

Associations Between Physical Activity and Inflammatory Bowel Disease: Results from a Canadian National Survey

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Abstract

Objective: Inflammatory bowel disease (IBD) is increasing in prevalence and incidence worldwide, particularly in Canada. Crohn's disease (CD) and ulcerative colitis (UC), the two most common forms of IBD, are characterized by inflammation of the gut. Physical activity is known to reduce chronic inflammation, but its potential preventive effect on IBD remains inconclusive. This study investigated the relationship between physical activity and IBD in the Canadian population.

Methods: The sample of 111,647 respondents were drawn from the Canadian Community Health Survey (2013-2014). Multinomial logistic regression was used to analyze the association between physical activity levels and IBD status (CD, UC, and no IBD), adjusting for the potential confounders of age, sex, body mass index, and type of smoker.

Results: The highest proportion of inactivity was found in the disease groups of CD (52.4%) and UC (45.0%), followed by no IBD (42.6%). The adjusted odds ratio of having CD were 1.42 (95% CI 0.99-2.03) and 1.59 (95% CI 1.14-2.23) for moderately active and inactive respondents, respectively, relative to active respondents. There was a trend in the UC group with the highest odds ratio of having UC observed in the moderately active respondents (OR 1.27, 95% CI 0.85-1.89) compared to active respondents, but this did not reach statistical significance.

Conclusion: Moderate activity and inactivity, relative to activity, were associated with higher odds of having CD and UC, with a stepwise trend observed in the CD group. Physical activity may offer a potential avenue for preventing IBD and informing future public health interventions if future studies demonstrate causality.

Introduction

Inflammatory bowel disease (IBD) is a chronic, multifactorial condition, characterized by inflammation of the gastrointestinal (GI) tract and an increased risk of comorbidities and colorectal cancer.¹⁻³ Crohn's disease (CD) and ulcerative colitis (UC) are two of the most common forms of IBD with important clinical distinctions.⁴ CD affects the entire GI tract from the oral cavity to the anus, and spreads to all layers of the gut.^{1,2} In contrast, UC targets the colon and the rectum and is limited to the innermost mucosal layer.^{1,2,5} Since the middle of the twentieth century, IBD has been increasing in prevalence worldwide, now affecting over 3.5 million people in North America and Europe.^{6,7} North America has the second highest prevalence worldwide, at 319 and 249 cases per 100,000 population for CD and UC, respectively.⁸ IBD is not only a common condition in North America, but also one that is being increasingly diagnosed; Canada has one of the highest incidences of IBD in the world, at 13.4 and 11.8 cases per 100,000 population for CD and UC, respectively, across all age groups.^{6,9} These high rates of incidence and prevalence in Canada are projected to continue increasing over the next decade.

The rise in IBD parallels the worldwide epidemiological transition to an increased prevalence of chronic diseases associated with lifestyle and environmental risk factors such as increased stress, smoking, poor diet, and physical inactivity.^{2,3,10-12} Regular physical activity has been shown to reduce inflammation through downregulation of pro-inflammatory mediators, induction of anti-inflammatory mediators, and alleviation of stress.^{13,14} In rats, physical activity prior to induction of UC significantly reduces inflammatory markers, lesions, and mucosal damage, and increases the expression of anti-inflammatory cytokine interleukin-10.¹⁵ However, much of the research to date has focused on physical activity's effect on general inflammation and is inconclusive regarding its preventive impacts on specific inflammatory diseases such as CD and UC.¹⁴⁻¹⁶ These inconclusive findings have been attributed to methodological inconsistencies including variations in the type, intensity, and duration of physical activity, lack of control groups, and

unclear distinctions between pre- and post-onset of IBD.¹⁴⁻¹⁷

The effect of physical activity on the development of CD and UC remains unclear. This study investigates the relationship between decreased physical activity and higher odds of IBD, in a multivariable model adjusted for potential confounders. The data used to investigate this relationship are from the 2013-2014 Canadian Community Health Survey (CCHS), a population-based national survey that is specific to the Canadian demographic. In the context of an increasing prevalence of IBD, physical activity offers a population health avenue worthy of further investigation.

Methods

Study Design

The CCHS is a cross-sectional, national survey conducted in 2013 and 2014.¹⁸ Every CCHS iteration gathers information on health and disease status, healthcare utilization, social relationships, and healthcare determinants from the Canadian population aged 12 and older. The survey includes all provinces and territories, representing more than 98% of the population. Those excluded are persons living on reserves and Aboriginal settlements, full-time Canadian Forces members, institutionalized individuals, children aged 12 to 17 years in care, and persons living in select remote Quebec health regions. Details of sampling and interview methods can be found on the Statistics Canada website.¹⁸ Ethical approval for the use of these data is covered under The University of British Columbia's publicly available data clause in Policy #89 for research involving human subjects.¹⁹

Analytic Sample

To investigate the relationship between physical activity and IBD, this analysis included all individuals who provided valid responses to physical activity and IBD status, as well as to the potential confounders of age, sex, body mass index (BMI), and type of smoker.

Figure 1 shows the inclusion and exclusion process for the analytic sample drawn from 127,462 respondents to the CCHS 2013-2014 survey. Of the total respondents, 5826 were excluded for other types of bowel disorders such as irritable bowel syndrome and bowel incontinence. Of the remaining 121,636 eligible respondents, 438 provided invalid responses (Other, Not Applicable, Don't Know, Refusal, Not Stated) to

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the type of bowel disorder, 3802 to physical activity level, 5055 to BMI, and 694 to type of smoker. These respondents were excluded from the sample. The final analytic sample consisted of 111,647 respondents (88% of the CCHS 2013-2014 sample).

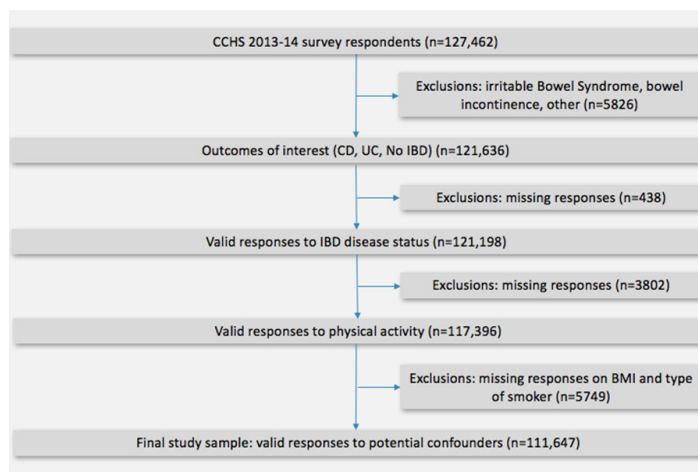


Figure 1 | Inclusion and exclusion process to generate the final analytic sample to investigate the relationship between physical activity and IBD.

Study Variables

The categorical outcome variable for IBD (CD, UC, or No IBD) was obtained from responses to two consecutive questions in the CCHS survey. All respondents were asked, “Do you have a bowel disorder such as Crohn’s disease, ulcerative colitis, irritable bowel syndrome, or bowel incontinence?” Respondents who answered “Yes,” “Don’t Know,” or “Refusal” were subsequently asked, “What kind of bowel disease do you have?” Those who answered “Yes” to CD or UC were assigned to the respective categories, and those who answered “No” to the first question were assigned to the reference group. The survey prompted respondents that chronic health conditions such as IBD are expected to last or have already lasted six months or more and are diagnosed by a health professional.

The categorical explanatory variable for physical activity was generated by Statistics Canada. Survey participants provided the frequency and number of minutes they spent on transportation or leisure-time physical activities in the past three months, such as walking or biking to school or work and sporting activities. Based on the reported frequency and duration of activities, Statistics Canada calculated the energy expenditure (EE) and metabolic equivalent of exercise as compared to when the body is at rest. Statistics Canada categorized the respondents as active (EE >3 kcal/kg/day), moderately active (EE = 1.5-3.0 kcal/kg/day), or inactive (EE <1.5 kcal/kg/day), based on daily EE for transportation and leisure-time physical activities.

Potential confounders of the relationship of interest included age (four groupings to reflect risk groups),^{2,20} sex (female or male), BMI (neither overweight nor obese, overweight, or obese), and type of smoker (daily smoker, former or occasional smoker, or never smoked). These potential confounders were selected based on the literature and conceptual understanding of IBD.^{14,20,21} BMI was a derived variable calculated by CCHS, based on weight and height.

Analysis Plan

Analyses were conducted using SAS University Edition (SAS Institute Inc., Cary, NC) and probability weights provided by Statistics Canada were applied to account for uneven probabilities of selection and to calculate estimates of variance. The CCHS Public Use Microdata File is covered under the Statistics Act that applies confidentiality rules for the use of the data and prevents the disclosure of confidential

information.¹⁸

Initial descriptive statistics were generated to explore the data and characteristics of the study sample were compared using the chi-squared test. A multinomial, logistic regression model was created to investigate the relationship between physical activity and IBD.²² The model was subsequently adjusted for confounding by age, sex, BMI, and type of smoker. A secondary analysis used a continuous BMI measure in place of the categorical BMI classes in the multinomial model.

Results

As shown in Table 1, the analytic sample of 111,647 respondents was equally distributed among sexes and variably distributed among age categories, with the smallest proportion of respondents aged 50 to 59 years (17.9%). Most of the sample were considered neither overweight nor obese (48.6%) and had never smoked (43.5%). Notable differences in IBD status were found in different age categories and type of smoker. The rates of CD and UC were lowest in the youngest age group and the “never smoked” group for CD, compared to the overall sample. The overall sample’s IBD status differed significantly by levels of physical activity, sex, age, and type of smoker.

For the main study variables of IBD status and physical activity, nearly all of the study sample reported no IBD (99.1%), with the rest reporting CD (0.4%) or UC (0.5%). The largest proportion of respondents were classified as inactive (42.6%), followed by active (31.6%) and moderately active (25.8%). The highest prevalence of inactive respondents was found in the CD group (52.4%), followed by UC (45.0%) and no IBD (42.6%).

Table 1 | Descriptive statistics of study sample investigating the relationship between physical activity level and IBD, from CCHS (2013-2014).

^aChi-squared tests with overall sample were significant at P <0.05

Variable	Overall (weighted %) (N = 111,647)	IBD status (weighted %)		
		Crohn’s disease (N = 586)	Ulcerative colitis (N = 673)	No IBD (N = 110,388)
Physical activity level^a				
Active	34,211 (31.6)	131 (20.9)	155 (25.1)	33,925 (31.6)
Moderately active	28,803 (25.8)	159 (26.7)	160 (30.0)	28,484 (25.8)
Inactive	48,633 (42.6)	296 (52.4)	358 (45.0)	47,979 (42.6)
Sex^a				
Male	52,073 (51.2)	221 (45.6)	238 (41.2)	51,614 (51.3)
Female	59,574 (48.8)	365 (54.4)	435 (58.8)	58,774 (48.7)
Age^a				
12-29 years	23,269 (26.2)	75 (13.1)	37 (8.8)	23,157 (26.3)
30-49 years	25,303 (31.9)	175 (43.7)	140 (35.6)	24,988 (31.8)
50-59 years	19,406 (17.9)	122 (19.4)	138 (21.5)	19,146 (17.9)
60 years or more	43,669 (24.1)	214 (23.7)	358 (34.2)	43,097 (24.0)
BMI				
Neither overweight nor obese	50,523 (48.6)	282 (45.6)	305 (46.5)	49,936 (48.7)
Overweight	37,784 (33.0)	182 (33.7)	211 (32.5)	37,391 (33.0)
Obese	23,340 (18.3)	122 (20.7)	157 (21.0)	23,061 (18.3)
Type of smoker^a				
Never smoked	42,874 (43.5)	155 (29.4)	186 (31.1)	42,533 (43.6)
Former or occasional	52,303 (42.5)	309 (47.5)	388 (51.1)	51,606 (42.4)
Daily	16,470 (14.0)	122 (23.0)	99 (17.8)	16,249 (14.0)

The bi-variable analyses showed a negative association between amount of physical activity and having either CD or UC. The odds of having CD and UC were increased for those who were moderately active and inactive, compared to active respondents. For respondents with CD, as the level of physical activity decreased from active to moderately active to inactive, the odds ratios (ORs) increased from 1.0 to 1.57 (95% confidence interval [CI] 1.10-2.26) and 1.87 (95% CI 1.35-2.58), respectively, indicating a stepwise association between less physical activity and the odds of having CD. This stepwise trend was not reflected for UC patients, even though the odds of having UC were

higher for those with less activity. The odds of having UC were in fact higher for moderately active respondents (OR 1.47, 95% CI 0.98-2.20) compared to inactive respondents (OR 1.33, 95% CI 0.98-1.81). The confidence intervals for the association of physical activity and UC included the OR estimate of 1.0. In contrast, the CIs for CD patients did not cross 1.0. Based on these results, increasing inactivity showed a step-wise association with CD and possible, but non-significant, association with UC.

To explore confounding effects, the multivariable model showed that the main relationship between physical activity and IBD was attenuated but maintained the same trend as in the bi-variable model. The odds of CD were increased for those with increasing levels of inactivity, in a stepwise fashion (Table 2). The moderately active level had a CI crossing 1.0. The odds of having UC with increasing levels of inactivity did not reflect this stepwise trend. The OR of having UC for moderately active respondents and inactive respondents were 1.27 (95% CI 0.85-1.89) and 1.07 (95% CI 0.79-1.46) compared to active respondents, respectively. Taken together, the adjusted data in Table 2 suggested a stepwise, increased odds of having CD for increasing levels of inactivity, while the highest odds of having UC were associated with the moderately active respondents.

In both bi-variable and multivariable models, the potential confounders of sex, age, and type of smoker were associated with IBD disease status. Looking at age, respondents aged 30 to 49 years showed the highest odds for having CD, whereas respondents aged 60 years or older showed the highest odds for having UC. Respondents who were female or who smoked at a higher frequency also had increased odds of having CD or UC. Although the CI for the association between sex and CD included 1.0, the distribution of the CIs suggested increased odds of having CD for females. Conversely, the ORs for the association between BMI and IBD were close to 1.0 and the distribution of the 95% CIs included 1.0, indicating this was not a strong confounding relationship. These variables were included in the final model adjusted for confounding, based on their associations with IBD and confounders identified a priori in the study design. It is well demonstrated in previous research that smoking and BMI are associated respectively with physical activity and IBD, particularly CD,^{23,24} and are thus important variables to include in multivariable analyses.

Table 2 | Unadjusted and adjusted logistic regression odds ratios (OR), investigating the relationship between physical activity level and IBD, from CCHS (2013-2014).
*CI, confidence interval

Variable	Crohn's disease		Ulcerative colitis	
	Unadjusted OR (95% CI ^a)	Adjusted OR (95% CI ^a)	Unadjusted OR (95% CI ^a)	Adjusted OR (95% CI ^a)
Physical activity level				
Active	1.0	1.0	1.0	1.0
Moderately active	1.57 (1.10, 2.26)	1.42 (0.99, 2.03)	1.47 (0.98, 2.20)	1.27 (0.85, 1.89)
Inactive	1.87 (1.35, 2.58)	1.59 (1.14, 2.23)	1.33 (0.98, 1.81)	1.07 (0.79, 1.46)
Sex				
Male	1.0	1.0	1.0	1.0
Female	1.25 (0.95, 1.65)	1.33 (0.99, 1.80)	1.50 (1.12, 2.01)	1.53 (1.16, 2.03)
Age				
12-29 years	1.0	1.0	1.0	1.0
30-49 years	2.75 (1.83, 4.14)	2.30 (1.50, 3.52)	3.36 (2.00, 5.64)	3.07 (1.86, 5.07)
50-59 years	2.18 (1.34, 3.54)	1.72 (1.07, 2.77)	3.62 (2.15, 6.10)	3.19 (1.91, 5.31)
60 years or more	1.98 (1.34, 2.92)	1.60 (1.06, 2.41)	4.27 (2.69, 6.78)	3.79 (2.40, 5.99)
BMI				
Neither overweight nor obese	1.0	1.0	1.0	1.0
Overweight	1.09 (0.79, 1.50)	1.00 (0.70, 1.41)	1.03 (0.74, 1.44)	0.91 (0.65, 1.25)
Obese	1.21 (0.86, 1.69)	1.01 (0.72, 1.42)	1.20 (0.85, 1.69)	1.01 (0.71, 1.42)
Type of smoker				
Never smoked	1.0	1.0	1.0	1.0
Former or occasional	1.66 (1.22, 2.26)	1.58 (1.16, 2.15)	1.69 (1.25, 2.28)	1.46 (1.09, 1.96)
Daily	2.44 (1.62, 3.67)	2.22 (1.44, 3.41)	1.79 (1.12, 2.84)	1.68 (1.05, 2.70)

A secondary analysis used a continuous measure of BMI along with other confounders, rather than categorical BMI classes. In the multivariable model adjusted for the continuous measure of BMI, the main relationship showed similar effects and trends as models adjusted for the categorical measure of BMI. Increasing levels of inactivity were associated with higher odds of having CD, with ORs of 1.42 (95% CI 0.99-2.04) and 1.60 (95% CI 1.14-2.25) for moderately active and inactive respondents, respectively, compared to active respondents. The ORs of having UC for moderately active and inactive respondents compared to active individuals were 1.27 (95% CI 0.85-1.89) and 1.07 (95% CI 0.79-1.46), respectively. This continuous measure of BMI showed ORs similarly close to 1.0 and CIs including 1.0, indicating a likely null association with IBD. Both measures of BMI did not appear to be strong confounders for IBD.

Discussion

CD and UC are the two most common forms of IBD and are characterized by chronic inflammation of the GI tract.¹⁴ Physical activity has been shown to reduce inflammatory pathologies by regulating inflammatory markers, cytokines, and mediators.^{13,14} The purpose of this study was to investigate the effect of low levels of physical activity on the odds of having CD, UC, and no IBD condition. Quantitative analysis of the population-based CCHS data sample found that inactivity was associated with increased odds of having CD and UC. The effect of physical activity followed a dose-response pattern for CD patients, whereby the highest odds of having UC were found in moderately active respondents. These effect measures followed a similar pattern when adjusted for age, sex, BMI, and type of smoker, although UC CIs crossed the null and were not statistically significant. Importantly, causality may not be inferred from the statistical analyses performed, as the data come from a cross-sectional survey and do not distinguish the temporal relationship between reported physical activity levels and IBD status. The results described here only highlight associations between physical activity and IBD. As hypothesized, these findings suggest that physical activity is associated with lower odds of having CD. While the analyses did show an association of moderate physical activity with lower odds of having UC, the association remained non-significant.

The results from this study are consistent with previous research. Existing evidence in the literature, including a meta-analysis by Wang *et al.*, determined that increasing levels of physical activity showed an inverse association with IBD.^{14-17,21} Importantly, studies that have investigated the effect of physical activity on CD and UC separately have found a similar, significant, inverse association with CD and a weaker, non-significant inverse association with UC.^{14,16,21} The magnitude of the increased odds of CD and UC in this study are comparable to the associations in previous studies.^{14,16,21} While this cross-sectional study could not explore the temporal relationship between physical activity and IBD, other previous case-control and cohort studies have shown similar associations using measures of sedentary activity, standing time, metabolic equivalent tasks (MET), and the Godin leisure time activity index.^{14,16,21} Contrastingly, one case-control study by Hlavaty *et al.* showed nearly twofold higher ORs of having CD and UC in less physically active individuals compared to active individuals than the ORs seen in this study.¹⁵ Their research, however, studied the frequency of childhood sporting activities, which may have had a cumulative effect and therefore magnified the inverse association.¹⁵

Consistent with evidence in the literature, despite the lack of a statistically significant inverse association between physical activity and UC, this study showed that physical activity of various forms may be associated with lower odds of having CD and UC. These results may be useful for informing public health interventions. The benefits of physical activity on IBD have been attributed to the regulation of pro- and anti-inflammatory markers and increased expression of

anti-inflammatory cytokines, mediated by myokines released during exercise.^{10,13,14} Downstream effects of this regulation include stress reduction and decreased number of mucosal lesions associated with IBD.^{13,14} Curiously, as shown in this study, UC may benefit more from moderate and low-intensity activities, in line with previous research that indicates that there is potential for inflammatory flare-ups resulting from intense exercise.^{17,25} Strenuous periods of exercise may release pro-inflammatory cytokines and trigger a more intense or even systemic inflammation. A study by Bilski et al. found effects of moderate versus acute physical activity similar to the results of this current study, based on these mechanisms.¹⁰

This study is strengthened by the population-based, representative sample, providing adequate power to the statistical analysis. It does, however, have limitations that may affect the interpretation of the results. Firstly, the CCHS is cross-sectional and is subject to issues of temporality and reverse causality. It is not possible to discern from the survey data whether physical activity preceded the onset of CD or UC, which poses a bias since those with IBD may face difficulties of exercising and become sedentary as a result of disease status.²⁶ However, this study showed similar magnitudes of the preventive effect of exercise on IBD compared to other prospective cohort studies and studies that measured childhood physical activity.^{14,16,21} Further longitudinal studies are warranted to elucidate the relationship between prior physical activity and subsequent onset of IBD.

Another limitation is the potential for reporting bias in surveys. However, self-reported IBD has been well validated in the literature and in other Internet-based surveys, showing high concordance with physician reports.²⁷⁻²⁹ The categorical measure of physical activity may also be biased, as it relies on broad categories of activity level and does not use the gold standard of MET.¹⁴ However, this is mitigated by the derivation by Statistics Canada, where the duration and frequency of various types of transportation and leisure activities were amalgamated to produce the physical activity index used in this study.

Finally, the interpretation of the results may be limited by the categorical measure of BMI and unmeasured confounders in CCHS. Literature suggests that many IBD individuals are overweight,³⁰ yet this higher-risk group was combined with the normal weight group in the categorical variable of BMI in the CCHS. This may have increased the odds of having CD and UC in the reference group, thus diluting the observed associations and biasing them towards the null. The true effect may be stronger with a better reference category for this confounder. Additionally, the risk, if any, of IBD for those at a high BMI may be a function of respondents being overweight and obese, rather than any one-unit increase along the categorical BMI index. These limitations were assessed in the secondary analysis, using a continuous BMI measure that may better capture the increased risk of disease and fully adjust for the potential confounding by BMI. The results of the secondary analysis did not differ from the main model using the categorical measure of BMI. Other potential confounders remain unexplored in the model in this study, such as family history, ethnicity, and disease severity. As the temporal relationship between physical activity and IBD was not explored in this study, and the severity of IBD may preclude individuals from physical activity, further studies are needed to illustrate the impact of severity on activity. As these variables were not captured fully in CCHS, the final model here did not account for their confounding effects, if any.

Further studies are warranted to elucidate the temporality of physical activity and IBD, as well as to use gold standard measures that are more robust to reporting biases. Nevertheless, this study has potential implications for public health interventions and guidelines for preventing IBD. These results add to the growing body of evidence for the preventive effects of physical activity, at various levels and in different forms. As IBD is rising in prevalence worldwide, and especially

in Canada, a thorough understanding of the preventive mechanism of physical activity on IBD offers strategies to prevent the disease and inform future public health interventions.

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