentages for individuals who reported (1) a perceived level of trauma greater than five compared to individuals who report (2) a perceived level of trauma less than or equal to five. Individuals were excluded from this analysis if they did not report an ACE in the 12-month CTES or did not report a perceived level of trauma for their recorded ACEs. A total of 253 respondents were retained for this analysis. Using frequencies/percentages and means as appropriate, covariate variables were compared for cohort members who reported a perceived level of trauma greater than five to those who reported a perceived level of trauma less than or equal to five. Differences between the two groups were tested using χ^2 tests of independence for categorical variables and t-tests for continuous variables.

The mean of the annual average estimates, standard errors, and the median of the annual average estimates were calculated for each of the healthcare use measures comparing persons

who report a perceived level of trauma greater than five and persons who report a perceived level of trauma less than or equal to five. GLMs with GEEs and a negative binomial distribution were used to test for differences in count outcome measures for the two groups. For binary outcome measures we used GLMs with GEEs and a logit function. GEEs were used to account for clustering of visits within individuals over time. An autoregressive correlation structure was assumed for the repeated measurements.

Crude rates of healthcare use measures were compared using unadjusted negative binomial regression. The adjusted models included all covariates described previously. RRs for discrete counts and ORs for binary measures along with 95% CIs were reported for all models. Model fit was assessed using the QIC. When compared across models, a lower QIC value indicates better fit.

IV. Results

Objective 1: Estimate Prevalence of ACEs in Individuals with IBD

A total of 345 individuals from the Manitoba IBD Cohort Study with an IBD diagnosis completed the 12-month CTES pertaining to ACEs and could be linked to our Manitoba administrative databases. Of this number, 74.2% reported experiencing at least one ACE. The characteristics of cohort members exposed to one or more ACE and cohort members never exposed to an ACE are described in Table 4.1.

Due to small cell sizes for higher score categories comorbidity as measured by the CCI could not be reported. However, no significant differences between cohort members exposed to an ACE and cohort members never exposed to an ACE were identified. This was also true for cohort members undergoing an IBD-related surgery in the year prior to CTES completion. Cohort members exposed to one or more ACEs had a mean PSS score close to three points greater than cohort members never exposed to an ACE. No other significant differences in the characteristics of cohort members exposed to one or more ACEs and cohort members never exposed to an ACE existed.

Table 4.1. Characteristics of Manitoba IBD Cohort Study respondents, stratified by ACE exposure, N = 345

	Exposed to ≥ 1 ACE	**Never exposed to ACE**
n (%)	256 (74.2)	89 (25.8)
Sex		
Male	95 (37.1)	43 (48.3)
Female	161 (62.9)	46 (51.7)
Age (years)		
18 – 44	153 (59.8)	50 (56.2)
45+	103 (40.2)	39 (43.8)
Income Quintile *		
One (lowest income)	63 (24.6)	16 (18.0)

Two	50 (19.5)	22 (24.7)
Three	50 (19.5)	17 (19.1)
Four	20 (7.8)	7 (7.9)
Five (highest income)	57 (22.5)	19 (21.3)
Smoking Status		
Never/Not daily	222 (86.7)	79 (88.8)
Daily	34 (13.3)	10 (11.2)
Alcohol Use		
Never/Less than once a week	151 (59.0)	45 (50.6)
1-3 times per week	63 (24.6)	25 (28.1)
>3 times per week	11 (4.3)	10 (11.2)
No response	31 (12.1)	9 (10.1)
Body Mass Index *		
Healthy weight	107 (41.8)	37 (41.6)
Underweight / Overweight / Obese	144 (56.3)	50 (56.2)
Social Functioning	47.3 (SD: 8.3)	48.7 (SD: 7.6)
Comorbidity	s	s
Perceived Psychological Stress	**21.8 (SD: 7.0)**	**19.1 (SD: 7.1)**
IBD Disease Type		
Crohn's Disease	128 (50.0)	39 (43.8)
Ulcerative /Indeterminate colitis	128 (50.0)	50 (56.2)
Disease Activity *		
Minimally active / inactive disease	80 (31.3)	34 (38.2)
Moderately active disease	75 (29.3)	25 (28.1)
Very active disease	100 (39.1)	30 (33.7)
Previous IBD-related Surgery		
Yes	11 (4.3)	3 (3.4)
No	245 (95.7)	86 (96.6)
Time between diagnosis and 12m survey completion (years)	5.3 (SD: 2.1)	5.7 (SD: 1.9)

* Some cohort members were missing data; therefore, column percentages do not sum to 100
s Indicates suppression due to small cell sizes

Bold values indicate a statistically significant difference between cohort members exposed to one or more ACE and cohort members never exposed to an ACE at α=0.05

Cohort members could report up to six types of ACEs: (1) physical abuse, (2) sexual abuse, (3) an upheaval between parents, (4) death of a very close friend or family member, (5) experience of a severe illness or injury, and (6) any other upheaval thought to significantly shape one's life or personality. In total, the Manitoba IBD Cohort experienced 501 ACEs. Cohort members experiencing no ACEs (25.8%), one type of ACE (33.6%), two types of ACEs (21.2%), and three or more types of ACEs (19.4%) were fairly evenly distributed. The characteristics of cohort members exposed to different numbers of ACEs are described in Table 4.2. More females than males were exposed to three or more types of ACEs (25.1% vs 10.9%). Cohort members exposed to three or more ACEs exhibited a mean SF score approximately five-points lower than persons experiencing no ACEs, one ACE, or two ACEs. Cohort members exposed to three or more ACEs also had higher PSS scores. While SF scores remained stable across members experiencing no ACEs, one ACE, and two ACEs, PSS scores increased across the categories. Additionally, cohort members exposed to three or more ACEs had a higher prevalence of individuals undergoing IBD-related surgeries in the 12-months prior to CTES completion than all other ACE count categories.

Table 4.2. Characteristics of Manitoba IBD Cohort Study respondents, stratified by number of types of ACEs, N=345

	0 ACEs	**1 ACE**	**2 ACEs**	**3+ ACEs**
n (%)	89 (25.8)	116 (33.6)	73 (21.2)	67 (19.4)
Sex				
Male	**43 (48.3)**	**47 (40.5)**	**33 (45.2)**	**15 (22.4)**
Female	**46 (51.7)**	**69 (59.5)**	**40 (54.8)**	**52 (77.6)**
Age (years)				
18 – 44	50 (56.2)	70 (60.3)	46 (63.0)	37 (55.2)

45+	39 (43.8)	46 (39.7)	27 (37.0)	30 (44.8)
Income Quintile *				
One (lowest income)	16 (18.0)	23 (19.8)	19 (26.0)	21 (31.3)
Two	22 (24.7)	21 (18.1)	11 (15.1)	18 (26.9)
Three	17 (19.1)	25 (21.6)	12 (16.4)	13 (19.4)
Four	7 (7.9)	12 (10.3)	6 (8.2)	s
Five (highest income)	19 (21.3)	26 (22.4)	20 (27.4)	s
Smoking Status				
Never/Not daily	79 (88.8)	103 (88.8)	61 (83.6)	58 (86.6)
Daily	10 (11.2)	13 (11.2)	12 (16.4)	9 (13.4)
Alcohol Use				
Never/Less than once a week	45 (50.6)	63 (54.3)	47 (64.4)	41 (61.2)
1-3 times per week	25 (28.1)	29 (25.0)	s	s
>3 times per week	10 (11.2)	8 (6.9)	s	s
No response	9 (10.1)	16 (13.8)	8 (11.0)	7 (10.4)
Body Mass Index *				
Healthy weight	37 (41.6)	48 (41.4)	34 (46.6)	25 (37.3)
Underweight / Overweight / Obese	50 (56.2)	65 (56.0)	37 (50.7)	42 (62.7)
Social Functioning *	**48.7 (SD: 7.6)**	**48.4 (SD: 7.6)**	**48.6 (SD: 7.0)**	**43.8 (SD: 9.8)**
Comorbidity				
0	s	103 (88.8)	s	58 (86.6)
1 or more	s	13 (11.2)	s	9 (13.4)
Perceived Psychological Stress	**19.1 (SD: 7.1)**	**20.7 (SD: 6.6)**	**21.4 (SD: 6.7)**	**23.9 (SD: 7.6)**
IBD Disease Type				
Crohn's Disease	39 (43.8)	55 (47.4)	40 (54.8)	33 (49.3)
Ulcerative / Indeterminate colitis	50 (56.2)	61 (52.6)	33 (45.2)	34 (50.7)
Disease Activity *				
Minimally / Inactive disease	34 (38.2)	42 (36.2)	22 (30.1)	16 (23.9)
Moderately active disease	25 (28.1)	30 (25.9)	27 (37.0)	18 (26.9)

Very active disease	30 (33.7%)	44 (37.9%)	23 (31.5%)	33 (49.2%)
Previous IBD-related Surgery				
Yes	**s**	**s**	**s**	**9 (13.4)**
No	**s**	**s**	**s**	**58 (86.6)**
Time between diagnosis and 12m survey completion (years)	5.7 (SD: 1.9)	5.5 (SD: 2.1)	5.2 (SD: 2.1)	5.1 (SD: 2.1)

* Some persons were missing data; therefore, column percentages do not sum to 100
s Indicates suppression due to small cell sizes
Bold values indicate a statistically significant difference between persons exposed to no ACEs, one ACE, two ACEs, and three or more ACEs at α=0.05

Objective 2: Test the association between ACEs, which included number and types of ACEs, and non-IBD- / IBD-related healthcare use amongst individuals with a confirmed IBD diagnosis

We determined if there were any significant differences in healthcare use measures between cohort members exposed to one or more ACEs compared to cohort members never exposed to an ACE. The mean annual estimates, standard deviations, and medians for each healthcare use measure for persons exposed to one or more ACE and persons never exposed to an ACE are presented in Table 4.3. Hospitalizations for the 60-month observation period following CTES completion were reported using frequencies and percentages.

The mean annual estimates for cohort members exposed to one or more ACE were slightly higher than for cohort members not exposed to at least one ACE for non-IBD-related GP visits, non-IBD-related SP visits, IBD-related SP visits, as well as, psychotropic, antibiotic, and other prescription medication dispensations. However, the differences were not statistically significant at $\alpha = 0.05$. Estimates were also not significantly different for cohort members exposed to one or more ACE and cohort members never exposed to an ACE for IBD-related GP visits, non-IBD and IBD-related hospital days, and IBD-related medication dispensations. The percentage of cohort members exposed to one or more ACE who were admitted to hospital for

non-IBD- (48.4%) and IBD-related (63.7%) reasons were very similar to the percentage of cohort members never exposed to an ACE who were admitted to hospital for non-IBD- (50.6%) and IBD-related (69.7%) reasons over the 60-month observation period following CTES completion.

Table 4.3. Annual healthcare use for Manitoba IBD Cohort Study respondents, stratified by ACE exposure, $N = 345$.

		Exposed to ≥ 1 ACE	**Never exposed to ACE**
n (%)		256 (74.2)	89 (25.8)
GP visits (non-IBD)		Mean: 5.5	Mean: 4.7
		SD: 5.3	SD: 3.9
		Median: 4.1	Median: 4.0
GP visits (IBD)		Mean: 1.7	Mean: 1.7
		SD: 3.3	SD: 3.2
		Median: 0.6	Median: 0.4
SP visits (non-IBD)		Mean: 5.5	Mean: 4.8
		SD: 9.2	SD: 5.6
		Median: 2.6	Median: 2.8
SP visits (IBD)		Mean: 3.6	Mean: 3.0
		SD: 6.8	SD: 3.9
		Median: 2.0	Median: 1.6
Hospitalized (non-IBD)	Yes	124 (48.4)	45 (50.6)
	No	132 (51.6)	44 (49.4)
Hospitalized (IBD)	Yes	163 (63.7)	62 (69.7)
	No	93 (36.3)	27 (30.3)
Hospital days (non-IBD)		Mean: 0.68	Mean 0.63
		SD: 1.8	SD: 1.7
		Median: 0.0	Median: 0.2
Hospital days (IBD)		Mean: 1.2	Mean: 1.2
		SD: 4.8	SD: 2.9
		Median: 0.2	Median: 0.2
IBD drug dispensations		Mean: 5.4	Mean: 5.4

	SD: 5.6	SD: 6.2
	Median: 4.2	Median: 3.6
Psychotropic drug dispensations	Mean: 2.5	Mean: 1.6
	SD: 5.8	SD: 3.9
	Median: 0.0	Median: 0.0
Antibiotic drug dispensations	Mean: 1.0	Mean: 0.82
	SD: 1.3	SD: 1.1
	Median: 0.6	Median: 0.6
Other drug dispensations	Mean: 11.0	Mean: 8.1
	SD: 17.1	SD: 10.3
	Median: 4.9	Median: 5.0

SD Indicates standard deviation

We determined if there were any significant differences in healthcare use measures between cohort members categorized by the number of different types of ACEs they were exposed to: no ACEs, one ACE, two ACEs, or 3 or more ACEs (ACE count). The mean annual estimates, standard deviations, and medians for each healthcare use measure for cohort members categorized by ACE count are presented in Table 4.4. Hospitalizations for the 60-month observation period following CTES completion were reported using frequencies and percentages.

In general, exposure to three or more types of ACEs was associated with a slight increase in non-IBD-related GP visits and non-IBD-related SP visits when compared to cohort members exposed to no ACEs, one type of ACE, or two types of ACEs. Cohort members exposed to one type of ACE or three or more types of ACEs also displayed slightly higher counts for psychotropic and other prescription drug dispensations when compared to cohort members exposed to no ACE or two types of ACEs. While these trends were observed, no statistically significant differences between ACE counts existed. Annual estimates for IBD-related GP visits

and IBD-related SP visits did not fluctuate between ACE count categories. This was also true for non-IBD and IBD-related hospital days. Moreover, the percentage of cohort members exposed to no ACE (50.6%), one (41.4%), two (53.4%), or three or more (55.2%) types of ACEs who were admitted to hospital for non-IBD-related reasons over the 60-month observation period was fairly consistent. Similarly, the percentage of cohort members exposed to no ACE (69.7%), one (68.1%), two (54.8%), or three or more (65.7%) types of ACEs who were admitted to hospital for IBD-related reasons also remained stable over the 60-month observation period.

Table 4.4. Annual healthcare use for Manitoba IBD Cohort Study respondents, stratified by number of types of ACEs (ACE Count), *N = 345*.

		0 ACEs	**1 ACE**	**2 ACEs**	**3+ ACEs**
n (%)		89 (25.8)	116 (33.6)	73 (21.2)	67 (19.4)
GP visits (non-IBD)		Mean: 4.7	Mean: 5.7	Mean: 4.3	Mean: 6.3
		SD: 3.9	SD: 5.1	SD: 3.3	SD: 6.8
		Median: 4.0	Median: 4.6	Median: 3.6	Median: 4.2
GP visits (IBD)		Mean: 1.7	Mean: 1.7	Mean: 1.9	Mean: 1.4
		SD: 3.2	SD: 3.8	SD: 3.4	SD: 2.2
		Median: 0.4	Median: 0.8	Median: 0.6	Median: 0.6
SP visits (non-IBD)		Mean: 4.8	Mean: 4.5	Mean: 5.7	Mean: 7.0
		SD: 5.6	SD: 8.5	SD: 8.1	SD: 11.2
		Median: 2.8	Median: 2.4	Median: 3.0	Median: 3.0
SP visits (IBD)		Mean: 3.0	Mean: 3.7	Mean: 3.8	Mean: 3.0
		SD: 3.9	SD: 6.6	SD: 9.1	SD: 3.7
		Median: 1.6	Median: 2.2	Median: 1.6	Median: 1.8
Hospitalized (non-IBD)	Yes	45 (50.6)	48 (41.4)	39 (53.4)	37 (55.2)
	No	44 (49.4)	68 (58.6)	34 (46.6)	30 (44.8)
Hospitalized (IBD)	Yes	62 (69.7)	79 (68.1)	40 (54.8)	44 (65.7)
	No	27 (30.3)	37 (31.9)	33 (45.2)	23 (34.3)
Hospital days (non-IBD)		Mean: 0.63	Mean: 0.52	Mean: 0.74	Mean: 0.91
		SD: 1.7	SD: 1.3	SD: 2.2	SD: 1.9
		Median: 0.2	Median: 0.0	Median: 0.2	Median: 0.2

Hospital days (IBD)	Mean: 1.2	Mean: 1.1	Mean: 1.8	Mean: 0.84
	SD: 2.9	SD: 2.8	SD: 8.2	SD: 2.0
	Median: 0.2	Median: 0.2	Median: 0.2	Median: 0.2
IBD drugs	Mean: 5.4	Mean: 5.9	Mean: 5.1	Mean: 5.0
	SD: 6.2	SD: 5.7	SD: 5.7	SD: 5.3
	Median: 3.6	Median: 4.5	Median: 3.4	Median: 3.3
Psychotropic drugs	Mean: 1.6	Mean: 2.7	Mean: 1.6	Mean: 3.0
	SD: 3.9	SD: 7.1	SD: 3.9	SD: 4.8
	Median: 0.0	Median: 0.0	Median: 0.0	Median: 0.2
Antibiotic drugs	Mean: 0.82	Mean: 0.95	Mean: 0.97	Mean: 1.0
	SD: 1.1	SD: 1.2	SD: 1.2	SD: 1.5
	Median: 0.6	Median: 0.6	Median: 0.6	Median: 0.6
Other drugs	Mean: 8.1	Mean: 11.5	Mean: 9.0	Mean: 12.1
	SD: 10.3	SD: 20.2	SD: 13.7	SD: 14.1
	Median: 5.0	Median: 4.4	Median: 3.8	Median: 7.4

SD indicates standard deviation

Of the 345 cohort respondents, 12.2% reported exposure to physical abuse and 13.0% reported exposure to sexual abuse. We determined if there were any significant differences in healthcare use measures between cohort members exposed to physical and sexual abuse compared to cohort members never exposed to physical and sexual abuse. The mean annual estimates, standard deviations, and medians for each healthcare use measure for cohort members exposed to physical and sexual abuse are reported in Table 4.5. Hospitalizations for the 60-month observation period following CTES completion were reported using frequencies and percentages.

On average, cohort members who were exposed to physical abuse and sexual abuse visit their GP for non-IBD-related reasons more times per year than cohort members never exposed to abuse. Additionally, cohort members who were exposed to physical abuse visit their specialist

for non-IBD-related reasons more often than cohort members who were not exposed to physical abuse. These relationships were statistically significant at $\alpha = 0.05$. Exposure to physical and sexual abuse did not result in significant increases in the mean annual estimates for other measures of healthcare use. While exposure to physical abuse resulted in slightly more non-IBD-related hospitalizations (57.1%) when compared to cohort members who were not exposed to physical abuse (47.7%), this trend was not statistically significant. Exposure to physical abuse did not influence the number of cohort members admitted to hospital for IBD-related reasons.

Table 4.5. Annual healthcare use for Manitoba IBD Cohort Study respondents, stratified by exposure to physical abuse and sexual abuse, $N = 345$.

		Physical Abuse		**Sexual Abuse**	
		Yes	**No**	**Yes**	**No**
n (%) *		42 (12.2)	300 (87.0)	45 (13.0)	300 (87.0)
GP visits (non-IBD)		**Mean: 7.3**	**Mean: 4.9**	**Mean: 6.7**	**Mean: 5.0**
		SD: 7.0	**SD: 4.5**	**SD: 7.3**	**SD: 4.5**
		Median: 4.9	**Median: 3.8**	**Median: 4.0**	**Median: 4.0**
GP visits (IBD)		Mean: 1.1	Mean: 1.8	Mean: 1.9	Mean: 1.7
		SD: 2.0	SD: 3.4	SD: 5.2	SD: 2.9
		Median: 0.4	Median: 0.6	Median: 0.4	Median: 0.6
SP visits (non-IBD)		**Mean: 7.7**	**Mean: 4.7**	Mean: 6.4	Mean: 5.1
		SD: 11.2	**SD: 7.3**	SD: 10.8	SD: 8.0
		Median: 4.1	**Median: 2.6**	Median: 2.8	Median: 2.7
SP visits (IBD)		Mean: 3.1	Mean: 3.5	Mean: 2.8	Mean: 3.5
		SD: 4.1	SD: 6.5	SD: 3.7	SD: 6.5
		Median: 1.7	Median: 1.9	Median: 1.4	Median: 2.0
Hospitalized (non-IBD)	Yes	24 (57.1)	143 (47.7)	22 (48.9)	147 (49.0)
	No	18 (42.9)	157 (52.3)	23 (51.1)	153 (51.0)
Hospitalized (IBD)	Yes	26 (61.9)	197 (65.7)	29 (64.4)	196 (65.3)
	No	16 (38.1)	103 (34.3)	16 (35.6)	104 (34.7)
Hospital days (non-IBD)		Mean: 1.0	Mean: 0.6	Mean: 0.6	Mean: 0.7
		SD: 2.2	SD: 1.7	SD: 1.0	SD: 1.8

	Median: 0.2	Median: 0.0	Median: 0.0	Median: 0.0
Hospital days (IBD)	Mean: 1.0	Mean: 1.2	Mean: 0.80	Mean: 1.3
	SD: 2.4	SD: 4.7	SD: 2.2	SD: 4.7
	Median: 0.1	Median: 0.2	Median:0.2	Median: 0.2
IBD drugs	Mean: 5.7	Mean: 5.4	Mean: 5.8	Mean: 5.4
	SD: 5.8	SD: 5.8	SD: 5.5	SD: 5.8
	Median: 4.6	Median: 4.0	Median: 4.6	Median: 3.6
Psychotropic drugs	Mean: 3.5	Mean: 2.1	Mean: 3.3	Mean: 2.1
	SD: 5.5	SD: 5.3	SD: 5.3	SD: 5.3
	Median: 0.3	Median: 0.0	Median: 0.4	Median: 0.0
Antibiotic drugs	Mean: 1.0	Mean: 0.9	Mean: 1.1	Mean: 0.9
	SD: 1.6	SD: 1.2	SD: 1.5	SD: 1.2
	Median: 0.4	Median: 0.6	Median: 0.6	Median: 0.6
Other drugs	Mean: 13.6	Mean: 9.7	Mean: 13.2	Mean: 9.8
	SD: 15.4	SD: 15.6	SD: 17.7	SD: 15.3
	Median: 7.6	Median: 4.5	Median: 5.2	Median: 4.9

* Some cohort members were missing data; therefore, row percentages do not sum to 100
SD indicates standard deviation
Bold values indicate a significant difference between persons exposed to physical abuse or sexual abuse at α=0.05

Of the Manitoba IBD Cohort, 51.3% reported exposure to the death of a very close friend or family member, 20.9% reported exposure to a severe illness or injury, and 20.3% reported exposure to parental upheaval. We determined if there were any significant differences in healthcare use measures between cohort members exposed to the death of a very close friend or family member, a severe illness or injury, and an upheaval between parents compared to cohort members never exposed to these traumatic experiences. The mean annual estimates, standard deviations, and medians for each healthcare use measure for cohort members exposed to the death of a very close friend or family member, a severe illness or injury, and an upheaval

between parents are reported in Table 4.6. Hospitalizations for the 60-month observation period following CTES completion were reported using frequencies and percentages.

Cohort members who were exposed to an upheaval between parents had an increased annual estimate for non-IBD-related SP visits compared to cohort members who did not experience an upheaval between parents. Additionally, cohort members who were exposed to an upheaval between parents were hospitalized significantly less (52.9%) for their IBD than cohort members who were not exposed to an upheaval between parents (68.1%). No other significant differences in summary values existed across healthcare use measures for those exposed to a death of a very close friend or family member, an experience of an extreme illness or injury, or an upheaval between parents.

Table 4.6. Annual healthcare use for Manitoba IBD Cohort Study respondents, stratified exposure to death of a close friend/family member, severe illness/injury, and upheaval between parents, $N = 345$.

	Death		**Illness/Injury**		**Parent Upheaval**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**
n (%) *	177 (51.3)	168 (48.7)	72 (20.9)	272 (78.8)	70 (20.3)	273 (79.1)
GP visits (non-IBD)	Mean: 5.4	Mean: 5.1	Mean: 4.8	Mean: 5.4	Mean: 5.6	Mean: 5.2
	SD: 5.2	SD: 4.6	SD: 4.4	SD: 5.1	SD: 6.4	SD: 4.5
	Med: 4.2	Med: 4.0	Med: 3.6	Med: 4.2	Med: 3.9	Med: 4.2
GP visits (IBD)	Mean: 1.7	Mean: 1.6	Mean: 1.5	Mean: 1.7	Mean: 1.5	Mean: 1.7
	SD: 2.9	SD: 3.6	SD: 2.6	SD: 3.4	SD: 2.6	SD: 3.4
	Med: 0.8	Med: 0.6	Med: 0.6	Med: 0.6	Med: 0.6	Med: 0.6
SP visits (non-IBD)	Mean: 5.3	Mean: 5.4	Mean: 5.0	Mean: 5.2	**Mean: 7.4**	**Mean: 4.7**
	SD: 7.4	SD: 9.4	SD: 6.0	SD: 8.4	**SD: 14.6**	**SD: 5.8**
	Med: 2.8	Med: 2.7	Med: 2.6	Med: 2.8	**Med: 2.4**	**Med: 2.8**
SP visits (IBD)	Mean: 3.8	Mean: 3.1	Mean: 4.1	Mean: 3.3	Mean: 2.8	Mean: 3.6
	SD: 8.0	SD: 3.5	SD: 9.3	SD: 5.1	SD: 3.2	SD: 6.8

		Med: 1.8	Med: 1.9	Med: 1.9	Med: 1.9	Med: 1.6	Med: 2.0
Hospitalized (non-IBD)	Yes	86 (48.6)	83 (49.4)	34 (47.2)	135 (49.6)	38 (54.3)	129 (47.3)
	No	91 (51.4)	85 (50.6)	38 (52.8)	137 (50.4)	32 (45.7)	144 (52.7)
Hospitalized (IBD)	Yes	113 (63.8)	112 (66.7)	44 (61.1)	181 (66.5)	**37 (52.9)**	**186 (68.1)**
	No	64 (36.2)	56 (33.3)	28 (38.9)	91 (33.5)	**33 (47.1)**	**87 (31.9)**
Hospital days (non-IBD)		Mean: 0.7	Mean: 0.6	Mean: 0.9	Mean: 0.6	Mean: 0.7	Mean: 0.7
		SD: 1.9	SD: 1.5	SD: 2.7	SD: 1.4	SD: 1.4	SD: 1.8
		Med: 0.0	Med: 0.0	Med: 0.0	Med: 0.0	Med: 0.2	Med: 0.0
Hospital days (IBD)		Mean: 1.4	Mean: 1.0	Mean: 1.7	Mean: 1.1	Mean: 0.8	Mean: 1.3
		SD: 5.7	SD: 2.5	SD: 8.2	SD: 2.7	SD: 2.1	SD: 4.8
		Med: 0.2	Med: 0.2	Med: 0.2	Med: 0.2	Med: 0.0	Med: 0.2
IBD drugs		Mean: 5.2	Mean: 5.6	Mean: 5.8	Mean: 5.3	Mean: 5.1	Mean: 5.5
		SD: 5.5	SD: 6.0	SD: 5.5	SD: 5.8	SD: 6.4	SD: 5.6
		Med: 3.4	Med: 4.2	Med: 4.8	Med: 3.6	Med: 3.3	Med: 4.2
Psychotropic drugs		Mean: 2.4	Mean: 2.1	Mean: 3.0	Mean: 2.0	Mean: 2.1	Mean: 2.3
		SD: 5.5	SD: 5.2	SD: 6.2	SD: 5.1	SD: 5.0	SD: 5.5
		Med: 0.0	Med: 0.0	Med: 0.0	Med: 0.0	Med: 0.0	Med: 0.0
Antibiotic drugs		Mean: 1.0	Mean: 0.9	Mean: 0.8	Mean: 1.0	Mean: 1.0	Mean: 0.9
		SD: 1.2	SD: 1.3	SD: 1.1	SD: 1.3	SD: 1.6	SD: 1.1
		Med: 0.6	Med: 0.5	Med: 0.5	Med: 0.6	Med: 0.5	Med: 0.6
Other drugs		Mean: 11.2	Mean: 9.2	Mean: 10.0	Mean: 10.3	Mean: 9.6	Mean: 10.3
		SD: 18.3	SD: 12.6	SD: 12.1	SD: 16.5	SD: 12.9	SD: 16.3
		Med: 4.8	Med: 5.2	Med: 5.6	Med: 4.9	Med: 4.6	Med: 5.0

* Some cohort members were missing data; therefore, row percentages do not sum to 100
SD indicates standard deviation, Med indicates median
Bold values indicate a significant difference between persons exposed to the death of a very close friend or family member, a severe illness or injury, or an upheaval between parents at α=0.05

Furthermore, to test if exposure to one or more ACE influenced the rates/odds of healthcare use measures GLMs were analyzed. Table 4.7 summarizes the results of the

multivariable regression models for cohort members exposed to one or more ACE relative to those never exposed to an ACE. Both unadjusted rates and rates adjusted for confounding covariates are reported. The QIC values for adjusted models were significantly lower than those for unadjusted models, indicating inclusion of the covariates improved model fit.

Overall, the results in Table 4.7 show that exposure to one or more ACE was not associated with increased rates for any healthcare use measures in the Manitoba IBD Cohort Study respondents. While exposure to an ACE was not a significant predictor variable, certain confounding covariates were predictive of healthcare use.

Table 4.7. Unadjusted and adjusted rate ratio and odds ratio estimates (95% CIs) of healthcare use for Manitoba IBD Cohort Study respondents exposed to ≥ 1 ACE.

	Unadjusted Estimate (95% CI)	**Adjusted Estimate** (95% CI)
GP visits (non-IBD)	1.17 (0.95-1.44)	1.11 (0.91-1.35)
GP visits (IBD)	1.03 (0.65-1.63)	0.90 (0.61- 1.33)
SP visits (non-IBD)	1.06 (0.79-1.44)	1.01 (0.73-1.40)
SP visits (IBD)	1.21 (0.85-1.72)	1.00 (0.73-1.40)
Hospitalization (non-IBD)	1.11* (0.78-1.60)	1.24* (0.80-1.91)
Hospitalization (IBD)	1.14* (0.84-1.55)	1.16* (0.82-1.65)
Hospital days (non-IBD)	0.88 (0.44-1.74)	0.94 (0.56-1.57)
Hospital days (IBD)	1.11 (0.55-2.23)	1.05 (0.57-1.91)
IBD drugs	1.02 (0.78-1.33)	1.05 (0.77-1.42)

Psychotropic drugs	1.51 (0.85-2.68)	1.54 (0.84-2.82)
Antibiotic drugs	1.21 (0.88-1.66)	1.02 (0.72-1.44)
Other drugs	1.33 (0.96-1.85)	1.18 (0.88-1.58)

* Indicate Odds Ratio

The following summary describes the significant associations between confounding covariates and non-IBD and IBD-related GP and SP visits observed across the negative binomial regression models for cohort members exposed to one or more ACE (Table 4.8). Females displayed a 26% increased rate of non-IBD-related GP visits relative to men. Older age (>44 years) was associated with a 51% increase in the rate of non-IBD-related GP visits and a 91% increase in the rate of non-IBD-related SP visits compared to younger cohort members (18-44 years). In contrast, older age predicted a significant decrease in the rates of IBD-related GP and SP visits relative to younger age. A one-point increase in SF scores was associated with a 2% decrease in the rate of non-IBD-related GP visits, 5% decrease in the rate of IBD-related GP visits, 3% decrease in the rate of non-IBD-related SP visits, and 4% decrease in the rate of IBD-related SP visits. A CCI score of two or more was associated with a significant increase in the rate of non-IBD-related SP visits relative to a CCI score of zero. A one-point increase in PSS scores was associated with 4 % decrease in the rate of IBD-related GP visits and a 3% decrease in the rate of IBD-related SP visits. Moderate and severe disease activity compared to minimal disease activity predicted significantly increased rates of IBD-related GP and SP visits. Additionally, severe disease activity compared to minimal disease activity predicted a 37% increase in the rate of non-IBD-related GP visits. Finally, a one-year increase between IBD diagnosis and CTES completion predicted an 11% decrease in the rate of IBD-related GP visits.

Table 4.8. Rate ratio estimates (95% CIs) of GP and SP visits for Manitoba IBD Cohort Study respondents modelled for exposure to ≥ 1 ACE, adjusted for model covariates.

Confounding Covariate	**GP visits (non-IBD)**	**GP visits (IBD)**	**SP Visits (non-IBD)**	**SP Visits (IBD)**
Sex				
Male	REF	REF	REF	REF
Female	**1.26 (1.01-1.57)**	0.80 (0.56-1.14)	1.15 (0.85-1.57)	0.76 (0.57-1.01)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.51 (1.27-1.81)**	**0.53 (0.37-0.75)**	**1.91 (1.46-2.51)**	**0.66 (0.49-0.89)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	1.01 (0.77-1.32)	0.80 (0.50-1.27)	0.92 (0.65-1.32)	0.87 (0.57-1.33)
Three	1.08 (0.79=1.50)	1.29 (0.70-2.38)	0.81 (0.57-1.14)	0.85 (0.56-1.29)
Four	1.10 (0.69-1.78)	1.62 (0.83-3.17)	1.25 (0.68-2.31)	0.74 (0.43-1.29)
Five (highest income)	0.82 (0.62-1.08)	0.63 (0.39-1.01)	1.02 (0.67-1.56)	0.77 (0.48-1.22)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	1.02 (0.78-1.33)	0.92 (0.58-1.46)	0.75 (0.52-1.08)	0.96 (0.60-1.52)
Alcohol Use				
Never/Less than once a week	REF	REF	REF	REF
1-3 times per week	0.85 (0.69-1.04)	0.82 (0.55-1.22)	1.01 (0.72-1.41)	0.80 (0.59-1.08)
>3 times per week	1.07 (0.72-1.60)	1.28 (0.60-2.75)	0.76 (0.50-1.16)	0.73 (0.44-1.19)
No response	1.07	1.48	1.19	1.35

	(0.81-1.40)	(0.84-2.58)	(0.75-1.89)	(0.79-2.31)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.12 (0.92-1.37)	1.01 (0.70-1.47)	1.10 (0.85-1.43)	0.91 (0.68-1.21)
Social Functioning	**0.98 (0.97-0.99)**	**0.95 (0.93-0.98)**	**0.97 (0.95-0.99)**	**0.96 (0.93-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	0.96 (0.64-1.44)	0.57 (0.28-1.17)	1.51 (0.95-2.40)	1.13 (0.56-2.26)
2 or more	1.02 (0.63-1.65)	0.91 (0.23-3.56)	**3.55 (1.61-7.85)**	0.94 (0.49-1.80)
Perceived Psychological Stress	0.99 (0.98-1.01)	**0.96 (0.93-0.99)**	0.98 (0.96-1.00)	**0.97 (0.95-0.99)**
IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.04 (0.86-1.25)	1.20 (0.86-1.69)	1.09 (0.80-1.47)	1.00 (0.85-1.45)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.19 (0.94-1.49)	**1.97 (1.19-3.26)**	1.06 (0.71-1.57)	**2.01 (1.36-2.98)**
Very active disease	**1.36 (1.06-1.75)**	**1.99 (1.30-3.05)**	0.99 (0.68-1.43)	**2.24 (1.56-3.22)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.15 (0.81-1.63)	1.39 (0.84-2.30)	1.50 (0.96-2.34)	1.53 (0.84-2.80)
Time between diagnosis and 12m survey completion (years)	0.99 (0.94-1.03)	**0.89 (0.83-0.95)**	0.96 (0.90-1.03)	0.95 (0.87-1.04)

REF indicates reference category

Bold values indicate a statistically significant effect at α=0.05

The following summary describes the significant associations between confounding covariates and non-IBD and IBD-related hospitalizations and hospital days observed across the negative binomial and logistic regression models for cohort members exposed to one or more ACE (Table 4.9). Older age (>44 years) predicted a 53% decreased rate of IBD-related hospital days relative to younger age (18-44 years). Income quintiles four and two were associated with significantly increased odds for non-IBD-related hospitalization relative to the lowest income quintile. In contrast, income quintile five was associated with a 57% decreased rate for non-IBD-related hospital days when compared to the lowest income quintile. If cohort members chose to not respond to the alcohol use questionnaire, they exhibited an 89% increase in odds of non-IBD-related hospitalization relative to those who drank less than one time per week. A BMI measured as underweight, overweight, or obese relative to cohort members measured at a healthy weight predicted an 80% increase in the rate of non-IBD-related hospital days. A one-point increase in SF scores was associated with a 4% decreased odds of non-IBD-related hospitalization and an 8% decrease in the rates of both non-IBD and IBD-related hospital days. A CCI score of two or more was associated with a significant increase in the odds for non-IBD-related hospitalization and rates of non-IBD-related and IBD-related hospital days relative to a CCI score of zero. A one-point increase in PSS scores was associated with a 3% decreased odds of IBD-related hospitalization, 5% decreased rate of non-IBD-related hospital days, and a 7% decreased rate of IBD-related hospital days. Moderate and severe disease activity compared to minimal disease activity, predicted significantly increased odds of IBD-related hospitalization and increased rate of IBD-related hospital days. Finally, cohort members who had IBD-related surgery in the 12 months prior to CTES completion displayed increased odds of non-IBD-related hospitalization

and increased rate of non-IBD-related hospital days relative to cohort members who had no surgery.

Table 4.9. Rate ratio and odds ratio estimates (95% CIs) of hospitalizations and hospital days for Manitoba IBD Cohort Study respondents modelled for exposure to ≥ 1 ACE, adjusted for model covariates.

Confounding Covariate	Hospitalized (non-IBD)*	Hospitalized (IBD)*	Hospital days (non-IBD)	Hospital days (IBD)
Sex				
Male	REF	REF	REF	REF
Female	1.03 (0.71-1.48)	0.85 (0.62-1.18)	1.35 (0.82-2.21)	0.89 (0.53-1.50)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.19 (0.83-1.71)	0.93 (0.65-1.31)	1.01 (0.60-1.69)	**0.47 (0.26-0.84)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	**2.05 (1.22-3.42)**	1.21 (0.76-1.91)	1.21 (0.57-2.56)	0.56 (0.26-1.20)
Three	1.15 (0.66-1.98)	0.99 (0.61-1.60)	0.86 (0.39-1.89)	0.50 (0.25-1.00)
Four	**2.24 (1.11-4.49)**	1.06 (0.63-1.80)	1.51 (0.59-3.90)	0.67 (0.25-1.80)
Five (highest income)	0.87 (0.50-1.51)	1.11 (0.67-1.81)	**0.43 (0.18-0.99)**	0.47 (0.21-1.06)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.69 (0.38-1.26)	0.60 (0.34-1.05)	0.55 (0.23-1.33)	0.88 (0.35-2.22)
Alcohol Use				
Never/Less than once a week	REF	REF	REF	REF

1-3 times per week	0.89 (0.57-1.40)	0.93 (0.65-1.33)	0.70 (0.38-1.29)	0.74 (0.42-1.32)
>3 times per week	1.36 (0.64-2.90)	0.91 (0.37-2.24)	0.87 (0.40-1.90)	0.71 (0.30-1.66)
No response	**1.89 (1.08-3.31)**	1.03 (0.59-1.77)	1.78 (0.80-3.95)	1.13 (0.42-3.04)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.34 (0.94-1.91)	1.01 (0.73-1.38)	**1.80 (1.08-3.01)**	1.01 (0.57-1.81)
Social Functioning	**0.96 (0.94-0.99)**	0.97 (0.94-1.00)	**0.92 (0.87-0.97)**	**0.92 (0.86-0.97)**
Comorbidity				
0	REF	REF	REF	REF
1	0.68 (0.26-1.82)	1.03 (0.48-2.19)	1.58 (0.47-5.29)	1.15 (0.26-5.01)
2 or more	**7.50 (2.88-19.50)**	1.38 (0.78-2.46)	**9.82 (3.91-24.62)**	**2.95 (1.18-7.33)**
Perceived Psychological Stress	0.98 (0.95-1.01)	**0.97 (0.94-0.99)**	**0.95 (0.92-0.98)**	**0.93 (0.89-0.97)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.07 (0.76-1.50)	1.12 (083-1.53)	1.23 (0.76-2.01)	1.11 (0.68-1.82)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.87 (0.55-1.38)	**1.81 (1.18-2.79)**	0.94 (0.44-1.99)	**2.78 (1.34-5.77)**
Very active disease	**0.53 (0.33-0.86)**	**1.75 (1.14-2.69)**	**0.42 (0.25-0.73)**	**2.04 (1.06-3.92)**

Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**3.14 (1.66-5.94)**	1.51 (0.78-2.93)	**3.09 (1.49-6.40)**	1.73 (0.54-5.50)
Time between diagnosis and 12m survey completion (years)	1.03 (0.95-1.12)	0.99 (0.91-1.07)	0.89 (0.73-1.07)	0.92 (0.76-1.10)

* indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

The following summary describes the significant associations between confounding covariates and drug dispensations categorized as, IBD, psychotropic, antibiotic, and other drug dispensations, observed across the negative binomial regression models for cohort members exposed to one or more ACE (Table 4.10). Females displayed a 44% decreased rate of IBD drug dispensations when compared to men. Older age (>44 years) was a significant predictor of a decreased rate of antibiotic drug dispensations and an increased rate of other prescription drug dispensations relative to younger age. Income quintile three was associated with a significantly increased rate of psychotropic prescription drug dispensations relative to the lowest income quintile. If cohort members chose to not respond to the alcohol use questionnaire, they exhibited an increased rate of antibiotic drug dispensations relative to cohort members reporting alcohol use at less than one time per week. A one-point increase in SF scores was associated with a 6% decrease in the rate of psychotropic drug dispensations and a 3% decrease in the rate of other drug dispensations. A CCI score of one or more relative to a score of zero predicted significantly increased rates of antibiotic drug dispensations. A one-point increase in PSS scores was associated with a 2% decrease in the rate of other drug dispensations. Finally, very active disease

relative to minimally active or inactive disease associated with a 45% increased rate of IBD drug dispensations and a 55% increased rate of other drug dispensations.

Table 4.10. Rate ratio estimates (95% CIs) of IBD, psychotropic, antibiotic, and other prescription drug dispensations for Manitoba IBD Cohort Study respondents modelled for exposure to ≥ 1 ACE, adjusted for model covariates.

Confounding Covariate	IBD drugs	Psychotropic drugs	Antibiotic drugs	Other drugs
Sex				
Male	REF	REF	REF	REF
Female	**0.66 (0.50-0.86)**	1.63 (0.99-2.69)	1.33 (0.98-1.81)	1.22 (0.93-1.59)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.84 (0.65-1.09)	1.21 (0.69-2.09)	**0.75 (0.57-0.99)**	**2.39 (1.88-3.05)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.87 (0.61-1.26)	1.56 (0.72-3.40)	1.18 (0.80-1.76)	1.05 (0.72-1.51)
Three	1.00 (0.66-1.51)	**2.66 (1.26-5.60)**	1.32 (0.92-1.88)	1.05 (0.70-1.59)
Four	1.01 (0.65-1.56)	1.25 (0.40-3.89)	1.35 (0.78-2.33)	1.06 (0.68-1.64)
Five (highest income)	0.99 (0.70-1.40)	1.66 (0.70-4.01)	0.96 (0.62-1.50)	0.82 (0.54-1.23)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.92 (0.64-1.31)	1.39 (0.64-2.99)	1.22 (0.81-1.82)	0.80 (0.48-1.31)
Alcohol Use				
Never/Less than once a week	REF	REF	REF	REF

1-3 times per week	0.98 (0.74-1.31)	0.76 (0.37-1.54)	0.81 (0.57-1.14)	0.77 (0.58-1.01)
>3 times per week	0.87 (0.46-1.64)	0.65 (0.17-2.54)	0.90 (0.50-1.63)	0.99 (0.49-2.01)
No response	1.20 (0.82-1.76)	1.25 (0.64-2.43)	**2.16 (1.41-3.33)**	1.48 (0.95-2.30)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.00 (0.79-1.27)	1.55 (0.96-2.50)	0.94 (0.71-1.25)	1.24 (0.96-1.61)
Social Functioning	0.99 (0.97-1.01)	**0.94 (0.90-0.98)**	0.98 (0.97-1.00)	**0.97 (0.95-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.26 (0.74-2.16)	1.96 (0.91-4.24)	**1.94 (1.12-3.33)**	1.50 (0.65-3.49)
2 or more	0.81 (0.47-1.40)	1.97 (0.43-8.95)	**3.26 (1.18-9.03)**	1.26 (0.52-3.06)
Perceived Psychological Stress	0.99 (0.96-1.01)	1.03 (0.97-1.08)	0.99 (0.97-1.01)	**0.98 (0.96-0.99)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	0.92 (0.73-1.17)	0.84 (0.49-1.43)	1.15 (0.90-1.47)	1.06 (0.82-1.38)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.39 (0.99-1.95)	0.77 (0.39-1.51)	**1.47 (1.01-2.14)**	1.06 (0.78-1.44)
Very active disease	**1.45 (1.04-2.02)**	1.13 (0.54-2.38)	**1.91 (1.33-2.75)**	**1.55 (1.10-2.17)**

Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.79 (0.44-1.44)	0.81 (0.38-1.73)	1.49 (0.82-2.69)	1.36 (0.83-2.23)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.03)	0.95 (0.84-1.08)	0.98 (0.91-1.06)	0.98 (0.91-1.06)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

To test if exposure to different ACE counts influenced the rates/odds of healthcare use measures GLMs were analyzed. Table 4.11 summarizes the results of the multivariable regression models for healthcare use measures for IBD Cohort Study members categorized into groups based on the number of different types of ACEs. Cohort members experiencing one type of ACE, two types of ACEs, and three or more types of ACEs were compared to cohort members who never experienced an ACE. Models that did and did not adjust for confounding covariates were fit to the data; adjustment for confounding covariates resulted in much lower QIC values, indicating better model fit. The unadjusted and adjusted rates/odds are displayed in the table. These results show no statistically significant differences in healthcare use for persons with different counts of ACE types relative to those never exposed to any type of ACE. While exposure to different ACE counts was not a significant predictor variable, certain confounding covariates were predictive of healthcare use (Appendix D).

Table 4.11. Unadjusted and adjusted rate ratios and odds ratio estimates (95% CIs) of healthcare use for Manitoba IBD Cohort Study participants exposed to different types of ACEs (ACE Count).

	1 ACE (95% CI)		**2 ACEs** (95% CI)		**3+ ACEs** (95% CI)	
	UA	**A**	**UA**	**A**	**UA**	**A**
GP visits	1.25	1.22	0.93	0.96	1.29	1.08

(non-IBD)	(0.98-1.58)	(0.98-1.52)	(0.73-1.20)	(0.75-1.22)	(0.94-1.76)	(0.75-1.54)
GP visits (IBD)	1.03 (0.59-1.82)	0.95 (0.60-1.50)	1.18 (0.67-2.06)	1.01 (0.61-1.68)	0.86 (0.50-1.47)	0.68 (0.41-1.10)
SP visits (non-IBD)	0.95 (0.63-1.44)	0.83 (0.61-1.14)	1.17 (0.79-1.73)	1.23 (0.84-1.79)	1.15 (0.79-1.66)	1.08 (0.56-2.10)
SP visits (IBD)	1.28 (0.85-1.93)	1.12 (0.78-1.59)	1.31 (0.72-2.39)	1.03 (0.65-1.62)	0.98 (0.66-1.45)	0.71 (0.45-1.11)
Hospitalized (non-IBD)	1.11* (0.71-1.74)	1.20* (0.74-1.95)	1.23* (0.72-1.76)	1.41* (0.86-2.32)	1.12* (0.69-1.84)	1.12* (0.60-2.09)
Hospitalized (IBD)	1.21* (0.86-1.72)	1.29* (0.88-1.91)	1.11* (0.72-1.70)	1.20* (0.74-1.94)	1.06* (0.69-1.62)	0.91* (0.53-1.54)
Hospital days (non-IBD)	0.72 (0.34-1.49)	0.86 (0.48-1.56)	1.11 (0.42-2.93)	1.40 (0.64-3.06)	0.89 (0.42-1.91)	0.65 (0.25-1.66)
Hospital days (IBD)	1.02 (0.52-2.01)	1.20 (0.60-2.38)	1.64 (0.52-5.24)	1.32 (0.56-3.09)	0.67 (0.33-1.35)	0.54 (0.23-1.23)
IBD drugs	1.12 (0.83-1.50)	1.12 (0.82-1.54)	0.94 (0.66-1.33)	1.00 (0.66-1.49)	0.93 (0.66-1.33)	0.96 (0.64-1.46)
Psychotropic drugs	1.66 (0.83-3.32)	1.82 (0.95-3.47)	1.00 (0.47-2.10)	1.29 (0.58-2.86)	1.79 (0.95-3.37)	1.36 (0.56-3.31)
Antibiotic drugs	1.18 (0.83-1.69)	1.11 (0.76-1.63)	1.20 (0.80-1.78)	1.11 (0.74-1.66)	1.27 (0.81-1.98)	0.76 (0.48-1.21)
Other drugs	1.43 (0.95-2.16)	1.20 (0.87-1.64)	1.10 (0.71-1.71)	1.25 (0.82-1.90)	1.42 (0.96-2.09)	1.08 (0.72-1.63)

* Indicate Odds Ratio; UA indicates unadjusted, A indicates adjusted

To test if exposure to physical abuse and sexual abuse influenced the rates/odds of healthcare use measures GLMs were analyzed. Table 4.12 summarizes the results of the negative binomial regressions modelling discrete healthcare use measures and the logit regressions modelling binary healthcare use measures for cohort members exposed to physical abuse and sexual abuse relative to those never exposed to abuse. While both adjusted and unadjusted rates

were analyzed, adjusted rates for confounding covariates had a much lower QIC values indicating better model fit. Unadjusted and adjusted rates for confounding covariates are displayed in the table. These results show that after adjustment for confounding covariates, exposure to sexual abuse and physical abuse did not predict increased rates of healthcare use. Although not statistically significant, cohort members exposed to sexual abuse displayed a 55% decreased rate for days spent as an inpatient in hospital for IBD-related reasons compared to cohort members never exposed to sexual abuse. While exposures to physical and sexual abuse were not significant predictor variables, certain confounding covariates were predictive of healthcare use (Appendix E).

Table 4.12: Unadjusted and adjusted rate ratio and odds ratio estimates (95% CIs) of healthcare use for Manitoba IBD Cohort Study participants exposed to physical abuse and sexual abuse.

	Exposed to Physical Abuse (95% CI)		**Exposed to Sexual Abuse (95% CI)**	
	UA	**A**	**UA**	**A**
GP visits (non-IBD)	**1.37 (1.01-1.86)**	1.20 (0.84-1.72)	1.26 (0.91-1.75)	1.06 (0.77-1.44)
GP visits (IBD)	0.62 (0.34-1.13)	0.64 (0.38-1.08)	1.14 (0.50-2.61)	0.81 (0.41-1.63)
SP visits (non-IBD)	1.36 (0.93-1.99)	1.36 (0.70-2.66)	1.07 (0.73-1.58)	0.82 (0.60-1.13)
SP visits (IBD)	0.86 (0.55-1.36)	0.86 (0.57-1.32)	0.75 (0.48-1.17)	0.66 (0.44-1.01)
Hospitalized (non-IBD)	0.88* (0.45-1.73)	0.76* (0.44-1.29)	0.90* (0.53-1.51)	0.89* (0.53-1.50)
Hospitalized (IBD)	0.70* (0.33-1.50)	0.74* (0.43-1.27)	0.95* (0.60-1.50)	0.77* (0.45-1.31)
Hospital days (non-IBD)	1.05 (0.76-1.47)	0.68 (0.33-1.39)	0.78 (0.40-1.53)	0.60 (0.27-1.32)
Hospital days	1.58	0.82	0.50	0.45

(IBD)	(0.89-2.82)	(0.39-2.75)	(0.22-1.11)	(0.19-1.03)
IBD drugs	1.08 (0.65-1.80)	1.13 (0.80-1.60)	1.06 (0.79-1.42)	1.15 (0.83-1.59)
Psychotropic drugs	1.30 (0.87-1.94)	1.40 (0.65-3.01)	1.55 (0.89-2.72)	1.33 (0.60-2.96)
Antibiotic drugs	0.88 (0.45-1.73)	0.74 (0.47-1.18)	1.13 (0.72-1.77)	0.89 (0.62-1.29)
Other drugs	0.70 (0.33-1.50)	1.17 (0.78-1.77)	1.30 (0.84-2.01)	0.93 (0.62-1.38)

* Indicate Odds Ratio, UA indicates unadjusted, A indicates adjusted

To test if exposure to the death of a very close friend or family member, a severe illness or injury, and an upheaval between parents influenced the rates/odds of healthcare use measures GLMs were analyzed. Table 4.13 summarizes the results of the negative binomial regressions modelling discrete healthcare use measures and the logit regressions modelling binary healthcare use measures for cohort members exposed to the death of a very close friend or family member, a severe illness or injury, and an upheaval between parents, relative to those who were never exposed to these ACEs. While both adjusted and unadjusted rates were analyzed, adjusted rates for confounding covariates had a much lower QIC values indicating better model fit. The unadjusted and adjusted rates are displayed in the table. These results show that cohort members exposed to an upheaval between parents visited their specialists for IBD-related reasons at a 38% decreased rate than members who were not exposed to an upheaval between parents. Additionally, exposure to an upheaval between parents resulted in 37 percent decreased odds of hospital admission and a 40 percent decreased rate in hospital days for IBD-related reasons relative to cohort members never exposed to an upheaval between parents. There were no other statistically significant differences between relative rates of healthcare use measures for persons

exposed death, illness, or parental upheavals. Although not statistically significant, trending towards significance included, cohort members exposed to the death of a very close friend or family member displayed 40 percent higher odds of hospital admission for non-IBD-related reasons. Moreover, cohort members experiencing a severe illness or injury had a 70 percent increased rate of psychotropic medications relative to cohort members who did not experience a severe illness or injury. Certain confounding covariates were predictive of increased and decreased healthcare use when modelled with exposure to the death of a very close friend or family member, severe illness or injury, and parent upheavals (Appendix F).

Table 4.13. Unadjusted and adjusted rate ratio and odds ratio estimates (95% CI) of healthcare use for Manitoba IBD Cohort Study participants exposed to death of a close friend/family member, severe illness/injury, and upheaval between parents.

	Exposed to death of family/friend (95% CI)		**Exposed to illness/injury** (95% CI)		**Exposed to parent upheaval** (95% CI)	
	UA	**A**	**UA**	**A**	**UA**	**A**
GP visits (non-IBD)	1.09 (0.90-1.33)	1.02 (0.84-1.23)	0.91 (0.72-1.15)	0.88 (0.70-1.11)	1.00 (0.75-1.34)	0.94 (0.70-1.26)
GP visits (IBD)	1.09 (0.72-1.66)	1.10 (0.76-1.59)	0.87 (0.54-1.39)	0.84 (0.57-1.22)	0.88 (0.55-1.40)	0.78 (0.51-1.19)
SP visits (non-IBD)	0.99 (0.73-1.34)	1.02 (0.79-1.32)	1.02 (0.73-1.42)	0.99 (0.73-1.34)	1.21 (0.75-1.95)	1.16 (0.70-1.92)
SP visits (IBD)	1.29 (0.90-1.83)	1.09 (0.83-1.43)	1.27 (0.73-2.21)	1.09 (0.76-1.55)	0.77 (0.54-1.09)	**0.62 (0.45-0.86)**
Hospitalization (non-IBD)	1.22* (0.861.72)	1.38* (0.96-1.97)	0.91* (0.59-1.40)	1.01* (0.66-1.54)	0.98* (0.63-1.57)	0.99* (0.64-1.53)
Hospitalization (IBD)	1.13* (0.84-1.50)	1.13* (0.83-1.55)	1.20* (0.82-1.76)	1.17* (0.77-1.76)	0.69* (0.46-1.05)	**0.63* (0.41-0.97)**
Hospital days (non-IBD)	1.10 (0.61-1.99)	1.28 (0.79-2.06)	1.27 (0.53-3.00)	1.23 (0.65-2.32)	0.82 (0.44-1.51)	0.65 (0.35-1.22)
Hospital days	1.51	1.36	1.63	1.28	0.57	**0.40**

(IBD)	(0.75-3.02)	(0.78-2.36)	(0.52-5.14)	(0.68-2.39)	(0.28-1.16)	**(0.21-0.77)**
IBD drugs	0.94 (0.75-1.17)	0.89 (0.69-1.13)	1.09 (0.85-1.41)	1.13 (0.86-1.49)	0.92 (0.67-1.25)	0.94 (0.66-1.34)
Psychotropic drugs	1.15 (0.69-1.92)	0.93 (0.56-1.54)	1.53 (0.87-2.67)	1.70 (0.93-3.11)	0.88 (0.47-1.67)	0.69 (0.32-1.49)
Antibiotic drugs	1.17 (0.88-1.55)	1.08 (0.82-1.43)	0.87 (0.61-1.22)	0.78 (0.58-1.03)	1.10 (0.74-1.65)	0.91 (0.66-1.26)
Other drugs	1.23 (0.90-1.69)	1.03 (0.80-1.32)	0.99 (0.70-1.38)	1.05 (0.78-1.42)	0.86 (0.60-1.25)	0.90 (0.66-1.21)

* Indicate Odds Ratio
UA indicates unadjusted, A indicates adjusted
Bold values indicate a significant difference between persons exposed to one or more ACE and persons never exposed to an ACE at α=0.05

Objective 3: Test the association between perceived level of trauma of ACEs and IBD- and non-IBD-related healthcare use amongst individuals with a confirmed IBD diagnosis.

A total of 253 individuals from the Manitoba IBD Cohort Study were exposed to an ACE and completed the 12-month CTQ questions pertaining to perceived level of trauma for ACEs. Approximately half of these cohort members (48.6%) report a high perceived level of trauma. The characteristics of cohort members who experienced a high level of trauma in relation to their ACEs and cohort members who experienced a low level of trauma in relation to their ACEs are displayed in Table 4.14. The table shows that significantly more females report a high level of trauma compared to males (55.3% vs. 37.2%). While less than half (48.5%) of the cohort members reporting a low level of trauma were characterized as either underweight, overweight, or obese, close to two thirds (64.2%) of cohort members reporting a high level of trauma fell into this underweight/overweight/obese category. Higher levels of reported trauma (i.e., score >5) were associated with both lower social functioning scores (45.6 ± 9.0 vs 48.8 ± 7.3) and higher perceived psychological stress scores (22.7 ± 7.4 vs 21.0 ± 6.6) than lower levels of reported

trauma (i.e., score ≤5). Additionally, more cohort members who had reported a high trauma ACE (7.3%) underwent an IBD-related surgery in the year prior to CTES completion than cohort members who had experienced a low trauma ACE (1.5%) and underwent an IBD-related surgery in the year prior to CTES completion. There were no other significant differences between cohort members experiencing at least one ACE who report a high perceived level of trauma and cohort members experiencing at least one ACE who report a low perceived level of trauma.

Table 4.14. Characteristics of Manitoba IBD Cohort Study respondents, stratified by perceived level of trauma, $N = 253$.

	High Perceived Trauma	**Low Perceived Trauma**
n (%)	123 (48.6)	130 (51.4)
Sex		
Male	**35 (28.5)**	**59 (45.4)**
Female	**88 (71.5)**	**71 (54.6)**
Age (years)		
18 – 44	70 (56.9)	83 (63.8)
45+	53 (43.1)	47 (36.2)
Income Quintile *		
One (lowest)	30 (24.4)	31 (23.8)
Two	30 (24.4)	19 (14.6)
Three	23 (18.7)	27 (20.8)
Four	10 (8.1)	10 (7.7)
Five (highest)	20 (16.3)	37 (28.5)
Smoking Status		
Never/Not daily	103 (83.7)	116 (89.2)
Daily	20 (16.3)	14 (10.8)
Alcohol Use		
Never/Less than once a week	73 (59.3)	77 (59.2)
1-3 times per week	29 (23.6)	34 (26.2)
>3 times per week	6 (4.9)	5 (3.8)
No response	15 (12.2)	14 (10.8)
Body Mass Index *		

Healthy weight	**43 (35.0)**	**63 (48.5)**
Underweight / Overweight / Obese	**79 (64.2)**	**63 (48.5)**
Social Functioning	**45.6 (SD: 9.0)**	**48.8 (SD: 7.3)**
Comorbidity		
0	108 (87.8)	121 (93.1)
1 or more	15 (12.2)	9 (6.9)
Perceived Psychological Stress	**22.7 (SD: 7.4)**	**21.0 (SD: 6.6)**
IBD Disease Type		
Crohn's Disease	67 (54.5)	60 (46.2)
Ulcerative / indeterminate colitis	56 (45.5)	70 (53.8)
Disease Activity *		
Minimally / inactive disease	36 (29.3)	44 (33.8)
Moderately active disease	32 (26.0)	40 (30.8)
Very active disease	54 (43.9)	46 (35.4)
Previous IBD-related Surgery		
Yes	**9 (7.3)**	**2 (1.5)**
No	**114 (92.7)**	**128 (98.5)**
Time between diagnosis and 12m survey completion (years)	5.3 (SD: 2.1)	5.3 (SD: 2.1)

* Some cohort members were missing data; therefore, column percentages do not sum to 100
s Indicates suppression due to small cell sizes
Bold values indicate a statistically significant difference between cohort members reporting high trauma and cohort members reporting low trauma ACE at α=0.05

We determined if there were any significant differences in healthcare use measures between cohort members reporting high perceived trauma and low perceived trauma. The mean annual estimates, standard deviations, and medians for each healthcare use measure for cohort members exposed to one or more ACE who report a perceived level of trauma greater than five (high perceived trauma) and cohort members exposed to one or more ACE who report a perceived level of trauma less than or equal to five (low perceived trauma) are presented in Table 4.15. For hospitalizations, frequencies and percentages of the cohort who experienced at least

one hospitalization during the 60-month observation period following CTES completion are provided.

On average, cohort members who report high perceived trauma saw their GP for non-IBD-related reasons more times per year than cohort members who report low perceived trauma (6.1 ± 6.0 vs 4.6 ± 3.9). This relationship was statistically significant at $\alpha = 0.05$. While the mean annual estimate for non-IBD-related specialists visits for cohort members exposed to high ACE trauma relative to low ACE trauma was slightly increased, no statistically significant differences were observed. All other annual healthcare use estimates revealed minimal differences between the two groups.

Table 4.15. Descriptive statistics for annual healthcare use for Manitoba IBD Cohort Study respondents, stratified by perceived level of trauma, N = 253.

		High Perceived Trauma	**Low Perceived Trauma**
n (%)		123 (48.6)	130 (51.4)
GP visits (non-IBD)		**Mean: 6.1**	**Mean: 4.6**
		SD: 6.0	**SD: 3.9**
		Median: 4.2	**Median: 3.5**
GP visits (IBD)		Mean: 1.4	Mean: 2.0
		SD: 2.3	SD: 4.0
		Median: 0.6	Median: 0.8
SP visits (non-IBD)		Mean: 6.0	Mean: 4.8
		SD: 8.4	SD: 9.8
		Median: 3.6	Median: 2.2
SP visits (IBD)		Mean: 3.4	Mean: 3.7
		SD: 6.3	SD: 7.3
		Median: 2.0	Median: 1.9
Hospitalized (non-IBD)	Yes	66 (53.7)	75 (57.7)
	No	57 (46.3)	55 (42.3)
Hospitalized	Yes	79 (64.2)	82 (63.1)

(IBD)	No	44 (35.8)	48 (36.9)
Hospital days (non-IBD)		Mean: 0.78	Mean 0.54
		SD: 1.6	SD: 1.9
		Median: 0.2	Median: 0.0
Hospital days (IBD)		Mean: 1.0	Mean: 1.4
		SD: 2.9	SD: 6.2
		Median: 0.2	Median: 0.2
IBD drugs		Mean: 4.9	Mean: 6.0
		SD: 5.3	SD: 5.9
		Median: 3.6	Median: 4.4
Psychotropic drugs		Mean: 2.6	Mean: 2.4
		SD: 5.0	SD: 6.5
		Median: 0.0	Median: 0.0
Antibiotic drugs		Mean: 1.1	Mean: 0.9
		SD: 1.3	SD: 1.3
		Median: 0.6	Median: 0.4
Other drugs		Mean: 12.2	Mean: 9.1
		SD: 18.1	SD: 15.3
		Median: 6.0	Median: 3.8

SD indicates standard deviation
Bold values indicate a statistically significant difference between cohort members reporting high perceived trauma and cohort members reporting low perceived trauma at α=0.05

Finally, to test if report of high perceived trauma influenced the rates/odds of healthcare use measures GLMs were analyzed. Table 4.16 summarizes the results of the negative binomial and logistic models for cohort members exposed to one or more ACE who report high perceived trauma relative to cohort members exposed to one more ACE who report low perceived trauma. Both unadjusted rates and rates adjusted for confounding covariates are displayed in the table; as expected, adjusted rates were lower than unadjusted rates. The models that were adjusted for confounding covariates also had much lower QIC values, indicating better model fit.

The unadjusted estimates show that report of high perceived trauma was associated with a 30% increased rate of non-IBD-related GP visits. However, the adjusted results display no difference in the rates of non-IBD-related GP visits between cohort members who report high perceived trauma and cohort members who report low perceived trauma. Moreover, the adjusted results show that report of high ACE trauma predicted a 49% decrease in the rate of IBD-related GP visits and a 52% decrease in the rate of IBD-related hospital days. Report of high perceived trauma did not predict any other variations in healthcare use rates or odds.

Table 4.16. Unadjusted and adjusted rate ratio and odds ratio estimates of healthcare use for Manitoba IBD Cohort Study respondents exposed to ≥ 1 ACE reporting high perceived trauma.

	Unadjusted Estimate (95% CI)	**Adjusted Estimate** (95% CI)
GP visits (non-IBD)	**1.28**	1.04
	(1.02-1.61)	(0.83-1.31)
GP visits (IBD)	0.70	**0.51**
	(0.45-1.11)	**(0.35-0.74)**
SP visits (non-IBD)	1.19	0.97
	(0.81-1.76)	(0.71-1.34)
SP visits (IBD)	0.91	0.77
	(0.56-1.46)	(0.55-1.10)
Hospitalization (non-IBD)	1.47*	1.20*
	(0.96-2.25)	(0.75-1.92)
Hospitalization (IBD)	0.86*	0.70*
	(0.61-1.22)	(0.46-1.05)
Hospital days (non-IBD)	1.36	1.01
	(0.63-2.91)	(0.35-2.94)
Hospital days (IBD)	0.68	**0.48**
	(0.27-1.71)	**(0.24-0.97)**
IBD drugs	0.79	0.81
	(0.62-1.02)	(0.61-1.06)

Psychotropic drugs	1.05 (0.59-1.89)	0.82 (0.40-1.72)
Antibiotic drugs	1.20 (0.87-1.67)	0.96 (0.70-1.33)
Other drugs	1.30 (0.88-1.93)	0.89 (0.65-1.22)

* Indicate Odds Ratio
Bold values indicate a statistically significant difference between cohort members reporting high perceived trauma and cohort members reporting low perceived trauma at α=0.05

V. Discussion

Summary

This study had three objectives: (1) estimate the prevalence of ACEs in individuals with IBD, (2) test the associations of the number and type of ACEs and healthcare use, and (3) test the association of perceived level of trauma from ACEs and healthcare use in individuals with IBD.

Of the 345 respondents to the CTES collected in the Manitoba IBD Cohort Study at the 12-month survey, approximately three quarters were exposed to one or more ACE. The ACEs that were investigated in this study included three commonly defined ACEs, physical abuse, sexual abuse, and parental upheaval, and three other traumatic experiences, which were the death of a very close friend or family member, a severe illness or injury, and any other major upheaval thought to shape one's life or personality significantly. The types of ACE categories were not mutually exclusive. An ACE count was also collected; the Manitoba IBD Cohort Study members were exposed to a total of 501 ACEs. Cohort members were categorized based on their ACE count: no ACEs, one type of ACE, two types of ACEs, and three or more types of ACE.

Exposure to one or more ACEs was not associated with increased healthcare use. Similarly, number of ACEs (ACE count) was not associated with healthcare use rates. Exposure to physical and sexual abuse was not associated with increased healthcare use after adjustments for confounding covariates. However, both forms of abuse were associated with higher mean annual estimates for non-IBD-related GP visits during unadjusted analysis. Additionally, exposure to physical abuse and parental upheavals were associated with increased mean annual estimates for non-IBD-related SP visits before adjustment for confounding covariates. However, after modelling and covariate adjustments, no significant differences were observed. In contrast,

following covariate adjustment, exposure to parental upheaval was associated with decreased IBD-related healthcare use including SP visits, hospitalizations, and hospital days.

High perceived trauma from ACEs was associated with increased mean annual estimates for non-IBD-related GP visits before adjustment for confounding covariates. However, after modelling and covariate adjustments no significant increases were observed. In contrast, following covariate adjustments, high perceived trauma from ACEs was associated with decreased IBD-related healthcare use including, GP visits and hospital days.

Discussion

The number of individuals exposed to one or more ACEs in this study was higher than previously reported in other population-based studies (McDonald et al., 2015; Metzler et al., 2017). This higher prevalence may result from the different types of ACEs included in this study. Moreover, we included exposure to any other upheaval thought to significantly shape one's life or personality; this type of ACE is likely to include a wide variety of experiences not captured in other ACE measures. When population estimates are compared to IBD cohort estimates, similar results are produced for two commonly defined ACEs, sexual abuse and parental upheavals. Statistics Canada reported the prevalence of sexual abuse at 10.0%, the IBD Cohort Study reported 13.0% (Afifi et al., 2014). Likewise, population data from the US ACE Study reported the prevalence of parental upheavals at 23.3%, the IBD Cohort Study reported 20.3% (Metzler et al., 2017). While the prevalence of sexual abuse and parental upheavals were similar amongst population and cohort estimates, the prevalence of physical abuse in the IBD cohort was low compared to Canadian estimates reported by Statistics Canada (12.2% vs. 26.0%) (Afifi et al.,

2014). However, the estimate from the cohort study (12.2%) was similar to the estimate reported by the Alberta ACE Study for the general population (11.0%) (McDonald et al., 2015).

ACEs have been associated with the evolution of psychological stress (Nurius et al., 2015); therefore, we expected perceived psychological stress to be higher among cohort members exposed to one or more ACE compared to cohort members never exposed to an ACE. Our findings were consistent with previous research. Moreover, perceived psychological stress gradually increased alongside exposure to more types of ACEs.

While previous research suggests that exposure to ACEs is associated with increased healthcare use (Anda et al., 2008; Bellis et al., 2017; Bonomi et al., 2008; Koskenvuo & Koskenvuo, 2015), after consideration of confounding covariates, the various number and types of ACEs were not predictive of increased non-IBD or IBD-related healthcare use in our study. As well, reports of higher perceived trauma from ACE exposure did not associate with increased non-IBD or IBD-related healthcare use. Cohort members were exposed to their ACEs prior to the age of 17. For cohort members exposed to at least one ACE, the mean number of years between exposure to their first ACE and CTES survey completion was 30.5 years. While this factor has not been recognized by previous ACE research, it is possible that the long period of time between ACE exposure and healthcare use measurement may have contributed to the null findings. Even though this study found that the number of ACEs, different types of ACEs, and higher perceived trauma from ACEs did not predict increased healthcare use in persons with IBD, ACEs may still have a significant impact on persons with IBD. Mean annual estimates for non-IBD-related healthcare use including, GP and SP visits, indicate that persons with IBD who were exposed to physical abuse, sexual abuse, and parental upheavals are utilizing more healthcare than persons with IBD who were not exposed to physical abuse, sexual abuse, and

parental upheavals. While GLMs indicate that this increase in utilization cannot be attributed to ACE exposure, other confounding covariates, for example social functioning, comorbidity, and disease activity may play a mediating role between ACE exposure and healthcare utilization.

It was unexpected that exposure to parental upheavals would associate with decreased IBD-related healthcare use, including SP visits, hospitalizations, and hospital days. It was also unexpected that high levels of perceived trauma from ACEs would be associated with decreased IBD-related healthcare use including GP visits and hospital days. There is no previous literature or evidence to explain why these trends may exist however, we can speculate that reduced social functioning and uneasiness around authoritative figures may play an important role. It is important to acknowledge that ACE exposure and higher levels of perceived ACE trauma may prevent persons with IBD from accessing the IBD-related healthcare services they require to properly manage their disease.

Significance and Recommendations for Future Research

Our main finding was that persons with IBD may have a higher prevalence of ACEs than previously reported population estimates, although the size of the estimate may be influenced by the method of measurement. While the number, type, and perceived level of ACE trauma did not necessarily predict worse outcomes for persons with IBD as measured by health care utilization, other outcomes should be explored. Descriptive statistics suggest that perceived psychological stress and social functioning may be significantly associated with ACE exposure. These are important outcomes to consider as people with IBD often report that their symptoms increase during periods of high stress. An increase in symptoms can have a significant impact on an individual's life (Bernstein et al., 2010; Lix et al., 2008). Exposure to physical and sexual abuse

was associated with increased mean annual estimates for non-IBD-related healthcare utilization and this may reflect the distress experienced by these individuals. As exposure to parental upheavals and higher levels of perceived ACE trauma were predictive of decreased IBD-related healthcare use, clinicians should consider inquiry into ACEs as a component of IBD care. Inquiry into ACEs may allow clinicians to better counsel their IBD patients in terms of managing psycho-social factors including stress, anxiety, and depression, and seeking out the appropriate supports (Graff, Walker, & Bernstein, 2009). While psychosocial screening in patients with IBD is not a new phenomenon, inquiry into ACEs has surfaced as a controversial topic (Finkelhor, 2017).

Implementation of ACE screening is supported by previously successful screening interventions. The Luebeck Interview developed and validated in a specialty GI service, is a clinician-administered scale that provides validation for broadening patient management (Kunzendorf et al., 2007). Additionally, the five-item Anxiety and Depression Detector has been validated and applied across primary care settings (Means-Christensen, Sherbourne, Roy-Byrne, Craske, & Stein, 2006). Screening tools have been used as successful indicators for social support, depression, anxiety, distress, and interest in receiving psychological care for persons with IBD (Graff et al., 2009; Mulrow et al., 1995). Low screening rates for ACEs can be partially attributed to a lack of appropriate assessment tools (Denton, Frogley, Jackson, John, & Querstret, 2017) and competing opinions. While some believe that ACE screening may itself provide opportunity for acknowledgement, reflection, and therapeutic benefit, critics of ACE screening argue that it may be disruptive, adding a sense of stigma and harming healthcare relationships (Finkelhor, 2017).

This study has some limitations. This study did not measure the ten commonly defined ACEs referenced in recent literature (Anda et al., 2010). Instead, in this study three commonly defined ACEs were measured, including physical abuse, sexual abuse, and parental upheavals. In addition, three other additional traumatic experiences were measured. While most studies involving ACEs measure a common ACE count ranging from zero to ten (Anda et al., 2010), this study focused on only six types of ACEs. The accuracy of ACE prevalence and associations between numbers and types of ACEs and healthcare use as well as, the relatability of our findings would be improved if we measured all ten commonly defined ACEs. Additionally, when looking at the length of time between when respondents were exposed to their first ACE and when they completed their CTES survey, we see that ACEs may have occurred years earlier and consequently respondents may have had the opportunity to develop effective coping mechanisms. The drive to optimize child health through healthy development, early interventions and public policy has increased significantly over the past thirty years (Sciaraffa, Zeanah, & Zeanah, 2018; Soleimanpour, Geierstanger, & Brindis, 2017). It is also possible that cohort members were unable to recall exposure or have an inaccurate perception of trauma from ACEs. ACEs were measured at any point in childhood (<17 years), however, this study did not account for variation in age at or length of exposure. Furthermore, due to a relatively small sample size, there may be insufficient power to detect an association between ACEs, perceived trauma, and healthcare use.

At the same time, this study has a number of strengths. Analysis of ACEs had remained entirely untapped in the IBD literature. The Manitoba IBD Cohort Study is population-based, which improves generalizability of these findings for all persons with IBD. Finally, this study

was able to include multiple measures of healthcare use that were objectively measured using provincial administrative health databases.

Both ACE and IBD literature would benefit from future research focused on their relationship. This study should be repeated assessing the ten commonly defined ACEs. Additionally, the association between ACEs and other IBD patient-outcomes should be assessed, such as psychological stress and social functioning. It may also be beneficial to test if demographic and behavioral risk factors, comorbid conditions, perceived psychological stress, and IBD disease characteristics play a mediating role in the relationship between ACEs and healthcare use. This could be done using structural equation modelling (SEM), which would require a much larger sample size. Moreover, it is possible that exposure to an ACE can serve as an important environmental trigger or risk factor for the development of IBD (Bernstein, 2016; Bernstein et al., 2010). While we do not have a matched control group for our Manitoba IBD Cohort Study to optimally interpret this finding, the high prevalence of ACEs among this IBD population does provide a rationale for more study in this area, preferably of a prospective nature.

Conclusions

In conclusion, the purpose of this study was to report the prevalence of ACEs in individuals with IBD, test the associations between number and types of ACEs and healthcare use, and test the associations between perceived level of trauma of ACEs and healthcare use in persons with IBD. In this study, we found that almost three quarters of our cohort were exposed to at least one ACE. This is a higher estimate than previously conducted population-based. Both physical abuse and sexual abuse were experienced by about 10 percent of the cohort. Parental

upheaval was more common; it was experienced by about one in five cohort members. The analytic models revealed no statistically significant associations between healthcare use and the number of ACEs, type of ACEs, and perceived trauma from ACEs. While ACEs did not predict increased healthcare use in persons with IBD, previous research suggests that ACEs may still have a significant impact on persons with IBD. Since clinicians managing persons with IBD have the opportunity to engage affected persons on their stress and past lives, this should be undertaken including inquiry about ACEs. It is possible that experiencing an ACE may drive stress and reduced functioning which in turn may influence disease activity and health care utilization and hence should be recognized and treated appropriately.

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Appendix A: Childhood Traumatic Experiences Scale (CTES)

Childhood Experiences

We are interested in the effect of stressful experiences during childhood on people's health and functioning later in life. The following two pages of questions are about experiences that people have while they are growing up - before the age of 17.

Many people have upsetting or difficult experiences during their growing up years. It can be upsetting to remember about these experiences. If you find that any of your recollections in answering these experiences are difficult and that you would like to discuss your concerns with a member of our staff, please let us know. We would be happy to talk to you now or at a later time that is convenient for you.

As with the other information provided in this study, your answers to these questions are confidential. You may decline to answer any of these questions if you wish.

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CTES

For the following questions, answer each item that is relevant. Be as honest as you can. Each question refers to any event that you may have experienced PRIOR TO THE AGE OF 17. Please fill in the bubble that corresponds to your answer using a dark pen.

1. Prior to the age of 17, did you experience a death of a very close friend or family member? ○ Yes ○ No **If yes**, how old were you? ☐☐

If yes, how traumatic was this?

Not at all (1)			Somewhat traumatic (4)			Extremely traumatic (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

If yes, how much did you confide in others about this traumatic experience at the time?

Not at all (1)						A great deal (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

2. Prior to the age of 17, was there a major upheaval between your parents (such as divorce, separation)? ○ Yes ○ No **If yes**, how old were you? ☐☐

If yes, how traumatic was this?

Not at all (1)			Somewhat traumatic (4)			Extremely traumatic (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

If yes, how much did you confide in others?

Not at all (1)						A great deal (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

3. Prior to the age of 17, did you have a traumatic sexual experience (raped, molested, etc.)? ○ Yes ○ No **If yes**, how old were you? ☐☐

If yes, how traumatic was this?

Not at all (1)			Somewhat traumatic (4)			Extremely traumatic (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

If yes, how much did you confide in others?

Not at all (1)						A great deal (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

4. Prior to the age of 17, were you the victim of violence (child abuse, mugged or assaulted) other than sexual? ○ Yes ○ No **If yes**, how old were you? ☐☐

If yes, how traumatic was this?

Not at all (1)			Somewhat traumatic (4)			Extremely traumatic (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

If yes, how much did you confide in others?

Not at all (1)						A great deal (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

5. Prior to the age of 17, were you extremely ill or injured? ○ Yes ○ No **If yes**, how old were you? ☐☐

If yes, how traumatic was this?

Not at all (1)			Somewhat traumatic (4)			Extremely traumatic (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

If yes, how much did you confide in others?

Not at all (1)						A great deal (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

6. Prior to the age of 17, did you experience any other major upheaval that you think may have shaped your life or personality significantly? ○ Yes ○ No **If yes**, how old were you? ☐☐

If yes, how traumatic was this?

Not at all (1)			Somewhat traumatic (4)			Extremely traumatic (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

If yes, how much did you confide in others?

Not at all (1)						A great deal (7)
1	2	3	4	5	6	7
○	○	○	○	○	○	○

Appendix B: Classification of Drug Types Based on ATC Codes and DINs

ATC Codes for IBD Drugs: A07EC01, A07EC02, A07EC03, A07EA02, A07EA04, A07EC04, A07EC06, L04AX03, L04AC05, L04AA33, L01BA01, L01BB02, L04AB02, L04AB04, L04AB06, L04AX01, H02AB02, H02AB04, H02AB06, H02AB07, H02AB09, H02AB10, H02AB01

DINs for IBD Drugs: 02244016, 02419475, 02419483, 02258595, 02258595, 02458349, 02458357, 02466872, 02324784, 02324776, 02413175, 02413183, 02417472, 02436841, 00016438, 00016446, 00249963, 00280437, 00030910, 00030929, 00016462, 00176842, 00285471, 00295094, 00349100, 00354309, 00416010, 00489158, 00501050, 00501069, 00504416, 00778621, 00786012, 00796603, 01946897, 01964070, 01964968, 01964976, 02240684, 02240685, 02240687, 02250055, 02261081, 02279363, 00030791, 00030961, 00030988, 00036129, 02245532, 02152541, 00021679, 02230619, 00021695, 00210188, 00232378, 00252417, 00271373, 00312770, 00550957, 00598194, 00610623, 01997580, 01914030, 02099683, 02171929, 02267217, 02063808, 00875856, 02112779, 00685925, 00685933, 00875848, 00263869, 00410640, 00445126, 00598461, 00598488, 00685925, 00685933, 01914030, 01997580, 02063808, 02064472, 02064480, 02099675, 02099683, 02112779, 02112787, 02171929, 02267217, 02297558, 02351463, 02004682, 02112795, 02112809, 00613568, 02064499, 02112752, 02153521, 02153548, 02153556, 02153564, 02242146, 00263869, 00410640, 00445126, 00598461, 00598488, 00685925, 00685933, 01914030, 01997580, 02063808, 02064472, 02064480, 02099675, 02099683, 02112779, 02112787, 02171929, 02267217, 02297558, 02351463, 02004682, 02112795, 02112809, 00613568, 02064499, 02112752, 02112760, 02153521, 02153548, 02153556, 02153564, 02242146, 00263869, 00410640, 00445126, 00598461, 00598488, 00685925, 00685933, 01914030, 01997580, 02063808, 02064472, 02064480, 02099675, 02099683, 02112779, 02112787, 02171929, 02246803, 02265257, 02267217, 02297558, 02348063, 02351463, 02399466, 00004596, 00004723, 00337854, 02231491, 02236799, 02236819, 02242907, 00004596, 00004723, 02231491, 02235352, 02236799, 02236819, 02242148, 02242907, 02243371, 02248843, 02343002, 02358573, 02415275

ATC Codes for Psychotropic Drugs: N03AF01, N03AG01, N03AX09, N05AA02, N05AA03, N05AB02, N05AB03, N05AB04, N05AB06, N05AB08, N05AC01, N05AC02, N05AC03, N05AC04, N05AD01, N05AD08, N05AE04, N05AF01, N05AF04, N05AF05, N05AG01, N05AG02, N05AH01, N05AH02, N05AH03, N05AH04, N05AN01, N05AX08, N05AX12, N05AX13, N05BA06, N05BA12, N06AA01, N06AA02, N06AA04, N06AA11, N06AA12, N06AA17, N06AA21, N06AB03, N06AB04, N06AB05, N06AB06, N06AB08, N06AB10, N06AF03, N06AF04, N06AG02, N06AX06, N06AX11, N06AX16, N06AX21, N06AX23, N06AA01, N06AA02, N06AA04, N06AA11, N06AA12, N06AA17, N06AA21, N06AB03, N06AB04, N06AB05, N06AB06, N06AB08, N06AB10, N06AF03, N06AF04, N06AG02, N06AX06, N06AX11, N06AX16, N06AX21, N06AX23

ATC Codes for Antibiotic Drugs: J01AA02, J01AA09, J01AA12, J01BA01, J01CA01, J01CA12, J01CA13, J01CE01, J01CE08, J01CE09, J01CE30, 'J01CF', J01CF02, J01CR03, J01CR05, J01DB03, J01DB04, J01DC01, J01DC02, J01DC03, J01DC05, J01DD01, J01DD02, J01DD04, J01DD07, J01DE01, J01DH02, J01DH03, J01DH04, J01DH51, J01DI01, J01DI54,

J01EE01, J01FA01, J01FF01, J01FF02, J01GA01, J01GB01, J01GB03, J01GB06, J01GB07, J01MA01, J01MA12, J01MA13, J01MA14, J01MA16, J01XA01, J01XA03, J01XB01, J01XB02, J01XC01, J01XX04, J01XX08, J01XX09, J01XX10, J01XX11, J01AA07, J01AA08, J01CA04, J01CE02, J01CE10, J01CR02, J01DB01, J01DC04, J01DC10, J01DD08, J01EA01, J01FA09, J01FA10, J01MA02, J01MA06, J01XD01, J01RA02, J01XE01, J01XX05,J01XX01, J01FA15, 'A01AB ', 'A02BD ', 'A07A ', 'D01 ', 'D06 ', 'G01AA', GA01F01, 'D07C ', 'D09AA ', 'D10AF ', 'G01 ', 'P01 ', 'R02AB ', 'R05X ', 'S01 ', 'S02 ', 'S03 ', 'J04 ', 'J01G ', 'J02', 'J04 ', 'J05 ', 'J06 ', 'J07 ',

DINs for Antibiotic Drugs: 000246026, 000012521, 002285401, 002409356, 000312363, 000002100, 000002119, 000002127, 000002135, 000004049, 000004057, 000004065, 000004073, 000605719, 000872644, 000872652, 001933345, 001933353, 002043149, 002043157, 002043173, 002068540, 002226995, 002227002, 002227010, 002227029, 002227037, 002441705, 002441713, 002441721, 002441748, 002441756, 000564974, 000564982, 000564990, 000857548, 002173425, 002173433, 002173441, 002173697, 002246640, 002246641, 002246642, 002248939, 002248940, 002248941, 001916912, 001916920, 000002208, 000002216, 000002224, 000002232, 000002240, 000002259, 000883727, 000883735, 000883743, 000883751, 001930672, 001930680, 002001101, 002001128, 002001136, 002001144, 002003465, 002003473, 002043246, 002043254, 002043270, 002060086, 002060094, 002060108, 002220237, 002220245, 002220253, 002220261, 002220288, 002220296, 002247375, 002300443, 002300478, 002300508, 002041596, 002291924, 000002402, 002041588, 002043785, 000002151, 000002178, 000002186, 000407593, 000407607, 000407615, 001912194, 001912410, 001912429, 001975447, 002367408, 002367416, 002367424, 002400081, 001916939, 002247880, 002083590, 002083604, 002083612, 002170795, 002170809, 002170817, 002299623, 002299631,002299658, 002305593, 002305607, 002305615, 002305623, 002305631, 002305658, 002308444, 002308452, 002308460, 002330547, 002362619, 002362627, 002362635, 002370158, 002370166, 002370174, 002377748, 002391511, 002391538, 002391546, 002401312, 002401320, 002401339, 002420430, 002439131, 002452545, 002452553, 002452561, 002452588, 002452596, 000015369, 000244406, 000752525, 002060051, 000322288, 000322296, 000411434, 000411442, 000411450, 001919601, 001919628, 001919636, 002108119, 002108127, 002108135, 002233853, 002233854, 002233855, 002237137, 002237138, 002237140, 002237141, 002297191, 002297205, 002297213, 002308932, 002308959, 002308967, 002318830, 002401029, 002437104, 002437112, 002437120, 002452162, 000663697, 000663700, 000893668, 000893676, 001980653, 002128187, 002128195, 002240773, 002291711, 002291738, 000481890, 000497843, 000890936, 001927256, 001927264, 001935828, 001940252, 001986082, 002213532, 002213540, 002213559, 002237731, 002237732, 002237733, 002241638, 002241639, 002241640, 002422298, 002422301, 002422328, 000439312, 000439320, 000648930, 000878839, 002036274, 002036428, 000546208, 000546216, 000546224, 000839248, 001989758, 001989766, 001989804, 001989812, 002225085, 002225093, 002225107, 002261499, 002261502, 002261510, 002261529, 002352168, 002352176, 002352184, 002434083, 002434091, 002434105, 000640026, 000640034, 000640042, 000791679, 000886955, 000886963, 000886971, 000887129, 000888338, 001968092, 001974408, 001974416, 001980645, 002212218, 002212226, 002212234, 002213737, 002215012, 002215020, 002437848, 002437856, 002437864, 002439522, 000657387,

000657409, 000657417, 000851957, 000894699, 002250276, 002250284, 002250292, 002250306, 002257866, 002257874, 002287625, 002287633, 002287641, 002287668, 002289679, 002289687, 002289695, 002289709, 002289717, 002292262, 002292270, 002292289, 002292297, 002292815, 002292866, 002292874, 002292882, 002292904, 002325594, 002325608, 002325616, 002325624, 002325632, 002409968, 001919490, 001919504, 002163632, 002163640, 002319020, 002319039, 002218488, 002218496, 002219018, 002219026, 002378787, 002378795, 002413779, 002413787, 002415216, 002415224, 002421518, 002421526, 002430495, 002430509, 002436493, 002436507, 002247437, 002332906, 000717274, 000717282, 001911430, 001911449, 002351692, 002351706, 002357429, 002357437, 002358336, 002358344, 002439840, 002439859, 002441225, 002441233, 002313103, 002446685, 002446901, 000550078, 000550086, 000000175, 000000183, 000015415, 000607541, 000682268, 000682276, 001958518, 001958542, 002239952, 002297566, 002334844, 002334976, 002358816, 002368846, 002385473, 000260436, 002051826, 002130866, 002139286, 002230535, 002230540, 002385716, 002408503, 002408511, 002408538, 002440091, 000030732, 002241323, 002015862, 002243660, 000325449, 000325457, 000375764, 000381969, 000533688, 000608963, 000851825, 002230639, 002230640, 002241209, 002241210, 002285150, 002382814, 002384930, 002420287, 000223824, 000223832, 000259160, 000259179, 001913093, 001913530, 001913549, 001913565, 001989693, 001989707, 002082136, 002082144, 002082152, 002145731, 002145758, 002242652, 002268531, 002457008, 000397415, 002242971, 000503371, 000503398, 002049414, 001947710, 002155982, 002237334, 002256789, 002267462, 002274140, 002289946, 002301296, 002301903, 002304546, 002304759, 002311895, 002312123, 002377535, 002236839, 002236840, 002297825, 002314932, 002460122, 002239145, 002246414, 002243183, 002243184, 000015423, 000722146, 000803510, 000803537, 001990853, 001990861, 001990888, 002015110, 002139243, 002139375, 002139383, 002230191, 002230192, 002241807, 002241820, 002241821, 002342855, 002342863, 002378337, 002378345, 002394626, 002394634, 002394642, 002394650, 002396386, 002405822, 002405830, 002406535, 002406543, 002406551, 002406578, 002407914, 002407922, 002407930, 002407949, 002411032, 002411040, 002420295, 002420309, 002420317, 002420325, 002435713, 002435721, 002330717, 002330725, 000476420, 002244849, 002403544, 000004421, 002375893, 002049406, 000649074, 000870420, 000210196, 002243685, 002402637, 002429527, 002430827, 002441012, 002299909, 000030708, 002245571, 002255820, 002438631

Appendix C: Pregnancy-Related Exclusions

The following physician tariff codes, lab related work/diagnostic tests, and ICD-9-CM diagnoses codes are used in the definition and identification of prenatal care visits in the Medical Services data.

Pregnancy Visit Tariffs:

- 8400 – Complete Prenatal Assessment
- 8401 – Prenatal Visit
- 8402 – Postnatal Visit

Lab Related Work / Diagnostic Tests:

- 9521 – Hormonal Pregnancy Test

ICD-9-CM Codes:

- 630-639 – Ectopic and molar pregnancy and other pregnancy with abortive outcomes
- 640-649 – Diagnostic code indicating a complication related to pregnancy
- 650-659 – Other indication for care in pregnancy, labor and delivery
- 660-669 – Complications occurring in the course of labor and delivery
- V20 – Health supervision of infant or child
- V22 – Normal Pregnancy
- V23 – Supervision of High Risk Pregnancy
- V24 – Postpartum care and examination of lactating mother
- V27 – Outcome of delivery (includes live birth and stillbirth)
- V637 – Unspecified abortion

ICD-9-CM Procedure Codes:

- 66.62 – Salpingectomy with removal of tubal pregnancy
- 69.01 – Dilation and curettage for termination of pregnancy
- 69.51 – Aspiration curettage of uterus for termination of pregnancy
- 74.3 – Removal of extratubal ectopic pregnancy
- 74.91 – Hysterotomy to terminate pregnancy
- 75.0 – Intra-amniotic injection for abortion

An inpatient hospitalization where the main reason for the hospital stay was related to pregnancy or birth. Pregnancy and birth hospitalizations are defined by a major clinical category (MCC) code 13, and supplemented with hospitalizations with a Most Responsible Diagnosis code containing ICD-10-CA codes Z32-Z35 (for hospitalizations with an ungroupable Case Mix Group (CMG™) code only.) Only patients age 18 at older at time of admission are placed into this category.

Appendix D: Associations between Model Covariates and Healthcare Use for IBD Cohort Study Members Exposed to Different ACE counts

Supplementary Table 1. Rate ratio estimates (95% CIs) for models of GP and SP visit

Covariate	GP visits (non-IBD)	GP visits (IBD)	SP Visits (non-IBD)	SP Visits (IBD)
Sex				
Male	REF	REF	REF	REF
Female	1.25 (1.00-1.57)	0.84 (0.59-1.18)	1.17 (0.84-1.64)	0.79 (0.59-1.06)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.53 (1.28-1.83)**	**0.55 (0.39-0.78)**	**1.89 (1.43-2.49)**	**0.68 (0.50-0.92)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.99 (0.76-1.30)	0.80 (0.50-1.26)	0.95 (0.68-1.34)	0.87 (0.58-1.33)
Three	1.05 (0.78-1.43)	1.27 (0.71-2.29)	0.86 (0.61-1.20)	0.82 (0.55-1.23)
Four	1.08 (0.66-1.77)	1.60 (0.79-3.26)	1.24 (0.70-2.21)	0.71 (0.39-1.28)
Five (highest income)	0.82 (0.62-1.07)	**0.60 (0.38-0.97)**	1.05 (0.66-1.65)	0.74 (0.46-1.18)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	1.02 (0.79-1.31)	0.87 (0.56-1.36)	0.76 (0.52-1.12)	0.92 (0.58-1.46)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.85 (0.69-1.06)	0.84 (0.56-1.25)	1.01 (0.75-1.38)	0.82 (0.60-1.12)

>3 times per week	1.03 (0.69-1.53)	1.28 (0.59-2.75)	0.82 (0.52-1.28)	0.73 (0.44-1.22)
No response	1.04 (0.80-1.34)	1.42 (0.82-2.46)	1.25 (0.79-1.98)	1.30 (0.76-2.24)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.13 (0.93-1.37)	1.02 (0.70-1.47)	1.11 (0.85-1.43)	0.94 (0.71-1.25)
Social Functioning	0.99 (0.97-1.00)	**0.95 (0.92-0.98)**	**0.97 (0.95-0.99)**	**0.96 (0.93-0.99)**
Charlson Comorbidity Score				
0	REF	REF	REF	REF
1	0.93 (0.62-1.39)	0.63 (0.30-1.30)	1.61 (0.97-2.67)	1.13 (0.57-2.22)
2 or more	0.97 (0.62-1.50)	0.88 (0.23-3.31)	**4.06 (1.73-9.53)**	0.94 (0.50-1.79)
Perceived Psychological Stress	0.99 (0.98-1.01)	**0.96 (0.93-0.99)**	**0.98 (0.96-1.00)**	**0.97 (0.95-0.99)**
IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.04 (0.87-1.25)	1.20 (0.85-1.68)	1.07 (0.80-1.45)	1.11 (0.86-1.44)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.18 (0.94-1.49)	**1.94 (1.18-3.18)**	1.07 (0.74-1.55)	**2.03 (1.37-3.02)**
Very active disease	**1.35 (1.05-1.75)**	**1.98 (1.29-3.05)**	1.03 (0.72-1.47)	**2.30 (1.61-3.30)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.18 (0.80-1.74)	1.65 (0.96-2.82)	1.38 (0.83-2.31)	**2.04 (1.07-3.90)**

Time between diagnosis and 12m survey completion (years)	0.99 (0.94-1.03)	**0.89 (0.83-0.96)**	0.97 (0.91-1.03)	0.95 (0.87-1.04)

REF indicates reference category
Bold values indicate a statistically significant estimate at α=0.05

Supplementary Table 2: Rate ratio and odds ratio estimates (95% CIs) for hospitalizations and hospital days

Covariate	Hospitalized (non-IBD)*	Hospitalized (IBD)*	Hospital days (non-IBD)	Hospital days (IBD)
Sex				
Male	REF	REF	REF	REF
Female	1.05 (0.72-1.53)	0.88 (0.64-1.22)	1.41 (0.80-2.48)	0.98 (0.57-1.70)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.19 (0.83-1.71)	0.94 (0.67-1.33)	1.00 (0.61-1.65)	**0.50 (0.28-0.89)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	**2.05 (1.22-3.43)**	1.19 (0.76-1.88)	1.30 (0.66-2.56)	0.59 (0.28-1.23)
Three	1.14 (0.65-1.98)	0.97 (0.60-1.56)	0.92 (0.43-1.95)	**0.48 (0.26-0.92)**
Four	**2.19 (1.07-4.48)**	0.99 (0.57-1.73)	1.42 (0.56-3.60)	0.62 (0.22-1.73)
Five (highest income)	0.85 (0.49-1.49)	1.07 (0.64-1.76)	0.42 (0.17-1.02)	**0.43 (0.19-0.99)**
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.68 (0.37-1.24)	0.59 (0.34-1.02)	0.53 (0.22-1.31)	0.83 (0.32-2.13)
Alcohol Use				
Less than once a week	REF	REF	REF	REF

1-3 times per week	0.91 (0.58-1.42)	0.94 (0.66-1.34)	0.75 (0.40-1.38)	0.81 (0.45-1.47)
>3 times per week	1.39 (0.66-2.94)	0.91 (0.36-2.30)	0.88 (0.40-1.94)	0.71 (0.28-1.76)
No response	**1.88 (1.07-3.29)**	0.99 (0.57-1.72)	1.89 (0.85-4.15)	1.07 (0.42-2.76)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.34 (0.94-1.91)	1.02 (0.74-1.39)	**1.78 (1.10-2.88)**	1.02 (0.58-1.80)
Social Functioning	**0.96 (0.93-0.99)**	**0.97 (0.94-0.99)**	**0.92 (0.87-0.97)**	**0.92 (0.87-0.97)**
Charlson Comorbidity Score				
0	REF	REF	REF	REF
1	0.71 (0.26-1.94)	1.08 (0.52-2.27)	1.76 (0.53-5.87)	1.45 (0.35-6.04)
2 or more	**7.66 (2.91-20.16)**	1.38 (0.77-2.46)	**10.26 (3.94-26.68)**	**3.15 (1.27-7.79)**
Perceived Psychological Stress	0.98 (0.95-1.01)	**0.97 (0.94-0.99)**	**0.95 (0.91-0.98)**	**0.93 (0.89-0.97)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.07 (0.76-1.50)	1.12 (083-1.53)	1.17 (0.74-1.85)	1.06 (0.66-1.68)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.86 (0.53-1.37)	**1.79 (1.17-2.75)**	0.95 (0.45-2.02)	**2.71 (1.33-5.53)**
Very active disease	**0.53 (0.33-0.86)**	**1.74 (1.13-2.68)**	**0.43 (0.25-0.75)**	**2.17 (1.13-4.15)**

Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**3.33** **(1.77-6.25)**	1.73 (0.86-3.50)	**4.03** **(1.90-8.52)**	2.58 (0.80-8.38)
Time between diagnosis and 12m survey completion (years)	1.03 (0.95-1.12)	0.98 (0.91-1.07)	0.90 (0.75-1.07)	0.93 (0.78-1.10)

*indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant estimate at α=0.05

Supplementary Table 3. Rate ratio estimates (95% CIs) for IBD, psychotropic, antibiotic, and other prescription drug dispensations

Covariate	**IBD drugs**	**Psychotropic drugs**	**Antibiotic drugs**	**Other drugs**
Sex				
Male	REF	REF	REF	REF
Female	**0.66** **(0.50-0.87)**	1.60 (0.95-2.69)	1.38 (0.99-1.89)	1.22 (0.93-1.61)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.85 (0.66-1.10)	1.20 (0.70-2.07)	**0.75** **(0.57-0.99)**	**2.40** **(1.87-3.07)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.88 (0.61-1.26)	1.52 (0.72-3.23)	1.19 (0.80-1.79)	1.06 (0.74-1.52)
Three	0.98 (0.65-1.50)	**2.50** **(1.18-5.29)**	1.28 (0.90-1.82)	1.06 (0.70-1.60)
Four	0.99 (0.64-1.54)	1.12 (0.38-3.37)	1.27 (0.74-2.17)	1.04 (0.68-1.59)
Five (highest income)	0.98	1.52	0.94	0.81

	(0.69-1.37)	(0.66-3.51)	(0.61-1.46)	(0.54-1.23)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.92 (0.64-1.31)	1.38 (0.65-2.96)	1.16 (0.78-1.72)	0.78 (0.48-1.25)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.99 (0.74-1.32)	0.78 (0.38-1.57)	0.82 (0.59-1.16)	0.78 (0.59-1.02)
>3 times per week	0.86 (0.45-1.63)	0.66 (0.17-2.61)	0.90 (0.52-1.58)	0.98 (0.48-2.01)
No response	1.19 (0.81-1.75)	1.23 (0.63-2.40)	**2.15 (1.40-3.31)**	1.48 (0.95-2.30)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.00 (0.79-1.27)	1.57 (0.97-2.55)	0.95 (0.72-1.26)	1.25 (0.97-1.61)
Social Functioning	0.99 (0.97-1.01)	**0.94 (0.90-0.98)**	0.98 (0.96-1.00)	**0.97 (0.95-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.25 (0.74-2.11)	1.93 (0.87-4.27)	**2.12 (1.19-3.79)**	1.51 (0.65-3.50)
2 or more	0.79 (0.46-1.37)	1.80 (0.41-7.90)	**3.19 (1.20-8.45)**	1.25 (0.52-2.99)
Perceived Psychological Stress	0.99 (0.96-1.01)	1.02 (0.97-1.08)	0.99 (0.97-1.01)	**0.98 (0.96-0.99)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	0.92 (0.73-1.17)	0.85 (0.50-1.44)	1.15 (0.90-1.46)	1.07 (0.83-1.39)

Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.40 (0.99-1.99)	0.79 (0.41-1.51)	1.43 (0.99-2.08)	1.06 (0.78-1.44)
Very active disease	**1.46 (1.04-2.03)**	1.14 (0.55-2.37)	**1.90 (1.32-2.73)**	**1.56 (1.12-2.19)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.84 (0.46-1.54)	0.90 (0.39-2.05)	1.75 (0.95-3.21)	1.45 (0.88-2.3)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.03)	0.95 (0.84-1.07)	0.98 (0.91-1.05)	0.98 (0.91-1.06)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Appendix E: Associations between Model Covariates and Healthcare Use for IBD Cohort Study Members Exposed to Physical and Sexual Abuse

Supplementary Table 4. Rate ratio estimates (95% CIs) for models of GP and SP visit, Exposed to physical abuse

Covariate	GP visits (non-IBD)	GP visits (IBD)	SP Visits (non-IBD)	SP Visits (IBD)
Sex				
Male	REF	REF	REF	REF
Female	**1.30 (1.05-1.61)**	0.78 (0.55-1.11)	1.18 (0.89-1.55)	0.75 (0.57-1.01)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.49 (1.24-1.79)**	**0.55 (0.39-0.78)**	**1.95 (1.46-2.62)**	**0.67 (0.49-0.90)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	1.00 (0.76-1.32)	0.78 (0.49-1.25)	0.95 (0.66-1.37)	0.86 (0.56-1.32)
Three	1.09 (0.79-1.50)	1.25 (0.69-2.27)	0.85 (0.59-1.22)	0.82 (0.54-1.25)
Four	1.15 (0.72-1.83)	1.53 (0.77-3.01)	1.34 (0.73-2.46)	0.72 (0.41-1.27)
Five (highest income)	0.83 (0.63-1.10)	0.60 (0.37-0.96)	1.04 (0.67-1.60)	0.75 (0.47-1.19)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	1.04 (0.80-1.36)	0.86 (0.56-1.36)	0.77 (0.53-1.13)	0.95 (0.59-1.52)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.84 (0.68-1.04)	0.83 (0.56-1.23)	0.99 (0.72-1.34)	0.79 (0.59-1.07)

>3 times per week	1.10 (0.74-1.65)	1.23 (0.58-2.59)	0.79 (0.52-1.20)	0.72 (0.45-1.15)
No response	1.07 (0.82-1.41)	1.43 (0.83-2.48)	1.18 (0.72-1.34)	1.31 (0.75-2.30)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.11 (0.91-1.36)	1.04 (0.71-1.50)	1.10 (0.84-1.43)	0.93 (0.70-1.23)
Social Functioning	**0.98 (0.97-0.99)**	**0.95 (0.92-0.98)**	**0.97 (0.95-0.99)**	**0.96 (0.93-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	0.96 (0.64-1.43)	0.56 (0.28-1.12)	1.49 (0.93-2.39)	1.16 (0.59-2.31)
2 or more	0.84 (0.49-1.46)	1.00 (0.25-3.99)	**3.47 (1.25-9.68)**	1.04 (0.53-2.06)
Perceived Psychological Stress	0.99 (0.98-1.01)	**0.96 (0.93-0.99)**	0.98 (0.96-1.00)	**0.97 (0.95-0.99)**
IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.03 (0.85-1.24)	1.19 (0.85-1.67)	1.13 (0.85-1.49)	1.10 (0.84-1.44)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.19 (0.94-1.51)	**1.93 (1.17-3.18)**	1.09 (0.75-1.60)	**2.05 (1.38-3.03)**
Very active disease	**1.35 (1.05-1.74)**	**1.87 (1.21-2.89)**	1.05 (0.73-1.50)	**2.25 (1.56-3.24)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.06 (0.74-1.50)	1.69 (0.99-2.86)	1.19 (0.74-1.91)	1.63 (0.82-3.24)

Time between diagnosis and 12m survey completion (years)	0.98 (0.94-1.03)	**0.89 (0.83-0.96)**	0.96 (0.90-1.03)	0.95 (0.87-1.04)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 5. Rate ratio and odds ratio estimates (95% CIs) for models of hospitalizations and hospital days, Exposed to physical abuse

Confounding Covariate	Hospitalized (non-IBD)*	Hospitalized (IBD)*	Hospital days (non-IBD)	Hospital days (IBD)
Sex				
Male	REF	REF	REF	REF
Female	1.02 (0.71-1.47)	0.85 (0.61-1.17)	1.30 (0.79-2.16)	0.89 (0.52-1.51)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.26 (0.87-1.81)	0.96 (0.68-1.36)	1.01 (0.60-1.70)	**0.47 (0.26-0.85)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	**2.11 (1.25-3.54)**	1.18 (0.74-1.88)	1.21 (0.57-2.57)	0.54 (0.25-1.16)
Three	1.19 (0.68-2.09)	0.96 (0.59-1.57)	0.84 (0.39-1.85)	0.46 (0.23-0.92)
Four	**2.28 (1.12-4.66)**	1.01 (0.59-1.73)	1.43 (0.53-3.83)	0.62 (0.23-1.70)
Five (highest income)	0.90 (0.51-1.59)	1.09 (0.66-1.79)	**0.41 (0.17-0.98)**	0.45 (0.20-1.03)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.75 (0.42-1.35)	0.59 (0.33-1.05)	0.56 (0.23-1.38)	0.84 (0.32-2.21)
Alcohol Use				
Less than once a week	REF	REF	REF	REF

1-3 times per week	0.89 (0.57-1.40)	0.91 (0.64-1.30)	0.71 (0.39-1.28)	0.73 (0.42-1.27)
>3 times per week	1.26 (0.60-2.67)	0.86 (0.36-2.09)	0.87 (0.40-1.89)	0.69 (0.31-1.55)
No response	1.63 (0.91-2.95)	0.94 (0.54-1.64)	1.69 (0.73-3.94)	1.11 (0.41-3.02)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.35 (0.94-1.92)	1.02 (0.74-1.39)	**1.79 (1.10-2.92)**	1.04 (0.60-1.79)
Social Functioning	**0.97 (0.94-0.99)**	0.97 (0.95-1.00)	**0.92 (0.87-0.97)**	**0.92 (0.87-0.97)**
Comorbidity				
0	REF	REF	REF	REF
1	0.84 (0.33-2.14)	1.17 (0.55-2.47)	1.74 (0.54-5.59)	1.21 (0.31-4.68)
2 or more	**6.81 (2.08-22.29)**	1.59 (0.84-3.00)	**10.14 (3.72-27.69)**	**3.89 (1.56-9.74)**
Perceived Psychological Stress	0.99 (0.95-1.02)	0.97 (0.94-1.00)	**0.95 (0.92-0.98)**	**0.93 (0.90-0.97)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.02 (0.72-1.44)	1.12 (082-1.52)	1.20 (0.73-1.96)	1.13 (0.69-1.84)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.92 (0.57-1.47)	**1.89 (1.22-2.92)**	0.99 (0.47-2.07)	**2.85 (1.38-5.88)**
Very active disease	**0.58 (0.36-0.93)**	**1.79 (1.16-2.78)**	**0.43 (0.25-0.76)**	**2.01 (1.03-3.92)**

Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**2.53** **(1.37-4.68)**	1.47 (0.67-3.23)	**3.23** **(1.33-7.88)**	2.09 (0.59-7.38)
Time between diagnosis and 12m survey completion (years)	1.03 (0.94-1.12)	0.99 (0.91-1.07)	0.89 (0.74-1.07)	0.92 (0.76-1.11)

* indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 6. Rate ratio estimates (95% CIs) for models of IBD, psychotropic, antibiotic, and other prescription drug dispensations, Exposed to physical abuse

Confounding Covariate	**IBD drugs**	**Psychotropic drugs**	**Antibiotic drugs**	**Other drugs**
Sex				
Male	REF	REF	REF	REF
Female	**0.67** **(0.51-0.88)**	1.65 (1.02-2.66)	1.30 (0.96-1.78)	1.26 (0.97-1.64)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.83 (0.64-1.08)	1.19 (0.67-2.11)	0.77 (0.58-1.02)	**2.35** **(1.84-3.02)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.85 (0.59-1.21)	1.41 (0.63-3.15)	1.20 (0.80-1.80)	1.02 (0.70-1.49)
Three	0.98 (0.65-1.48)	**2.36** **(1.09-5.12)**	1.31 (0.91-1.88)	1.03 (0.68-1.55)
Four	1.00 (0.65-1.56)	1.25 (0.40-3.87)	1.31 (0.76-2.27)	1.11 (0.71-1.72)
Five (highest income)	0.98	1.60	0.96	0.83

	(0.70-1.39)	(0.66-3.86)	(0.62-1.47)	(0.55-1.25)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.91 (0.63-1.29)	1.36 (0.60-3.07)	1.19 (0.80-1.79)	0.81 (0.49-1.35)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.98 (0.74-1.30)	0.67 (0.34-1.36)	0.81 (0.57-1.14)	0.75 (0.57-0.99)
>3 times per week	0.88 (0.47-1.67)	057 (0.15-2.21)	0.87 (0.49-1.55)	1.01 (0.50-2.04)
No response	1.23 (0.84-1.79)	1.25 (0.60-2.57)	**2.05 (1.32-3.17)**	1.47 (0.94-2.32)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.00 (0.78-1.27)	1.49 (0.92-2.41)	0.95 (0.71-1.26)	1.24 (0.96-1.60)
Social Functioning	0.99 (0.96-1.01)	**0.94 (0.90-0.98)**	0.98 (0.97-1.00)	**0.97 (0.95-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.24 (0.71-2.16)	2.01 (0.91-4.45)	**2.18 (1.23-3.88)**	1.56 (0.64-3.80)
2 or more	0.74 (0.39-1.40)	2.24 (0.46-10.86)	**3.25 (1.04-10.18)**	0.94 (0.28-3.11)
Perceived Psychological Stress	0.99 (0.96-1.01)	1.03 (0.97-1.09)	0.99 (0.97-1.02)	**0.98 (0.96-0.99)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	0.92 (0.72-1.17)	0.87 (0.52-1.45)	1.12 (0.88-1.43)	1.04 (0.80-1.35)

Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.38 (0.98-1.95)	0.77 (0.39-1.51)	**1.50 (1.03-2.20)**	1.07 (0.79-1.45)
Very active disease	**1.41 (1.01-1.97)**	1.05 (0.49-2.24)	**1.95 (1.35-2.82)**	**1.53 (1.09-2.16)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.82 (0.46-1.48)	0.78 (0.35-1.73)	1.43 (0.73-2.82)	1.30 (0.75-2.25)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.03)	0.95 (0.83-1.08)	0.98 (0.91-1.05)	0.98 (0.91-1.06)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 7. Rate ratio estimates (95% CIs) for models of GP and SP visit, Exposed to sexual abuse

Confounding Covariate	**GP visits (non-IBD)**	**GP visits (IBD)**	**SP Visits (non-IBD)**	**SP Visits (IBD)**
Sex				
Male	REF	REF	REF	REF
Female	**1.25 (1.01-1.55)**	0.82 (0.59-1.16)	1.18 (0.87-1.61)	0.79 (0.59-1.07)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.52 (1.27-1.81)**	**0.53 (0.37-0.75)**	**1.93 (1.48-2.52)**	**0.66 (0.49-0.88)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	1.00 (0.76-1.32)	0.83 (0.53-1.31)	0.95 (0.67-1.34)	0.94 (0.63-1.41)

Three	1.07 (0.78-1.48)	1.36 (0.74-2.50)	0.81 (0.58-1.13)	0.88 (0.59-1.32)
Four	1.10 (0.69-1.76)	1.70 (0.86-3.36)	1.29 (0.71-2.37)	0.77 (0.44-1.32)
Five (highest income)	0.82 (0.62-1.09)	0.63 (0.40-1.01)	1.03 (0.68-1.57)	0.79 (0.50-1.23)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	1.02 (0.78-1.33)	0.91 (0.58-1.45)	0.75 (0.52-1.08)	0.95 (0.61-1.49)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.84 (0.68-1.03)	0.83 (0.56-1.22)	1.02 (0.74-1.42)	0.81 (0.60-1.09)
>3 times per week	1.06 (0.71-1.59)	1.31 (0.61-2.82)	0.78 (0.51-1.19)	0.75 (0.47-1.19)
No response	1.06 (0.80-1.39)	1.48 (0.85-2.56)	1.19 (0.76-1.88)	1.33 (0.78-2.26)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.12 (0.92-1.36)	1.01 (0.69-1.49)	1.11 (0.85-1.43)	0.90 (0.69-1.19)
Social Functioning	0.99 (0.97-1.00)	**0.95 (0.93-0.98)**	**0.97 (0.95-0.99)**	**0.96 (0.93-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	0.99 (0.66-1.49)	0.55 (0.27-1.12)	1.54 (0.99-2.38)	1.07 (0.56-2.06)
2 or more	1.04 (0.64-1.68)	0.88 (0.23-3.36)	**3.52 (1.64-7.58)**	0.96 (0.51-1.81)
Perceived Psychological Stress	0.99 (0.98-1.01)	**0.96 (0.93-0.99)**	0.98 (0.96-1.00)	**0.97 (0.95-0.99)**

IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.04 (0.87-1.25)	1.21 (0.86-1.70)	1.09 (0.81-1.46)	1.11 (0.86-1.44)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.19 (0.95-1.51)	**1.98 (1.18-3.31)**	1.07 (0.73-1.58)	**2.03 (1.38-2.99)**
Very active disease	**1.37 (1.06-1.76)**	**1.96 (1.27-3.03)**	1.00 (0.70-1.44)	**2.32 (1.63-3.31)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.15 (0.81-1.63)	1.40 (0.84-2.34)	1.51 (0.97-2.35)	1.68 (0.89-3.18)
Time between diagnosis and 12m survey completion (years)	0.99 (0.94-1.04)	**0.89 (0.83-0.95)**	0.96 (0.90-1.03)	0.95 (0.87-1.04)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 8. Rate ratio and odds ratio estimates (95% CIs) for models of hospitalizations and hospital days, Exposed to sexual abuse

Confounding Covariate	**Hospitalized (non-IBD)***	**Hospitalized (IBD)***	**Hospital days (non-IBD)**	**Hospital days (IBD)**
Sex				
Male	REF	REF	REF	REF
Female	1.06 (0.73-1.54)	0.89 (0.64-1.23)	1.45 (0.85-2.45)	1.00 (0.58-1.72)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.22 (0.85-1.75)	0.94 (0.67-1.32)	1.01 (0.62-1.66)	**0.47 (0.27-0.81)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF

Two	**2.03**	1.23	1.32	0.66
	(1.21-3.39)	(0.78-1.94)	(0.68-2.60)	(0.33-1.34)
Three	1.14	1.00	0.90	0.55
	(0.66-1.97)	(0.61-1.61)	(0.43-1.88)	(0.29-1.05)
Four	**2.24**	1.07	1.65	0.70
	(1.11-4.51)	(0.63-1.79)	(0.64-4.22)	(0.27-1.78)
Five (highest income)	0.87	1.11	**0.43**	0.50
	(0.50-1.52)	(0.68-1.83)	**(0.19-0.98)**	(0.23-1.07)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.70	0.59	0.57	0.88
	(0.39-1.26)	(0.34-1.04)	(0.24-1.32)	(0.37-2.09)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.88	0.92	0.72	0.75
	(0.56-1.39)	(0.65-1.31)	(0.40-1.32)	(0.43-1.30)
>3 times per week	1.30	0.91	0.88	0.73
	(0.62-2.75)	(0.37-2.23)	(0.40-1.91)	(0.32-1.68)
No response	**1.83**	1.00	1.80	1.13
	(1.05-3.20)	(0.59-1.72)	(0.80-4.04)	(0.44-2.91)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.33	1.00	**1.79**	1.00
	(0.94-1.89)	(0.73-1.37)	**(1.10-2.92)**	(0.59-1.70)
Social Functioning	**0.96**	**0.97**	**0.92**	**0.91**
	(0.94-0.99)	**(0.94-1.00)**	**(0.87-0.97)**	**(0.86-0.97)**
Comorbidity				
0	REF	REF	REF	REF
1	0.73	1.10	1.51	1.21
	(0.28-1.92)	(0.52-2.31)	(0.47-4.89)	(0.32-4.51)
2 or more	**7.50**	1.39	**9.57**	**3.32**
	(2.76-20.93)	(0.77-2.52)	**(3.87-23.68)**	**(1.35-8.21)**

Perceived Psychological Stress	0.98 (0.95-1.01)	**0.97 (0.94-0.99)**	**0.95 (0.91-0.98)**	**0.93 (0.89-0.97)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.07 (0.76-1.50)	1.13 (084-1.54)	1.22 (0.76-1.98)	1.10 (0.69-1.76)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.88 (0.55-1.40)	**1.84 (1.20-2.84)**	0.98 (0.48-2.01)	**2.78 (1.38-5.60)**
Very active disease	**0.54 (0.33-0.87)**	**1.79 (1.16-2.75)**	**0.45 (0.26-0.75)**	**2.16 (1.15-4.03)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**3.14 (1.66-5.93)**	1.53 (0.77-3.04)	**3.28 (1.56-6.92)**	1.81 (0.63-5.18)
Time between diagnosis and 12m survey completion (years)	1.03 (0.95-1.12)	0.99 (0.91-1.07)	0.88 (0.73-1.07)	0.92 (0.77-1.10)

* indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 9: Rate ratio estimates (95% CIs) for models of IBD, psychotropic, antibiotic, and other prescription drug dispensations, Exposed to sexual abuse

Confounding Covariate	**IBD drugs**	**Psychotropic drugs**	**Antibiotic drugs**	**Other drugs**
Sex				
Male	REF	REF	REF	REF
Female	**0.65**	1.56	1.35	1.22

	(0.49-0.85)	(0.91-2.68)	(0.99-1.85)	(0.93-1.59)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.84 (0.65-1.09)	1.26 (0.72-2.21)	**0.75 (0.57-0.99)**	**2.38 (1.87-3.02)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.85 (0.60-1.22)	1.45 (0.64-3.28)	1.20 (0.81-1.79)	1.04 (0.72-1.51)
Three	1.00 (0.66-1.51)	**2.43 (1.14-5.15)**	1.32 (0.92-1.88)	1.03 (0.68-1.56)
Four	1.00 (0.65-1.53)	1.24 (0.39-3.94)	1.36 (0.79-2.36)	1.07 (0.69-1.67)
Five (highest income)	0.99 (0.70-1.40)	1.70 (0.69-4.18)	0.96 (0.62-1.49)	0.81 (0.54-1.21)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.92 (0.65-1.32)	1.41 (0.64-3.13)	1.20 (0.81-1.79)	0.80 (0.48-1.32)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.98 (0.74-1.30)	0.69 (0.35-1.39)	0.81 (0.58-1.15)	**0.76 (0.58-0.99)**
>3 times per week	0.85 (0.45-1.62)	0.55 (0.14-2.10)	0.90 (0.51-1.60)	0.98 (0.48-1.98)
No response	1.19 (0.81-1.75)	1.20 (0.59-2.45)	**2.16 (1.40-3.31)**	1.47 (0.94-2.29)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.01 (0.79-1.28)	1.52 (0.94-2.47)	0.94 (0.70-1.24)	1.25 (0.97-1.61)
Social Functioning	0.99	**0.94**	**0.98**	**0.97**

	(0.97-1.01)	**(0.90-0.98)**	**(0.96-1.00)**	**(0.95-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.27 (0.74-2.18)	2.21 (1.00-4.92)	**1.99 (1.14-3.48)**	1.60 (0.68-3.77)
2 or more	0.82 (0.47-1.42)	1.98 (0.41-9.53)	**3.25 (1.18-8.97)**	1.29 (0.53-3.12)
Perceived Psychological Stress	0.99 (0.96-1.01)	1.03 (0.97-1.08)	0.99 (0.97-1.01)	**0.98 (0.96-0.99)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	0.92 (0.72-1.16)	0.86 (0.51-1.45)	1.15 (0.91-1.47)	1.07 (0.83-1.39)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.37 (0.98-1.93)	0.77 (0.39-1.50)	**1.48 (1.01-2.16)**	1.10 (0.81-1.49)
Very active disease	**1.44 (1.03-2.01)**	1.08 (0.51-2.27)	**1.92 (1.34-2.76)**	**1.60 (1.14-2.25)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.76 (0.43-1.36)	0.78 (0.36-1.72)	1.48 (0.82-2.66)	1.37 (0.85-2.20)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.03)	0.95 (0.83-1.08)	0.98 (0.91-1.05)	0.98 (0.91-1.06)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Appendix F: Associations between Model Covariates and Healthcare Use for IBD Cohort Study Members Exposed to the Death of a Very Close Friend or Family Member, a Severe Illness/Injury, and an Upheaval between Parents

Supplementary Table 10: Rate ratio estimates (95% CIs) for models of GP and SP visit, Exposed to the death of a very close friend or family member

Confounding Covariate	GP visits (non-IBD)	GP visits (IBD)	SP Visits (non-IBD)	SP Visits (IBD)
Sex				
Male	REF	REF	REF	REF
Female	**1.26**	0.80	1.15	0.75
	(1.01-1.58)	(0.56-1.14)	(0.86-1.55)	(0.57-1.00)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.51**	**0.52**	**1.91**	**0.66**
	(1.27-1.80)	**(0.37-0.74)**	**(1.46-2.50)**	**(0.48-0.90)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	1.00	0.83	0.92	0.89
	(0.77-1.32)	(0.52-1.30)	(0.65-1.32)	(0.59-1.35)
Three	1.08	1.34	0.81	0.87
	(0.78-1.49)	(0.74-2.45)	(0.57-1.14)	(0.58-1.31)
Four	1.11	1.73	1.26	0.77
	(0.69-1.78)	(0.90-3.33)	(0.68-2.32)	(0.45-1.33)
Five (highest income)	0.82	0.63	1.02	0.77
	(0.62-1.09)	(0.39-1.00)	(0.67-1.56)	(0.49-1.22)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	1.02	0.92	0.75	0.95
	(0.78-1.32)	(0.58-1.46)	(0.52-1.08)	(0.60-1.50)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.84	0.84	1.01	0.80

	(0.68-1.03)	(0.56-1.26)	(0.74-1.39)	(0.59-1.09)
>3 times per week	1.06	1.32	0.76	0.73
	(0.71-1.59)	(0.61-2.87)	(0.50-1.17)	(0.45-1.18)
No response	1.06	1.52	1.20	1.38
	(0.81-1.39)	(0.87-2.66)	(0.75-1.90)	(0.80-2.36)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.12	1.03	1.10	0.90
	(0.91-1.36)	(0.71-1.51)	(0.85-1.43)	(0.68-1.20)
Social Functioning	**0.99**	**0.95**	**0.97**	**0.96**
	(0.97-1.00)	**(0.93-0.98)**	**(0.95-0.99)**	**(0.93-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	0.99	0.54	1.50	1.11
	(0.66-1.49)	(0.26-1.12)	(0.95-2.38)	(0.54-2.27)
2 or more	1.04	0.92	**3.58**	0.95
	(0.65-1.68)	(0.23-3.59)	**(1.61-7.92)**	(0.50-1.82)
Perceived Psychological Stress	0.99	**0.96**	0.97	**0.97**
	(0.98-1.01)	**(0.93-0.99)**	(0.96-1.00)	**(0.95-0.99)**
IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.04	1.19	1.09	1.11
	(0.86-1.25)	(0.85-1.67)	(0.81-1.46)	(0.85-1.44)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.19	**1.95**	1.06	**2.00**
	(0.94-1.51)	**(1.17-3.25)**	(0.72-1.55)	**(1.35-2.97)**
Very active disease	**1.37**	**1.93**	0.99	**2.22**
	(1.06-1.76)	**(1.25-2.97)**	(0.69-1.42)	**(1.55-3.18)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.15	1.35	1.50	1.51

	(0.81-1.64)	(0.81-2.26)	(0.95-2.34)	(0.81-2.81)
Time between diagnosis and 12m survey completion (years)	0.99 (0.94-1.03)	**0.89 (0.83-0.95)**	0.96 (0.90-1.03)	0.95 (0.87-1.04)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 11. Rate ratio and odds ratio estimates (95% CIs) for models of hospitalizations and hospital days, Exposed to the death of a very close friend or family member

Confounding Covariate	**Hospitalized (non-IBD)***	**Hospitalized (IBD)***	**Hospital days (non-IBD)**	**Hospital days (IBD)**
Sex				
Male	REF	REF	REF	REF
Female	1.03 (0.72-1.49)	0.86 (0.62-1.18)	1.34 (0.81-2.20)	0.86 (0.51-1.46)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.16 (0.81-1.67)	0.92 (0.65-1.31)	0.95 (0.56-1.61)	**0.47 (0.26-0.85)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	**2.07 (1.24-3.46)**	1.21 (0.76-1.91)	1.24 (0.60-2.55)	0.57 (0.27-1.21)
Three	1.19 (0.68-2.07)	1.00 (0.61-1.62)	0.89 (0.42-1.90)	0.53 (0.27-1.04)
Four	**2.38 (1.18-4.84)**	1.08 (0.64-1.83)	1.62 (0.65-4.02)	0.72 (0.27-1.94)
Five (highest income)	0.89 (0.50-1.56)	1.11 (0.68-1.82)	**0.44 (0.19-0.99)**	0.47 (0.21-1.04)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.69 (0.38-1.25)	0.59 (0.34-1.04)	0.56 (0.24-1.32)	0.86 (0.35-2.12)

Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.91 (0.58-1.42)	0.93 (0.65-1.34)	0.72 (0.40-1.32)	0.77 (0.43-1.36)
>3 times per week	1.33 (0.63-2.85)	0.90 (0.37-2.18)	0.93 (0.42-2.07)	0.70 (0.31-1.59)
No response	**1.98 (1.13-3.46)**	1.04 (0.60-1.78)	1.94 (0.90-4.18)	1.18 (0.44-3.18)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.35 (0.95-1.92)	1.00 (0.73-1.38)	**1.82 (1.08-3.06)**	0.98 (0.55-1.76)
Social Functioning	**0.96 (0.95-1.01)**	0.97 (0.94-1.00)	**0.92 (0.87-0.97)**	**0.91 (0.86-0.97)**
Comorbidity				
0	REF	REF	REF	REF
1	0.67 (0.26-1.77)	1.03 (0.48-2.19)	1.51 (0.45-5.10)	1.17 (0.24-5.56)
2 or more	**8.10 (3.05-21.55)**	1.38 (0.78-2.46)	**10.26 (4.10-25.71)**	**3.34 (1.34-8.32)**
Perceived Psychological Stress	0.98 (0.95-1.01)	0.97 (0.94-1.00)	**0.95 (0.92-0.98)**	**0.93 (0.89-0.96)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.07 (0.76-1.51)	1.13 (083-1.54)	1.21 (0.74-1.97)	1.09 (0.67-1.77)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.87 (0.55-1.38)	**1.82 (1.18-2.81)**	0.95 (0.46-1.97)	**2.77 (1.35-5.70)**

Very active disease	**0.53 (0.33-0.86)**	**1.76 (1.14-2.71)**	**0.41 (0.24-0.71)**	**2.02 (1.05-3.86)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**2.95 (1.55-5.58)**	1.48 (0.75-2.92)	**2.97 (1.36-6.45)**	1.69 (0.48-5.91)
Time between diagnosis and 12m survey completion (years)	1.03 (0.95-1.12)	0.99 (0.91-1.07)	0.89 (0.74-1.07)	0.92 (0.77-1.10)

* indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 12. Rate ratio estimates (95% CIs) for models of IBD, psychotropic, antibiotic, and other prescription drug dispensations, Exposed to the death of a very close friend or family member

Confounding Covariate	**IBD drugs**	**Psychotropic drugs**	**Antibiotic drugs**	**Other drugs**
Sex				
Male	REF	REF	REF	REF
Female	**0.65 (0.50-0.85)**	1.61 (0.98-2.63)	1.33 (0.97-1.81)	1.21 (0.93-1.58)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.85 (0.66-1.10)	1.26 (0.72-2.22)	**0.75 (0.56-1.00)**	**2.37 (1.87-3.02)**
Income Quintile *				
One (lowest income)	REF	REF	REF	REF
Two	0.87 (0.61-1.24)	1.51 (0.67-3.34)	1.20 (0.81-1.77)	1.03 (0.72-1.51)
Three	0.97 (0.65-1.46)	**2.49 (1.16-5.37)**	1.33 (0.93-1.89)	1.03 (0.68-1.55)
Four	0.97	1.27	1.37	1.07

	(0.62-1.50)	(0.40-4.05)	(0.80-2.36)	(0.69-1.67)
Five (highest income)	0.99 (0.70-1.40)	1.67 (0.69-4.06)	0.97 (0.63-1.51)	0.81 (0.54-1.22)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.93 (0.65-1.32)	1.40 (0.63-3.12)	1.21 (0.81-1.80)	0.80 (0.49-1.32)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.97 (0.73-1.29)	0.71 (0.35-1.42)	0.82 (0.58-1.17)	0.76 (0.58-0.99)
>3 times per week	0.84 (0.46-1.56)	0.54 (0.14-2.04)	0.90 (0.50-1.60)	0.97 (0.48-1.97)
No response	1.18 (0.80-1.74)	119 (0.58-2.44)	**2.18 (1.42-3.36)**	1.46 (0.95-2.26)
Body Mass Index *				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.00 (0.78-1.27)	1.50 (0.94-2.39)	0.94 (0.71-1.25)	1.25 (0.97-1.61)
Social Functioning *	0.99 (0.97-1.01)	**0.94 (0.90-0.98)**	0.98 (0.97-1.00)	**0.97 (0.95-1.00)**
Comorbidity				
0	REF	REF	REF	REF
1	1.33 (0.76-2.28)	2.25 (1.04-4.87)	**1.93 (1.09-3.41)**	1.58 (0.68-3.69)
2 or more	0.79 (0.46-1.36)	1.89 (0.40-8.95)	**3.34 (1.20-9.26)**	1.30 (0.53-3.15)
Perceived Psychological Stress	0.99 (0.96-1.01)	1.03 (0.97-1.08)	0.99 (0.97-1.01)	**0.98 (0.96-1.00)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF

Crohn's Disease	0.92 (0.73-1.17)	0.85 (0.51-1.42)	1.15 (0.90-1.47)	1.07 (0.83-1.39)
Disease Activity *				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.42 (1.01-1.99)	0.77 (0.39-1.52)	**1.47 (1.01-2.14)**	1.09 (0.80-1.47)
Very active disease	**1.48 (1.07-2.06)**	1.08 (0.51-2.26)	**1.91 (1.33-2.74)**	**1.59 (1.13-2.23)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.82 (0.45-1.51)	0.83 (0.38-1.81)	1.46 (0.81-2.63)	1.35 (0.83-2.20)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.03)	0.94 (0.83-1.07)	0.98 (0.91-1.06)	0.98 (0.91-1.06)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 13. Rate ratio estimates (95% CIs) for models of GP and SP visit, Exposed to severe illness or injury

Confounding Covariate	**GP visits (non-IBD)**	**GP visits (IBD)**	**SP Visits (non-IBD)**	**SP Visits (IBD)**
Sex				
Male	REF	REF	REF	REF
Female	**1.26 (1.01-1.57)**	0.79 (0.56-1.12)	1.15 (0.85-1.56)	0.76 (0.57-1.02)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.52 (1.27-1.82)**	**0.53 (0.38-0.76)**	**1.94 (1.47-2.55)**	**0.65 (0.48-0.89)**
Income Quintile				

One (lowest income)	REF	REF	REF	REF
Two	0.98 (0.74-1.29)	0.78 (0.49-1.25)	0.95 (0.66-1.37)	0.87 (0.58-1.32)
Three	1.05 (0.76-1.45)	1.24 (0.69-2.24)	0.83 (0.58-1.17)	0.85 (0.57-1.28)
Four	1.07 (0.66-1.74)	1.58 (0.82-3.08)	1.27 (0.69-2.34)	0.75 (0.43-1.29)
Five (highest income)	0.81 (0.61-1.07)	0.61 (0.38-0.97)	1.04 (0.68-1.60)	0.76 (0.48-1.20)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.99 (0.76-1.30)	0.89 (0.56-1.40)	0.75 (0.52-1.09)	0.97 (0.61-1.53)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.84 (0.68-1.03)	0.82 (0.56-1.20)	1.02 (0.73-1.41)	0.79 (0.58-1.07)
>3 times per week	1.04 (0.69-1.55)	1.27 (0.60-2.73)	0.76 (0.49-1.18)	0.74 (0.45-1.21)
No response	1.02 (0.78-1.35)	1.44 (0.84-2.48)	1.21 (0.76-1.92)	1.35 (0.78-2.33)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.12 (0.92-1.37)	1.04 (0.72-1.51)	1.10 (0.85-1.43)	0.90 (0.68-1.20)
Social Functioning	**0.98 (0.97-0.99)**	**0.95 (0.93-0.98)**	**0.97 (0.95-0.99)**	**0.96 (0.93-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.00 (0.67-1.51)	0.55 (0.27-1.13)	1.50 (0.96-2.36)	1.12 (0.57-2.23)
2 or more	1.00	0.86	**3.64**	0.94

	(0.62-1.60)	(0.22-3.46)	**(1.61-8.20)**	(0.49-1.83)
Perceived Psychological Stress	1.00	**0.96**	0.98	**0.97**
	(0.98-1.01)	**(0.93-0.99)**	(0.96-1.00)	**(0.95-0.99)**
IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.04	1.18	1.10	1.10
	(0.86-1.25)	(0.85-1.65)	(0.82-1.48)	(0.85-1.43)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.21	**1.99**	1.05	**2.01**
	(0.95-1.52)	**(1.20-3.29)**	(0.71-1.54)	**(1.36-2.97)**
Very active disease	**1.36**	**1.97**	1.01	**2.21**
	(1.06-1.75)	**(1.28-3.02)**	(0.70-1.45)	**(1.54-3.17)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.22	1.44	1.52	1.45
	(0.84-1.77)	(0.86-2.41)	(0.96-2.40)	(0.81-2.61)
Time between diagnosis and 12m survey completion (years)	0.99	**0.89**	0.96	0.95
	(0.94-1.03)	**(0.83-0.95)**	(0.90-1.03)	(0.87-1.04)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 14. Rate ratio and odds ratio estimates (95% CIs) for models of hospitalizations and hospital days, Exposed to severe illness or injury

Confounding Covariate	**Hospitalized (non-IBD)***	**Hospitalized (IBD)***	**Hospital days (non-IBD)**	**Hospital days (IBD)**
Sex				
Male	REF	REF	REF	REF
Female	1.05	0.87	1.34	0.89
	(0.73-1.50)	(0.63-1.20)	(0.81-2.22)	(0.52-1.51)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.20	0.92	0.99	**0.46**

	(0.84-1.73)	(0.65-1.30)	(0.59-1.66)	**(0.26-0.83)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	**1.98**	1.19	1.22	0.58
	(1.18-3.32)	(0.75-1.90)	(0.60-2.50)	(0.28-1.20)
Three	1.12	0.98	0.86	0.51
	(0.64-1.95)	(0.61-1.60)	(0.41-1.83)	(0.26-1.01)
Four	**2.20**	1.07	1.57	0.69
	(1.10-4.42)	(0.63-1.81)	(0.64-3.84)	(0.26-1.82)
Five (highest income)	0.86	1.10	**0.43**	0.49
	(0.50-1.50)	(0.67-1.81)	**(0.19-0.97)**	(0.22-1.08)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.70	0.61	0.57	0.93
	(0.39-1.26)	(0.35-1.06)	(0.25-1.31)	(0.38-2.25)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.88	0.92	0.69	0.73
	(0.56-1.37)	(0.64-1.31)	(0.38-1.24)	(0.41-1.29)
>3 times per week	1.31	0.92	0.92	0.71
	(0.62-2.76)	(0.38-2.25)	(0.40-2.09)	(0.30-1.67)
No response	**1.83**	1.01	1.82	1.13
	(1.04-3.21)	(0.58-1.75)	(0.83-3.99)	(0.42-3.00)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.34	1.01	**1.82**	1.00
	(0.94-1.90)	(0.74-1.37)	**(1.11-3.00)**	(0.58-1.71)
Social Functioning	**0.97**	0.97	**0.92**	**0.92**
	(0.94-0.99)	(0.95-1.00)	**(0.88-0.97)**	**(0.87-0.97)**
Comorbidity				
0	REF	REF	REF	REF
1	0.72	1.06	1.55	1.14

	(0.27-1.93)	(0.50-2.26)	(0.47-5.18)	(0.28-4.69)
2 or more	**7.47**	1.44	**9.96**	**3.06**
	(2.73-20.44)	(0.78-2.63)	**(3.86-25.72)**	**(1.19-7.86)**
Perceived Psychological Stress	0.98	**0.97**	**0.95**	**0.93**
	(0.95-1.02)	**(0.94-0.99)**	**(0.92-0.98)**	**(0.89-0.96)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.06	1.12	1.18	1.08
	(0.75-1.49)	(082-1.52)	(0.73-1.89)	(0.68-1.73)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.88	**1.83**	0.94	**2.79**
	(0.55-1.40)	**(1.19-2.82)**	(0.46-1.95)	**(1.37-5.70)**
Very active disease	**0.53**	**1.74**	**0.41**	**1.96**
	(0.33-0.86)	**(1.13-2.66)**	**(0.23-0.72)**	**(1.02-3.77)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**3.11**	1.44	**2.82**	1.52
	(1.68-5.77)	(0.76-2.74)	**(1.38-5.77)**	(0.50-4.61)
Time between diagnosis and 12m survey completion (years)	1.03	0.99	0.89	0.93
	(0.95-1.12)	(0.91-1.07)	(0.75-1.07)	(0.78-1.10)

* indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 15. Rate ratio estimates (95% CIs) for models of IBD, psychotropic, antibiotic, and other prescription drug dispensations, Exposed to severe illness or injury

Confounding Covariate	**IBD drugs**	**Psychotropic drugs**	**Antibiotic drugs**	**Other drugs**

Sex				
Male	REF	REF	REF	REF
Female	**0.67 (0.51-0.87)**	1.65 (1.01-2.70)	1.34 (0.99-1.81)	1.21 (0.93-1.59)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.83 (0.64-1.06)	1.19 (0.69-2.05)	**0.75 (0.57-0.99)**	**2.36 (1.85-3.01)**
Income Quintile *				
One (lowest income)	REF	REF	REF	REF
Two	0.87 (0.61-1.25)	1.63 (0.74-3.59)	1.12 (0.76-1.66)	1.02 (0.70-1.49)
Three	1.00 (0.66-1.51)	**2.75 (1.26-6.01)**	1.25 (0.88-1.79)	1.01 (0.66-1.55)
Four	1.02 (0.65-1.58)	1.54 (0.50-4.73)	1.26 (0.73-2.15)	1.07 (0.68-1.68)
Five (highest income)	0.98 (0.70-1.39)	1.76 (0.74-4.18)	0.93 (0.60-1.45)	0.80 (0.53-1.20)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.92 (0.65-1.32)	1.50 (0.67-3.39)	1.17 (0.78-1.75)	0.81 (0.49-1.32)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.98 (0.74-1.30)	0.69 (0.35-1.40)	0.81 (0.58-1.13)	0.75 (0.57-0.98)
>3 times per week	0.89 (0.47-1.67)	0.63 (0.17-2.41)	0.88 (0.49-1.58)	0.99 (0.49-2.02)
No response	1.20 (0.82-1.76)	1.35 (0.67-2.74)	**2.12 (1.38-3.24)**	1.45 (0.93-2.27)
Body Mass Index *				
Healthy weight	REF	REF	REF	REF

Underweight / Overweight / Obese	1.00 (0.79-1.27)	1.43 (0.89-2.30)	0.96 (0.72-1.27)	1.25 (0.97-1.61)
Social Functioning *	0.99 (0.97-1.01)	**0.94 (0.90-0.98)**	**0.98 (0.96-1.00)**	**0.97 (0.95-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.27 (0.74-2.18)	**2.16 (1.00-4.63)**	**1.97 (1.16-3.36)**	1.61 (0.68-3.81)
2 or more	0.84 (0.49-1.44)	2.33 (0.49-11.03)	**3.06 (1.12-8.40)**	1.29 (0.53-3.15)
Perceived Psychological Stress	0.99 (0.96-1.01)	1.02 (0.97-1.07)	0.97 (0.97-1.01)	**0.98 (0.96-0.99)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	0.91 (0.72-1.16)	0.82 (0.49-1.38)	1.16 (0.91-1.47)	1.06 (0.82-1.37)
Disease Activity *				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.38 (0.99-1.94)	0.79 (0.41-1.51)	**1.49 (1.02-2.16)**	1.09 (0.81-1.48)
Very active disease	**1.44 (1.03-2.01)**	1.14 (0.53-2.43)	**1.89 (1.32-2.70)**	**1.57 (1.12-2.20)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.75 (0.41-1.36)	0.66 (0.30-1.44)	1.62 (0.90-2.93)	1.33 (0.81-2.18)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.03)	0.95 (0.84-1.07)	0.98 (0.91-1.05)	0.98 (0.91-1.06)

REF indicates reference category

Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 16. Rate ratio estimates (95% CIs) for models of GP and SP visit, Exposed to an upheaval between parents

Confounding Covariate	GP visits (non-IBD)	GP visits (IBD)	SP Visits (non-IBD)	SP Visits (IBD)
Sex				
Male	REF	REF	REF	REF
Female	**1.26 (1.01-1.57)**	0.79 (0.56-1.13)	1.15 (0.86-1.54)	0.72 (0.54-0.95)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.50 (1.26-1.79)**	**0.53 (0.37-0.74)**	**1.95 (1.49-2.54)**	**0.68 (0.51-0.90)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	1.01 (0.76-1.33)	0.82 (0.52-1.28)	0.90 (0.63-1.30)	0.86 (0.57-1.28)
Three	1.07 (0.78-1.47)	1.27 (0.70-2.32)	0.80 (0.57-1.14)	0.84 (0.56-1.26)
Four	1.11 (0.68-1.81)	1.65 (0.83-3.24)	1.23 (0.67-2.24)	0.73 (0.42-1.28)
Five (highest income)	0.82 (0.62-1.08)	0.63 (0.38-1.03)	1.01 (0.65-1.56)	0.75 (0.48-1.18)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	1.01 (0.78-1.32)	0.94 (0.59-1.50)	0.76 (0.52-1.11)	0.99 (0.64-1.53)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.84 (0.68-1.03)	0.83 (0.57-1.22)	0.99 (0.73-1.36)	0.80 (0.60-1.07)

>3 times per week	1.06 (0.71-1.58)	1.27 (0.59-2.74)	0.77 (0.51-1.18)	0.70 (0.44-1.11)
No response	1.05 (0.80-1.38)	1.42 (0.82-2.47)	1.23 (0.74-2.02)	1.26 (0.73-2.18)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.12 (0.92-1.37)	1.03 (0.71-1.50)	1.10 (0.85-1.42)	0.90 (0.69-1.18)
Social Functioning	**0.98 (0.97-1.00)**	**0.95 (0.93-0.98)**	**0.97 (0.95-0.99)**	**0.96 (0.93-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.00 (0.65-1.54)	0.64 (0.31-1.32)	1.51 (0.92-2.49)	1.22 (0.64-2.35)
2 or more	1.06 (0.65-1.71)	0.99 (0.24-4.03)	**3.34 (1.56-7.13)**	1.09 (0.55-2.16)
Perceived Psychological Stress	1.00 (0.98-1.01)	**0.96 (0.93-0.99)**	0.98 (0.96-1.00)	**0.98 (0.96-0.99)**
IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.04 (0.87-1.25)	1.20 (0.86-1.67)	1.11 (0.82-1.49)	1.14 (0.88-1.48)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.20 (0.95-1.51)	**1.99 (1.20-3.31)**	1.06 (0.73-1.55)	**2.13 (1.46-3.12)**
Very active disease	**1.38 (1.06-1.78)**	**2.01 (1.31-3.09)**	0.99 (0.69-1.42)	**2.31 (1.64-3.25)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.16 (0.81-1.66)	1.42 (0.86-1.67)	1.46 (0.93-2.31)	1.61 (0.94-2.77)

Time between diagnosis and 12m survey completion (years)	0.99 (0.94-1.04)	**0.89 (0.83-0.96)**	0.96 (0.90-1.03)	0.95 (0.87-1.04)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 17. Rate ratio and odds ratio estimates (95% CIs) for models of hospitalizations and hospital days, Exposed to an upheaval between parents

Confounding Covariate	Hospitalized (non-IBD)*	Hospitalized (IBD)*	Hospital days (non-IBD)	Hospital days (IBD)
Sex				
Male	REF	REF	REF	REF
Female	1.04 (0.72-1.50)	0.84 (0.61-1.16)	1.36 (0.82-2.25)	0.76 (0.45-1.28)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.22 (0.84-1.75)	0.94 (0.67-1.33)	1.04 (0.63-1.70)	**0.50 (0.29-0.85)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	**1.99 (1.19-3.35)**	1.15 (0.72-1.81)	1.26 (0.61-2.58)	0.51 (0.24-1.06)
Three	1.14 (0.66-1.97)	0.96 (0.59-1.56)	0.85 (0.40-1.82)	0.50 (0.25-1.03)
Four	**2.23 (1.10-4.50)**	1.02 (0.60-1.74)	1.60 (0.62-4.17)	0.64 (0.24-1.74)
Five (highest income)	0.87 (0.50-1.52)	1.08 (0.65-1.78)	0.44 (0.19-1.01)	0.47 (0.22-1.03)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.71 (0.39-1.29)	0.62 (0.36-1.07)	0.59 (0.26-1.34)	0.98 (0.42-2.27)
Alcohol Use				

Less than once a week	REF	REF	REF	REF
1-3 times per week	0.88 (0.56-1.38)	0.93 (0.66-1.32)	0.70 (0.38-1.28)	0.72 (0.42-1.24)
>3 times per week	1.30 (0.62-2.75)	0.86 (0.35-2.08)	0.85 (0.40-1.81)	0.65 (0.30-1.43)
No response	**1.85 (1.05-3.28)**	0.94 (0.53-1.64)	1.67 (0.71-3.93)	1.00 (0.37-2.70)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.33 (0.94-1.89)	0.99 (0.73-1.36)	**1.82 (1.10-3.02)**	1.01 (0.60-1.70)
Social Functioning	**0.97 (0.94-0.99)**	0.97 (0.95-1.00)	**0.92 (0.88-0.97)**	**0.92 (0.87-0.97)**
Comorbidity				
0	REF	REF	REF	REF
1	0.70 (0.23-2.08)	1.09 (0.48-2.50)	1.78 (0.56-5.65)	1.51 (0.43-5.35)
2 or more	**7.53 (2.79-20.33)**	1.50 (0.80-2.82)	**11.25 (4.37-28.95)**	**4.60 (1.79-11.83)**
Perceived Psychological Stress	0.98 (0.95-1.02)	**0.97 (0.95-0.99)**	**0.95 (0.92-0.98)**	**0.94 (0.91-0.98)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.07 (0.76-1.51)	1.15 (085-1.56)	1.23 (0.76-1.98)	1.17 (0.72-1.91)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.87 (0.55-1.39)	**1.85 (1.20-2.84)**	0.98 (0.46-2.07)	**3.17 (1.59-6.33)**
Very active disease	**0.53**	**1.76**	**0.45**	**2.11**

	(0.33-0.86)	**(1.15-2.68)**	**(0.26-0.76)**	**(1.15-3.85)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**3.18** **(1.66-6.09)**	1.66 (0.86-3.17)	**3.24** **(1.57-6.70)**	1.80 (0.67-4.85)
Time between diagnosis and 12m survey completion (years)	1.03 (0.95-1.12)	0.99 (0.91-1.07)	0.89 (0.74-1.06)	0.92 (0.78-1.09)

* indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 18. Rate ratio estimates (95% CIs) for models of IBD, psychotropic, antibiotic, and other prescription drug dispensations, Exposed to an upheaval between parents

Confounding Covariate	**IBD drugs**	**Psychotropic drugs**	**Antibiotic drugs**	**Other drugs**
Sex				
Male	REF	REF	REF	REF
Female	**0.65** **(0.50-0.86)**	1.60 (0.99-2.58)	1.31 (0.96-1.78)	1.19 (0.91-1.55)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.85 (0.65-1.09)	1.23 (0.71-2.12)	0.77 (0.58-1.01)	**2.38** **(1.87-3.02)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.87 (0.60-1.25)	1.60 (0.74-3.48)	1.14 (0.76-1.71)	1.03 (0.71-1.49)
Three	1.00 (0.65-1.52)	**2.45** **(1.12-5.34)**	1.30 (0.91-1.86)	1.01 (0.67-1.53)
Four	1.01 (0.64-1.57)	1.30 (0.43-3.95)	1.35 (0.78-2.32)	1.07 (0.69-1.66)

Five (highest income)	0.99 (0.70-1.39)	1.68 (0.70-4.07)	0.96 (0.61-1.50)	0.81 (0.54-1.22)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.92 (0.64-1.31)	1.32 (0.60-2.94)	1.24 (0.83-1.86)	0.80 (0.49-1.32)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.98 (0.74-1.31)	0.73 (0.36-1.50)	0.81 (0.57-1.15)	0.76 (0.58-0.99)
>3 times per week	0.86 (0.46-1.61)	0.55 (0.14-2.10)	0.91 (0.51-1.63)	0.97 (0.48-1.95)
No response	1.19 (0.81-1.75)	1.11 (0.54-2.26)	**2.12 (1.38-3.27)**	1.42 (0.91-2.23)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.00 (0.78-1.27)	1.49 (0.92-2.40)	0.92 (0.70-1.23)	1.25 (0.97-1.61)
Social Functioning	0.99 (0.97-1.01)	**0.94 (0.90-0.98)**	0.98 (0.97-1.00)	**0.97 (0.95-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.26 (0.70-2.27)	**2.56 (1.20-5.46)**	**2.05 (1.12-3.74)**	1.68 (0.68-4.15)
2 or more	0.81 (0.48-1.39)	2.34 (0.47-11.63)	**3.41 (1.18-9.57)**	1.33 (0.54-3.25)
Perceived Psychological Stress	0.99 (0.96-1.01)	1.03 (0.97-1.09)	0.99 (0.97-1.02)	**0.98 (0.96-1.00)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	0.93	0.82	1.17	1.07

	(0.73-1.18)	(0.49-1.36)	(0.92-1.49)	(0.83-1.39)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.40 (0.99-1.98)	0.80 (0.40-1.58)	**1.48 (1.02-2.17)**	1.10 (0.81-1.49)
Very active disease	**1.46 (1.04-2.03)**	1.09 (0.53-2.28)	**1.89 (1.31-2.72)**	**1.60 (1.14-2.24)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.82 (0.44-1.51)	0.80 (0.39-1.65)	1.50 (0.83-2.72)	1.39 (0.86-2.25)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.03)	0.95 (0.83-1.08)	0.97 (0.91-1.05)	0.98 (0.91-1.06)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Appendix G: Associations between Model Covariates and Healthcare Use for IBD Cohort Members Reporting High Perceived Trauma from ACEs

Supplementary Table 19. Rate ratio estimates (95% CIs) for models of GP and SP visits

Covariate	GP visits (non-IBD)	GP visits (IBD)	SP Visits (non-IBD)	SP Visits (IBD)
Sex				
Male	REF	REF	REF	REF
Female	1.11 (0.86-1.44)	0.82 (0.56-1.22)	1.07 (0.75-1.51)	0.72 (0.53-0.98)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	**1.33 (1.08-1.65)**	**0.56 (0.37-0.85)**	**1.62 (1.18-2.21)**	**0.54 (0.39-0.77)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.97 (0.71-1.33)	0.72 (0.43-1.20)	0.83 (0.55-1.26)	0.71 (0.46-1.10)
Three	1.08 (0.76-1.53)	1.19 (0.63-2.26)	0.83 (0.56-1.24)	0.76 (0.49-1.17)
Four	1.27 (0.74-2.17)	1.03 (0.47-2.25)	1.14 (0.58-2.26)	**0.60 (0.36-0.98)**
Five (highest income)	0.85 (0.63-1.15)	0.60 (0.36-0.99)	0.95 (0.58-1.58)	0.67 (0.42-1.07)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	1.12 (0.84-1.50)	1.19 (0.70-2.02)	0.83 (0.54-1.27)	1.24 (0.75-2.04)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	0.75 (0.60-0.96)	0.83 (0.57-1.22)	1.02 (0.68-1.54)	0.97 (0.71-1.34)

>3 times per week	1.42 (0.84-2.40)	1.27 (0.59-2.74)	1.19 (0.73-1.94)	0.96 (0.53-1.76)
No response	1.02 (0.73-1.41)	1.42 (0.82-2.47)	1.22 (0.77-1.94)	1.11 (0.65-1.90)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.04 (0.83-1.30)	0.91 (0.62-1.34)	1.13 (0.82-1.55)	1.11 (0.81-1.52)
Social Functioning	0.99 (0.97-1.01)	**0.95 (0.92-0.97)**	**0.96 (0.94-0.99)**	**0.95 (0.91-0.98)**
Comorbidity				
0	REF	REF	REF	REF
1	1.09 (0.73-1.61)	0.63 (0.30-1.32)	1.52 (0.95-2.45)	1.17 (0.58-2.36)
2 or more	1.25 (0.82-1.91)	1.02 (0.24-4.29)	**4.45 (1.79-11.05)**	0.98 (0.48-2.00)
Perceived Psychological Stress	1.00 (0.98-1.02)	**0.97 (0.94-0.99)**	0.98 (0.95-1.01)	**0.96 (0.93-0.98)**
IBD Disease Type				
Ulcerative/Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.03 (0.83-1.26)	1.35 (0.94-1.93)	1.04 (0.75-1.44)	1.10 (0.83-1.45)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	1.21 (0.94-1.58)	**1.90 (1.09-3.28)**	1.01 (0.62-1.64)	**1.84 (1.24-2.74)**
Very active disease	**1.39 (1.04-1.86)**	**2.43 (1.59-3.73)**	0.82 (0.54-1.26)	**2.29 (1.57-3.34)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	1.17 (0.77-1.80)	1.71 (0.95-3.08)	**1.70 (1.07-2.70)**	**1.90 (1.03-3.49)**

Time between diagnosis and 12m survey completion (years)	1.01 (0.95-1.06)	**0.91 (0.85-0.98)**	0.94 (0.87-1.01)	0.93 (0.85-1.02)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 20. Rate ratio and odds ratio estimates (95% CIs) for models of hospitalizations and hospital days

Confounding Covariate	Hospitalized (non-IBD)*	Hospitalized (IBD)*	Hospital days (non-IBD)	Hospital days (IBD)
Sex				
Male	REF	REF	REF	REF
Female	0.81 (0.51-1.27)	0.87 (0.60-1.26)	1.30 (0.66-2.57)	0.86 (0.52-1.44)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	1.18 (0.75-1.84)	0.77 (0.50-1.20)	0.92 (0.49-1.74)	**0.32 (0.16-0.62)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	**2.53 (1.38-4.63)**	1.12 (0.65-1.95)	0.92 (0.39-2.17)	0.41 (0.19-0.86)
Three	1.36 (0.71-2.60)	0.96 (0.53-1.72)	0.90 (0.39-2.05)	0.58 (0.29-1.17)
Four	**2.56 (1.08-6.05)**	0.85 (0.44-1.64)	1.50 (0.53-4.26)	0.48 (0.23-1.02)
Five (highest income)	1.08 (0.56-2.07)	1.09 (0.63-1.89)	0.44 (0.17-1.16)	0.55 (0.23-1.32)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.61 (0.30-1.23)	0.67 (0.35-1.29)	0.60 (0.22-1.63)	1.37 (0.49-3.82)
Alcohol Use				
Less than once a	REF	REF	REF	REF

week				
1-3 times per week	0.84 (0.48-1.45)	1.08 (0.73-1.60)	0.93 (0.44-1.94)	0.90 (0.51-1.59)
>3 times per week	0.95 (0.30-3.02)	1.68 (0.54-5.26)	0.79 (0.22-2.80)	1.33 (0.49-3.64)
No response	**2.25 (1.14-4.41)**	0.86 (0.43-1.69)	1.51 (0.55-4.16)	1.02 (0.37-2.82)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.45 (0.92-2.30)	1.32 (0.91-1.91)	**2.13 (0.98-4.64)**	1.45 (0.84-2.50)
Social Functioning	0.98 (0.94-1.01)	**0.96 (0.92-0.99)**	**0.92 (0.86-1.00)**	**0.90 (0.85-0.96)**
Comorbidity				
0	REF	REF	REF	REF
1	0.66 (0.24-1.85)	1.10 (0.50-2.43)	1.44 (0.45-4.63)	1.51 (0.43-5.35)
2 or more	**11.29 (4.39-29.02)**	1.57 (0.77-3.20)	**13.53 (4.96-36.91)**	**4.60 (1.79-11.83)**
Perceived Psychological Stress	0.98 (0.94-1.02)	**0.96 (0.93-0.99)**	**0.95 (0.90-0.99)**	**0.94 (0.91-0.98)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	1.25 (0.83-1.89)	1.11 (077-1.61)	1.48 (0.82-2.68)	1.10 (0.67-1.82)
Disease Activity				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	0.85 (0.47-1.51)	**1.87 (1.12-3.13)**	0.71 (0.27-1.89)	**2.03 (1.03-4.00)**
Very active disease	0.63	**1.91**	**0.47**	**1.95**

	(0.36-1.11)	**(1.14-3.22)**	**(0.26-0.85)**	**(1.01-3.79)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	**3.50** **(1.60-7.68)**	1.89 (0.83-4.29)	**4.03** **(1.77-9.14)**	2.65 (0.75-9.35)
Time between diagnosis and 12m survey completion (years)	1.09 (0.99-1.20)	0.95 (0.87-1.05)	0.89 (0.71-1.11)	0.89 (0.76-1.05)

* indicates odds ratio estimates
REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05

Supplementary Table 21. Rate ratio estimates (95% CIs) for models of IBD, psychotropic, antibiotic, and other prescription drug dispensations

Confounding Covariate	**IBD drugs**	**Psychotropic drugs**	**Antibiotic drugs**	**Other drugs**
Sex				
Male	REF	REF	REF	REF
Female	**0.63** **(0.47-0.84)**	1.29 (0.73-2.30)	1.23 (0.88-1.72)	1.03 (0.77-1.37)
Age (years)				
18 – 44	REF	REF	REF	REF
45+	0.79 (0.57-1.09)	1.40 (0.74-2.64)	0.62 (0.46-0.84)	**1.94** **(1.47-2.57)**
Income Quintile				
One (lowest income)	REF	REF	REF	REF
Two	0.97 (0.65-1.43)	1.11 (0.50-2.47)	0.96 (0.61-1.52)	0.97 (0.63-1.50)
Three	0.90 (0.57-1.43)	2.08 (0.92-4.70)	1.14 (0.79-1.67)	0.91 (0.56-1.47)
Four	0.93 (0.52-1.64)	1.28 (0.38-4.34)	1.31 (0.71-2.41)	1.37 (0.85-2.21)

Five (highest income)	0.92 (0.63-1.33)	1.42 (0.54-3.79)	0.70 (0.44-1.12)	0.74 (0.48-1.14)
Smoking Status				
Never/Not daily	REF	REF	REF	REF
Daily	0.97 (0.66-1.43)	1.78 (0.69-4.57)	1.47 (0.93-2.33)	0.99 (0.58-1.70)
Alcohol Use				
Less than once a week	REF	REF	REF	REF
1-3 times per week	1.04 (0.76-1.42)	0.63 (0.30-1.35)	0.81 (0.57-1.15)	0.72 (0.53-0.97)
>3 times per week	0.85 (0.46-1.58)	**0.28 (0.09-0.85)**	0.91 (0.51-1.63)	1.22 (0.53-2.78)
No response	1.16 (0.76-1.79)	1.18 (0.57-2.44)	**2.12 (1.38-3.27)**	1.35 (0.80-2.30)
Body Mass Index				
Healthy weight	REF	REF	REF	REF
Underweight / Overweight / Obese	1.07 (0.81-1.41)	1.63 (0.92-2.87)	0.96 (0.71-1.29)	1.41 (1.06-1.87)
Social Functioning	0.98 (0.96-1.01)	**0.93 (0.88-0.98)**	**0.98 (0.95-1.00)**	**0.97 (0.94-0.99)**
Comorbidity				
0	REF	REF	REF	REF
1	1.29 (0.76-2.18)	**1.93 (0.85-4.39)**	**2.14 (1.23-3.73)**	2.04 (0.80-5.25)
2 or more	0.68 (0.38-1.22)	1.55 (0.25-9.60)	**4.19 (1.35-13.00)**	1.51 (0.62-3.72)
Perceived Psychological Stress	0.98 (0.95-1.01)	1.01 (0.95-1.08)	0.98 (0.95-1.00)	**0.97 (0.95-0.99)**
IBD Disease Type				
Ulcerative / Indeterminate colitis	REF	REF	REF	REF
Crohn's Disease	0.93	0.72	1.22	1.06

	(0.70-1.24)	(0.41-1.29)	(0.93-1.59)	(0.78-1.44)
Disease Activity *				
Minimally / Inactive disease	REF	REF	REF	REF
Moderately active disease	**1.65 (1.07-2.53)**	0.73 (0.36-1.49)	**1.63 (1.07-2.47)**	1.22 (0.86-1.75)
Very active disease	**1.62 (1.10-2.38)**	0.76 (0.34-1.73)	**1.72 (1.17-2.53)**	**1.81 (1.25-2.63)**
Previous IBD-related Surgery				
No	REF	REF	REF	REF
Yes	0.93 (0.52-1.67)	0.90 (0.36-2.24)	1.49 (0.80-2.80)	1.17 (0.72-1.91)
Time between diagnosis and 12m survey completion (years)	0.97 (0.91-1.04)	0.91 (0.79-1.04)	1.00 (0.93-1.09)	0.98 (0.90-1.07)

REF indicates reference category
Bold values indicate a statistically significant effect at α=0.05