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1 **Physical activity habits, limitations and predictors in people with**  
2 **inflammatory bowel disease: a large cross-sectional online survey**

3

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13

14 **Conflicts of Interest and Source of Funding**

15 The authors report no conflicts of interest. This work was supported by no funding sources.

## 16 **Abstract**

17 **Background:** Limited evidence suggests that physical activity has beneficial effects in people with  
18 inflammatory bowel disease (IBD). This study aimed to determine the physical activity habits of  
19 adults with IBD, the limitations to physical activity they experience because of their disease, and the  
20 extent to which their physical activity is affected by various demographic, clinical and psychological  
21 factors.

22 **Methods:** Data were collected on 859 adult participants (52% with Crohn's disease [CD], 75%  
23 female) via an online survey conducted between May and June 2016. Measures included physical  
24 activity (International Physical Activity Questionnaire), psychological symptoms (Hospital Anxiety  
25 and Depression Scale), fatigue (sub-items of IBD fatigue scale), exercise perceptions (Exercise  
26 Benefits/Barriers Scale) and disease activity. Regression analyses were used to identify predictors of  
27 physical activity.

28 **Results:** Only 17% of respondents were categorised as "high active". Self-reported physical activity  
29 levels decreased, and fatigue and psychological scores increased, with increasing disease activity.  
30 Walking was the most common activity performed (57% of respondents) and running/jogging the  
31 most commonly avoided (34%). Many participants (n=677) reported that IBD limited their physical  
32 activity for reasons including abdominal/joint pain (70%), fatigue/tiredness (69%), disease flare-up  
33 (63%), and increased toilet urgency (61%). Physical activity was independently associated with  
34 depression, disease activity and perceived barriers to exercise in people with CD, and depression and  
35 age in people with ulcerative or indeterminate colitis (all  $P \leq 0.038$ ).

36 **Conclusions:** This survey highlights several important factors that should be considered by designers  
37 of future physical activity interventions for people with IBD.

38

39 **Key Words:** Crohn's disease; exercise; depression; fatigue; physical activity; ulcerative colitis

## 40 **1. Introduction**

41 Physical activity and exercise are important lifestyle behaviours for the general population: they are  
42 associated with improvements in physical fitness and mental well-being (1, 2); they facilitate weight  
43 management (3); and, independently of these benefits, they have been associated with lower  
44 mortality rates (4). Physical activity/exercise may also be a useful adjunctive therapy for people with  
45 inflammatory bowel disease (IBD) by improving immune function and mood, reducing fatigue, and  
46 promoting gains in muscle and bone strength (5). However, the evidence for physical  
47 activity/exercise in IBD is sparse, with only a handful of intervention studies (6-9), some of which  
48 have methodological limitations such as short follow-up, no control group, and a small sample size.  
49 As such, it is perhaps unsurprising that there are currently no evidence-based physical activity  
50 guidelines that are specific to IBD.

51

52 Despite the numerous potential benefits of physical activity, there is evidence that a large  
53 proportion of the IBD population is physically inactive, and that people with IBD are less active than  
54 people without IBD (10, 11). Although the reasons for this are unclear, recent surveys have  
55 demonstrated that many patients cite limitations to physical activity due to IBD-related factors such  
56 as fatigue, joint pain, and lack of toilet access (12, 13). There is also evidence from other populations  
57 that depression disorders and symptoms, which have a reported prevalence in IBD of 15.2% and  
58 21.6%, respectively (14), may have an adverse impact on self-management behaviours such as  
59 physical activity (15). A better understanding of the modifiable correlates of physical activity in  
60 people with IBD will aid in the development of interventions with the potential to favourably-modify  
61 behavioural and health outcomes.

62

63 Given the lack of research in this area, the purpose of this study was to characterise the physical  
64 activity habits of adults with IBD, to explore limitations to physical activity that patients may face

65 because of their disease, and to identify factors that are associated with physical activity. An

66 additional objective was to explore clinical and psychological correlates of fatigue.

67

## 68 **2. Materials and Methods**

### 69 **2.1 Ethics approval**

70 The study was approved by the Northumbria University Faculty of Health and Life Sciences Research  
71 Ethics Committee in May 2016.

72

### 73 **2.2 Design**

74 A cross-sectional online survey was conducted.

75

### 76 **2.3 Participants**

77 Participants were a non-clinical population recruited via on-line advertisements on Twitter,  
78 Facebook and Instagram. They were invited to participate if they had a formal diagnosis of IBD and  
79 were at least 18 years of age. Respondents who were younger than 18 years old were excluded.

80

### 81 **2.4 Procedure**

82 The survey was conducted between May and June 2016. The link to the survey was included in the  
83 advertisements and interested respondents answered the survey directly through this link.

84 Survey Monkey was used as it allowed confidential access and facilitated data analysis. Study

85 information was provided at the commencement of the survey, and respondents had to provide

86 informed consent before they could participate. Contact details of the researchers were provided in  
87 case any queries arose.

88

### 89 **2.5 Survey**

90 The survey was anonymous. The first section collected participants' age, gender, employment status,  
91 smoking status, and whether they Crohn's disease (CD), ulcerative colitis (UC) or indeterminate

92 colitis (IC). The second section assessed duration of diagnosis, current treatments, surgical history,

93 disease activity, depression and anxiety symptoms, and fatigue. For people with CD, disease activity

94 was assessed using the PRO3 Index, with scores of <13, 13-21, 22-52 and ≥52 indicative of inactive,  
95 mildly active, moderately active, and severely active disease, respectively (16). For people with UC or  
96 IC, disease activity was assessed using the Patient-based Simple Clinical Colitis Activity Index (P-  
97 SCCAI), with scores of <5 and ≥5 indicative of inactive and active disease, respectively (17).  
98 Depression and anxiety symptoms were measured by using the Hospital Anxiety and Depression  
99 Scale (HADS) (18). Fatigue was assessed using items 4 and 5 of the IBD Fatigue Scale (19): “What was  
100 your AVERAGE fatigue level in the past two weeks?” (5-point ordinal scale ranging 0 [No fatigue] to 4  
101 [Severe fatigue]) and “How much of your waking time have you felt fatigued in the past two weeks”  
102 (5-point ordinal scale ranging 0 [None of the time] to 4 [All of the time]). A composite fatigue score  
103 was calculated by multiplying the responses to these two questions. The third section of the survey  
104 assessed participants’ physical activity habits using the International Physical Activity Questionnaire  
105 (IPAQ) – Short Form (20). Standard scoring criteria were used (<http://www.ipaq.ki.se>) to classify  
106 respondents as ‘inactive’, ‘minimally active’ or ‘HEPA active’ (health enhancing physical activity; a  
107 high activity category). Standard formulae were also used to produce a continuous indicator of  
108 physical activity; a total physical activity score in MET-min/week, computed as the sum of walking,  
109 moderate, and vigorous MET-min/week scores (<http://www.ipaq.ki.se>). Participants were also asked  
110 to list up to 3 types of physical activity, exercise or sport that they most frequently participated in  
111 over the past year, and up to 3 types of physical activity, exercise or sport that they avoided because  
112 of their IBD in the past year. The final section of the survey assessed participants’ perceived benefits  
113 and barriers to exercise using the Exercise Benefits/Barriers Scale (21), and their reasons (if  
114 applicable) for IBD limiting participation in physical activity.

115

## 116 **2.6 Statistical analysis**

117 All responses collected via Survey Monkey were inspected, downloaded into Excel, coded and  
118 analysed using descriptive statistics (means, standard deviations [SD], medians, interquartile ranges  
119 [IQR], frequencies, and percentages). All returned surveys were included in the analysis, regardless

120 of the amount of missing data. Consequently, the number of total responses for each survey item  
121 varied due to missing data and refusal/inability to answer.

122

123 Multivariable linear regression analyses were conducted to determine the combination of clinical  
124 and psychological indices that best explained the observed variations in physical activity and fatigue  
125 scores. Separate models were constructed for people with CD and people with UC or IC (combined).  
126 Inspection of the total physical score in MET-min/week demonstrated significant positive skew that  
127 was transformed to a normal distribution using logarithmic transformation. The fatigue composite  
128 score was treated as a continuous outcome, and inspection of the histogram demonstrated an  
129 approximately normal distribution.

130

131 A multi-stage strategy was used to develop our explanatory models. Firstly, correlation matrices  
132 were produced to explore the relationship between dependent variables (physical activity and  
133 fatigue) and potential predictor variables (age, gender, disease severity, disease duration,  
134 depression, anxiety, exercise barriers score, and exercise benefits score). Indices that demonstrated  
135 significant correlation (two-tailed  $p < 0.05$ ) with the dependent variable were then carried forward for  
136 inclusion in a 'stage 1' multivariable linear regression model. The final model was then constructed,  
137 retaining only those coefficients making a significant ( $p < 0.05$ ) contribution to the overall model fit.  
138 Analyses were conducted using IBM SPSS Statistics Version 22 (IBM United Kingdom Limited,  
139 Hampshire, UK).

140

141



## 142 **3. Results**

### 143 **3.1 Participant characteristics**

144 Overall, there were 859 eligible respondents to the survey, of whom 75.2% were female (Table 1).  
145 The mean (SD) age was 37.3 (11.6) years, 52% had CD, and the median (IQR) time since diagnosis  
146 was 87 (36 to 178) months. According to the PRO3 Index data, 28.3% of people with CD were in  
147 clinical remission, and 19.0%, 45.1% and 7.6% had mildly-, moderately-, or severely-active disease,  
148 respectively. Using the P-SCCAI data, 40.7% of people with UC or IC had inactive disease, and 59.3%  
149 had active disease. Table 2 shows data on current treatments and surgical history.

150

### 151 **3.2 Physical activity habits and limitations**

152 Of the 737 respondents who completed the IPAQ, 17.1% were classified as HEPA (i.e., high) active,  
153 49.6% as minimally active, and 33.3% as inactive (Table 3). The median total physical activity was  
154 1866 (594 to 4040) MET·min/week and mean daily sitting time was 429 (225) min. The proportion of  
155 physically-inactive individuals increased, in both disease sub-groups, with increasing disease activity.  
156 For example, 21.7% of people with mildly-active CD reported being physically inactive versus 62.1%  
157 of people with severely-active CD. The exercise barriers scores also increased, and the exercise  
158 benefits scores decreased, with increasing disease activity (Table 3).

159

160 Figure 1A shows that the respondents had participated in a wide range of activities/exercises in the  
161 past year, with walking being the most common activity by far (56.7%). There were no marked  
162 differences between disease sub-types. Similarly, the types of activity/exercise that were avoided  
163 because of IBD did not differ markedly between CD and UC/IC respondents (Figure 1B). Of the 712  
164 respondents, running/jogging was the most commonly avoided activity (32.2%).

165

166 Six hundred and seventy-seven participants (79%) reported that their IBD limited their participation  
167 in physical activity/exercise (Figure 2). The most common reasons were abdominal or joint pain (n =

168 473), fatigue or tiredness (n = 471), disease flare-up (n = 430), and increased toilet urgency (n = 411).  
169 The proportion of respondents providing reasons tended to be higher in CD versus UC/IC (e.g., 80.9%  
170 vs. 57.1% for abdominal or joint pain; 84.3% vs. 52.7% for fatigue or tiredness).

171

### 172 **3.3 Depression, anxiety and fatigue**

173 Of the whole IBD cohort, 33.1% and 22.3% of respondents had abnormal anxiety and depression  
174 scores (i.e., HADS scores of 11 to 21), respectively. The anxiety and depression scores were generally  
175 higher in CD versus UC/IC, with higher scores also seen in individuals with more-active disease (Table  
176 3).

177

178 Data on average fatigue levels in the past two weeks is presented in Figure 3. Fatigue scores were  
179 generally worse in people with CD, in females, in people with higher levels of disease activity, and in  
180 people with lower levels of physical activity. For example, “severe fatigue” was more frequently  
181 reported in people with CD than people with UC/IC (26.8% vs. 20.1%), in females than males (CD:  
182 27.3% vs. 25.5%; UC/IC: 20.8% vs. 11.5%), and in physically-inactive individuals than high-active  
183 individuals (CD: 33.8% vs. 19.0%; UC/IC: 38.5% vs. 9.4%).

184

### 185 **3.4 Predictors of physical activity and fatigue**

186 Table 4 shows the correlations between physical activity, fatigue and various demographic, clinical  
187 and psychological factors. In people with CD, variables that were significantly correlated with  
188 logarithmically-transformed total physical activity were disease activity ( $r = -0.228$ ,  $P < 0.01$ ),  
189 depression ( $r = -0.287$ ,  $P < 0.01$ ), anxiety ( $r = -0.120$ ,  $P < 0.05$ ), fatigue ( $r = -0.127$ ,  $P < 0.05$ ), exercise  
190 benefits score ( $r = 0.244$ ,  $P < 0.01$ ), and exercise barriers score ( $r = -0.292$ ,  $P < 0.01$ ), whereas variables  
191 that were significantly correlated with fatigue were duration of diagnosis ( $r = 0.110$ ,  $P < 0.05$ ), disease  
192 activity ( $r = 0.479$ ,  $P < 0.01$ ), depression ( $r = 0.538$ ,  $P < 0.01$ ), anxiety ( $r = 0.465$ ,  $P < 0.01$ ), and physical  
193 activity ( $r = -0.127$ ,  $P < 0.05$ ). In people with UC/IC, variables that were significantly correlated with

194 logarithmically-transformed total physical activity were age ( $r = -0.158, P < 0.01$ ), disease activity ( $r = -$   
195  $0.123, P < 0.05$ ), depression ( $r = -0.240, P < 0.01$ ), fatigue ( $r = -0.181, P < 0.01$ ), and exercise benefits  
196 score ( $r = 0.171, P < 0.01$ ), whereas variables that were significantly correlated with fatigue were  
197 disease activity ( $r = 0.393, P < 0.01$ ), depression ( $r = 0.572, P < 0.01$ ), anxiety ( $r = 0.453, P < 0.01$ ), and  
198 physical activity ( $r = -0.181, P < 0.01$ ).

199

200 The multivariable linear regression models for physical activity and fatigue are shown in Tables 5 and  
201 6, respectively. After adjusting for each of the included demographic, clinical and psychological  
202 factors, several variables were found to be independently associated with low physical activity levels  
203 including higher disease activity ( $B = -0.010, P = 0.038$ ), depression ( $B = -0.077, P = 0.002$ ) and exercise  
204 barriers ( $B = -0.035, P = 0.008$ ) scores for people with CD, and higher age ( $B = -0.016; P = 0.011$ ) and  
205 depression score ( $B = -0.053, P = 0.025$ ) for people with UC/IC. In the final models, these factors  
206 explained 12.3% and 7.3% of the observed variability in self-reported total physical activity in the CD  
207 and UC/IC groups, respectively.

208

209 Variables that were found to be independently associated with higher fatigue scores were longer  
210 time since diagnosis ( $B = 0.005, P = 0.011$ ), and higher disease activity ( $B = 0.076, P < 0.001$ ),  
211 depression ( $B = 0.324, P < 0.001$ ) and anxiety ( $B = 0.183, P = 0.001$ ) scores in people with CD, and  
212 female gender ( $B = -1.360; P = 0.006$ ), and higher depression ( $B = 0.454; P < 0.001$ ) and anxiety ( $B =$   
213  $0.180; P = 0.003$ ) scores in people with UC/IC. In the final models, these factors explained 37% and  
214 36% of the observed variability in self-reported fatigue in the CD and UC/IC groups, respectively.

215

## 216 4. Discussion

217 The main novel finding from this cross-sectional online survey was that physical activity was  
218 negatively and independently associated with depression, disease activity and exercise barriers in  
219 people with CD, and depression and age in people with UC/IC. Other key findings are as follows: the  
220 large majority of respondents, regardless of disease type, did not engage in physical activity at levels  
221 commensurate with public health guidelines; physical activity levels were lower and fatigue and  
222 psychological scores higher in people with higher levels of disease activity; walking was by far the  
223 most common type of physical activity performed, with running/jogging the most common activity  
224 avoided because of IBD; a large proportion of respondents provided reasons for IBD limiting their  
225 participation in physical activity, including pain, fatigue, flare-up and increased toilet urgency, and;  
226 independent predictors of fatigue were time since diagnosis, disease activity, depression and anxiety  
227 in people with CD, and gender, depression and anxiety in people with UC/IC.

228

229 There is a paucity of published data on predictors of physical activity in people with IBD. In a recent  
230 study in which 7-day accelerometry was used to objectively measure physical activity in 48 adults  
231 with CD, low body mass index ( $<21 \text{ kg/m}^2$ ), longer time since diagnosis, presence of systemic  
232 inflammation (indicated by serum C-reactive protein  $>3 \text{ mg/L}$ ) and low vitamin D3 ( $<50 \text{ nmol/L}$ ) were  
233 all independently associated with lower physical activity (zero bouts of moderate-to-vigorous  
234 physical activity during the 7-day accelerometer-wear period) (11). Unfortunately, the authors did  
235 not report how much of the variation in physical activity was explained by these variables. Of these  
236 predictor variables, only time since diagnosis was recorded in the current study, and we did not  
237 observe a significant association (Table 4). The reason for this discrepancy is unclear, but may be due  
238 to differences in the study populations and the way physical activity was measured and classified. In  
239 the present study, although large amounts of the variability in total physical activity remained  
240 unexplained by the regression models, it was notable that depressed mood emerged as being  
241 independently associated with less physical activity in both CD and UC/IC sub-groups. Such an

242 association, which has previously been reported for adults with type 2 diabetes (22), might be  
243 explained by depressed mood having an adverse impact on self-management behaviours (15);  
244 however, the evidence from randomised controlled trials is currently equivocal as to whether  
245 depression-specific management in depressed individuals leads to increased physical activity (23,  
246 24). We acknowledge that cross-sectional studies cannot assign causality and highlight that the  
247 inverse association between physical activity and depressed mood is likely bi-directional (25).  
248 Viewed this way, our findings may suggest a potential beneficial effect of regular physical activity on  
249 depressive symptoms in people with IBD. A recent meta-analysis of 35 randomised controlled trials  
250 (n=1356) showed that exercise training is moderately more effective than a control intervention for  
251 reducing symptoms of depression in adults with depression (2); however we are not aware of any  
252 prospective trials that have explored the potential mental health benefits of exercise training in  
253 people with IBD specifically. Given that a relatively high proportion of people with IBD have  
254 abnormal depression scores (22.3% in the current study), this seems an important area of focus for  
255 future research, and we are currently exploring the effects of continuous and interval-type aerobic  
256 exercise training on physical fitness, fatigue, mental well-being and disease activity in people with  
257 inactive or mildly-active CD (26). Future studies, are also needed to better understand the sources of  
258 the unexplained variance in physical activity. Such studies should ideally be prospective, include  
259 objective measurement of physical activity, and include a range of intrapersonal, social and physical  
260 environmental predictor variables.

261

262 Few studies have explored the physical activity habits and limitations of people with IBD (10, 12, 13),  
263 but such information has practical value in the promotion of physical activity in this population. In  
264 this study, walking was the most common form of physical activity that the respondents participated  
265 in within the last year. Indeed, 57% of respondents cited walking, whereas the next most common  
266 activities of cycling, running, swimming, and gym were each cited by less than 20% of respondents.  
267 This finding is consistent with previous research that has demonstrated walking to be the most

268 common recreational and sporting activity undertaken by the general adult population (27) and  
269 people with IBD (10, 12). Health promotion initiatives seeking to engage people with IBD in physical  
270 activity need to be sensitive to the preferred mode of physical activity when designing interventions.  
271 Achieving a better understanding of physical activity *levels* may also represent a meaningful step in  
272 health promotion efforts in this population. Although 83% of all respondents indicated having  
273 undertaken one or more forms of physical activity in the last year, the IPAQ data showed that the  
274 same proportion (i.e., 83%) was classified as either “minimally-active” or “inactive”. When compared  
275 against the results of the International Prevalence Study on Physical Activity (28), which also used  
276 the IPAQ short form to quantify physical activity levels, our findings suggest that people with IBD  
277 (and particularly those with more highly-active disease) are substantially less physically active than  
278 the general adult population. For example, 17% of our survey respondents were in the high physical  
279 activity category versus 62% of adults aged 18-65 years in the USA (28). The reasons for this are not  
280 fully understood, but might at least be partly explained by the fact that many people reported  
281 experiencing IBD-related limitations to physical activity such as pain, fatigue, disease flare-up and  
282 increased toilet urgency. Further research is needed to better understand the extent to which  
283 physical activity barriers and facilitators differ among specific sub-groups (e.g., CD versus UC/IC;  
284 active disease versus inactive disease), as this will assist in the design and tailoring of physical  
285 activity interventions.

286

287 A secondary objective of this study was to explore clinical and psychological correlates of fatigue.  
288 Fatigue is very common in IBD (29, 30). It is often associated with increased disease activity, pain,  
289 poor sleep quality, depression, and perceived stress (31). In the present study, fatigue was most  
290 prevalent in those with CD, females, those with high disease activity and those reporting lower levels  
291 of physical activity. Similar differences in prevalence of fatigue between CD and UC, gender and  
292 disease activity have been previously observed in a longitudinal study which, like ours, drew  
293 attention to patients with CD suffering more severe fatigue than those with UC, females being more

294 prone to it than males and fatigue levels increasing in line with disease severity (32). Another  
295 longitudinal study examined factors reducing fatigue and noted that regular exercise improved  
296 physical fatigue (33), corroborating our finding of fatigue being more prevalent in those reporting  
297 low levels of physical activity. In terms of predictors of fatigue, our adjusted models showed that  
298 both in CD and UC, anxiety and depression were associated with fatigue, which is consistent with the  
299 two previous longitudinal studies (32, 33) and the previous cross-sectional data summarised in a  
300 recent review (34). Graff et al. (32) explained this association by common pathways, and particularly  
301 pro-inflammatory cytokines contributing to mood changes, inflammation and fatigue, and  
302 neuroendocrine factors linking stress, inflammation and fatigue. Further, Graff et al. (32) also  
303 noticed that fatigue increases over time in IBD and that this process appears to be independent of  
304 disease activity, as some patients with inactive IBD also report significant levels of fatigue. In the  
305 present study, we observed a relationship between duration of illness (indicated by time since  
306 diagnosis) and fatigue in patients with CD. It is unclear why the same was not found in our  
307 participants with UC as that's contrary to previous observations. Further to this, disease activity  
308 predicted fatigue in CD and not UC. This perhaps could be explained by generally lower levels of  
309 fatigue reported in UC. Interestingly, at the multivariable level, female gender explained fatigue in  
310 UC but not in CD. Females in general report higher levels of fatigue than males (35). The fact that  
311 gender did not predict fatigue in CD may thus have more to do with our sample (predominantly  
312 female) than the actual differences between CD and UC. These predictors of fatigue, and particularly  
313 anxiety and depression which we identified as common for both CD and UC, may suggest that  
314 therapies targeting mental symptoms may be useful in also addressing fatigue comorbid with IBD.  
315 Solution-focused therapy has shown promise (36), however there are very few interventional studies  
316 in the area and more needs to be done to propose effective therapies for fatigue in IBD.  
317  
318 The strengths of this study include the use of a large clinically- and demographically-diverse sample  
319 and the exploration of a broad range of factors pertaining to physical activity. The limitations of this

320 study also need to be acknowledged. Firstly, as the data are cross-sectional, we cannot confirm the  
321 direction of relationships between physical activity, fatigue, and other disease and psychological  
322 variables. Secondly, the results might be prone to bias due to the exclusive use of self-reported data.  
323 For example, physical activity levels may have been under- or over-reported, and peoples' disease  
324 activity may have been incorrectly categorised. Thirdly, the fact that participants for this survey were  
325 self-selected and predominantly recruited via social network advertisements means that the results  
326 might not be directly generalisable to the wider IBD population. Of particular note, around 75% of  
327 respondents were female meaning that the results might not be directly relevant to males.

328

329 In summary, this large online survey has shown that the majority of respondents with IBD have low  
330 levels of physical activity. Associated factors included depression, disease activity and perceived  
331 barriers to exercise. A large proportion of respondents cited IBD-related limitations to physical  
332 activity such as pain, fatigue and increased toilet urgency. Given that regular physical activity may  
333 have numerous general and condition-specific benefits in people with IBD, attempting to increase  
334 participation of the IBD population in this vital health behaviour is probably a worthwhile pursuit.  
335 The results highlight several important factors that should be considered by designers of physical  
336 activity interventions for this population. Further research is now needed to better understand the  
337 barriers and facilitators of physical activity in specific sub-groups of patients, to determine the  
338 effects of different exercise programmes on important outcomes (e.g., fatigue, disease activity, and  
339 mental well-being), and to identify cost-effective interventions that have good potential for  
340 widespread implementation. Such efforts will help pave the way for the development of evidence-  
341 based physical activity guidelines for people with IBD.

342

#### 343 **Author Contributions**

344 KJ and GT contributed to the design of the survey. KJ collated the results and conducted the analyses  
345 under the supervision of AMW and GT. All authors interpreted the data. GT drafted the manuscript.



346 KJ and AMW contributed to revising this report and gave final approval for its submission. All  
347 authors had full access to all the data in the study and had final responsibility for the decision to  
348 submit for publication.

349 **References**

- 350 1. Milanović Z, Sporiš G, Weston M. Effectiveness of High-Intensity Interval Training (HIT) and  
351 Continuous Endurance Training for VO<sub>2</sub>max Improvements: A Systematic Review and Meta-Analysis  
352 of Controlled Trials. *Sports Med.* 2015;45(10):1469-81.
- 353 2. Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, et al. Exercise for depression.  
354 *Cochrane Database Syst Rev.* 2013(9):CD004366.
- 355 3. Verheggen RJ, Maessen MF, Green DJ, Hermus AR, Hopman MT, Thijssen DH. A systematic  
356 review and meta-analysis on the effects of exercise training versus hypocaloric diet: distinct effects  
357 on body weight and visceral adipose tissue. *Obes Rev.* 2016;17(8):664-90.
- 358 4. Fishman EI, Steeves JA, Zipunnikov V, Koster A, Berrigan D, Harris TA, et al. Association  
359 between Objectively Measured Physical Activity and Mortality in NHANES. *Med Sci Sports Exerc.*  
360 2016;48(7):1303-11.
- 361 5. Bilski J, Mazur-Bialy A, Brzozowski B, Magierowski M, Zahradnik-Bilska J, Wójcik D, et al. Can  
362 exercise affect the course of inflammatory bowel disease? Experimental and clinical evidence.  
363 *Pharmacol Rep.* 2016;68(4):827-36.
- 364 6. D'Inca R, Varnier M, Mestriner C, Martines D, D'Odorico A, Sturniolo GC. Effect of moderate  
365 exercise on Crohn's disease patients in remission. *Ital J Gastroenterol Hepatol.* 1999;31(3):205-10.
- 366 7. Ng V, Millard W, Lebrun C, Howard J. Low-intensity exercise improves quality of life in  
367 patients with Crohn's disease. *Clin J Sport Med.* 2007;17(5):384-8.
- 368 8. Sharma P, Poojary G, Vélez DM, Dwivedi SN, Deepak KK. Effect of Yoga-Based Intervention in  
369 Patients with Inflammatory Bowel Disease. *Int J Yoga Therap.* 2015;25(1):101-12.
- 370 9. Klare P, Nigg J, Nold J, Haller B, Krug AB, Mair S, et al. The impact of a ten-week physical  
371 exercise program on health-related quality of life in patients with inflammatory bowel disease: a  
372 prospective randomized controlled trial. *Digestion.* 2015;91(3):239-47.
- 373 10. Mack DE, Wilson PM, Gilmore JC, Gunnell KE. Leisure-time physical activity in Canadians  
374 living with Crohn disease and ulcerative colitis: population-based estimates. *Gastroenterol Nurs.*  
375 2011;34(4):288-94.
- 376 11. van Langenberg DR, Papandony MC, Gibson PR. Sleep and physical activity measured by  
377 accelerometry in Crohn's disease. *Aliment Pharmacol Ther.* 2015;41(10):991-1004.
- 378 12. DeFilippis EM, Tabani S, Warren RU, Christos PJ, Bosworth BP, Scherl EJ. Exercise and Self-  
379 Reported Limitations in Patients with Inflammatory Bowel Disease. *Dig Dis Sci.* 2016;61(1):215-20.
- 380 13. Chan D, Robbins H, Rogers S, Clark S, A P. Inflammatory bowel disease and exercise: results  
381 of a Crohn's and Colitis UK survey *Frontline Gastroenterology.* 2014;5:44-8.
- 382 14. Neuendorf R, Harding A, Stello N, Hanes D, Wahbeh H. Depression and anxiety in patients  
383 with Inflammatory Bowel Disease: A systematic review. *J Psychosom Res.* 2016;87:70-80.
- 384 15. McKellar JD, Humphreys K, Piette JD. Depression increases diabetes symptoms by  
385 complicating patients' self-care adherence. *Diabetes Educ.* 2004;30(3):485-92.
- 386 16. Khanna R, Zou G, D'Haens G, Feagan BG, Sandborn WJ, Vandervoort MK, et al. A  
387 retrospective analysis: the development of patient reported outcome measures for the assessment  
388 of Crohn's disease activity. *Aliment Pharmacol Ther.* 2015;41(1):77-86.
- 389 17. Bennebroek Evertsz' F, Nieuwkerk PT, Stokkers PC, Ponsioen CY, Bockting CL, Sanderman R,  
390 et al. The patient simple clinical colitis activity index (P-SCCAI) can detect ulcerative colitis (UC)  
391 disease activity in remission: a comparison of the P-SCCAI with clinician-based SCCAI and biological  
392 markers. *J Crohns Colitis.* 2013;7(11):890-900.
- 393 18. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.*  
394 1983;67(6):361-70.
- 395 19. Czubor-Dochan W, Norton C, Bassett P, Berliner S, Bredin F, Darvell M, et al. Development  
396 and psychometric testing of inflammatory bowel disease fatigue (IBD-F) patient self-assessment  
397 scale. *J Crohns Colitis.* 2014;8(11):1398-406.

- 398 20. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International  
399 physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.*  
400 2003;35(8):1381-95.
- 401 21. Sechrist KR, Walker SN, Pender NJ. Development and psychometric evaluation of the  
402 exercise benefits/barriers scale. *Res Nurs Health.* 1987;10(6):357-65.
- 403 22. Lysy Z, Da Costa D, Dasgupta K. The association of physical activity and depression in Type 2  
404 diabetes. *Diabet Med.* 2008;25(10):1133-41.
- 405 23. Williams JW, Katon W, Lin EH, Nöel PH, Worchel J, Cornell J, et al. The effectiveness of  
406 depression care management on diabetes-related outcomes in older patients. *Ann Intern Med.*  
407 2004;140(12):1015-24.
- 408 24. Lin EH, Katon W, Rutter C, Simon GE, Ludman EJ, Von Korff M, et al. Effects of enhanced  
409 depression treatment on diabetes self-care. *Ann Fam Med.* 2006;4(1):46-53.
- 410 25. Azevedo Da Silva M, Singh-Manoux A, Brunner EJ, Kaffashian S, Shipley MJ, Kivimäki M, et al.  
411 Bidirectional association between physical activity and symptoms of anxiety and depression: the  
412 Whitehall II study. *Eur J Epidemiol.* 2012;27(7):537-46.
- 413 26. Tew GA, Carpenter R, Seed M, Anderson S, Langmead L, Fairhurst C, et al. Feasibility of high-  
414 intensity interval training and moderate-intensity continuous training in adults with inactive or  
415 mildly active Crohn's disease: Study protocol for a randomised controlled trial *BMC*  
416 *Gastroenterology.* in review.
- 417 27. Bryan SN, Katzmarzyk PT. Patterns and trends in walking behaviour among Canadian adults.  
418 *Can J Public Health.* 2009;100(4):294-8.
- 419 28. Bauman A, Bull F, Chey T, Craig CL, Ainsworth BE, Sallis JF, et al. The International Prevalence  
420 Study on Physical Activity: results from 20 countries. *Int J Behav Nutr Phys Act.* 2009;6:21.
- 421 29. Minderhoud IM, Oldenburg B, van Dam PS, van Berge Henegouwen GP. High prevalence of  
422 fatigue in quiescent inflammatory bowel disease is not related to adrenocortical insufficiency. *Am J*  
423 *Gastroenterol.* 2003;98(5):1088-93.
- 424 30. Graff LA, Vincent N, Walker JR, Clara I, Carr R, Ediger J, et al. A population-based study of  
425 fatigue and sleep difficulties in inflammatory bowel disease. *Inflamm Bowel Dis.* 2011;17(9):1882-9.
- 426 31. Graff LA, Walker JR, Russell AS, Bissonnette R, Bernstein CN. Fatigue and quality of sleep in  
427 patients with immune-mediated inflammatory disease. *J Rheumatol Suppl.* 2011;88:36-42.
- 428 32. Graff LA, Clara I, Walker JR, Lix L, Carr R, Miller N, et al. Changes in fatigue over 2 years are  
429 associated with activity of inflammatory bowel disease and psychological factors. *Clin Gastroenterol*  
430 *Hepatol.* 2013;11(9):1140-6.
- 431 33. van Langenberg DR, Gibson PR. Factors associated with physical and cognitive fatigue in  
432 patients with Crohn's disease: a cross-sectional and longitudinal study. *Inflamm Bowel Dis.*  
433 2014;20(1):115-25.
- 434 34. Artom M, Czuber-Dochan W, Sturt J, Norton C. Targets for Health Interventions for  
435 Inflammatory Bowel Disease-fatigue. *J Crohns Colitis.* 2016;10(7):860-9.
- 436 35. Schwarz R, Krauss O, Hinz A. Fatigue in the general population. *Onkologie.* 2003;26(2):140-4.
- 437 36. Vogelaar L, van't Spijker A, Timman R, van Tilburg AJ, Bac D, Vogelaar T, et al. Fatigue  
438 management in patients with IBD: a randomised controlled trial. *Gut.* 2014;63(6):911-8.

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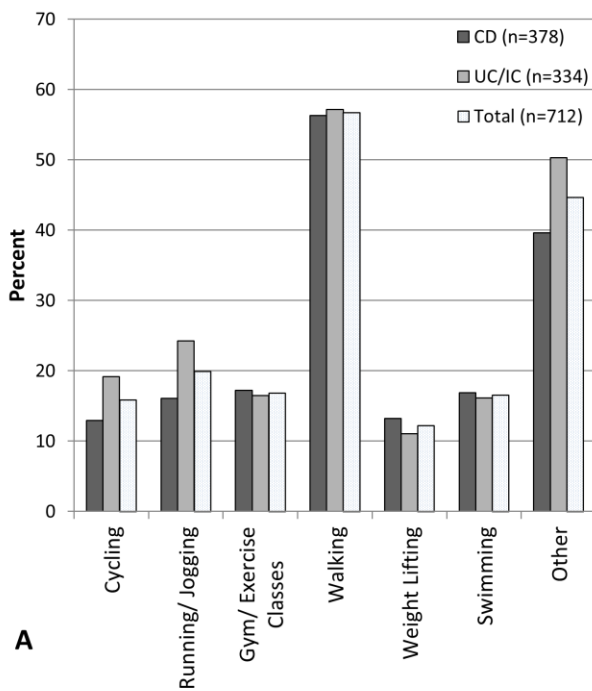
440 **Figure Legends**

441 **Figure 1** The most common types of physical activity/exercise that respondents participated  
442 in during the last year (Panel A) and avoided because of IBD (Panel B)

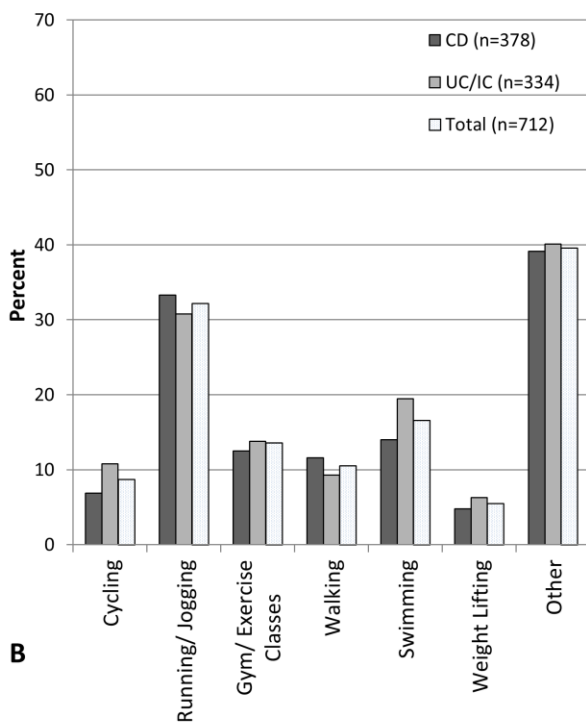
443 **Figure 2** Reasons given for IBD limiting participation in physical activity/exercise

444 **Figure 3** Average fatigue levels in the past two weeks (values in bars are %)

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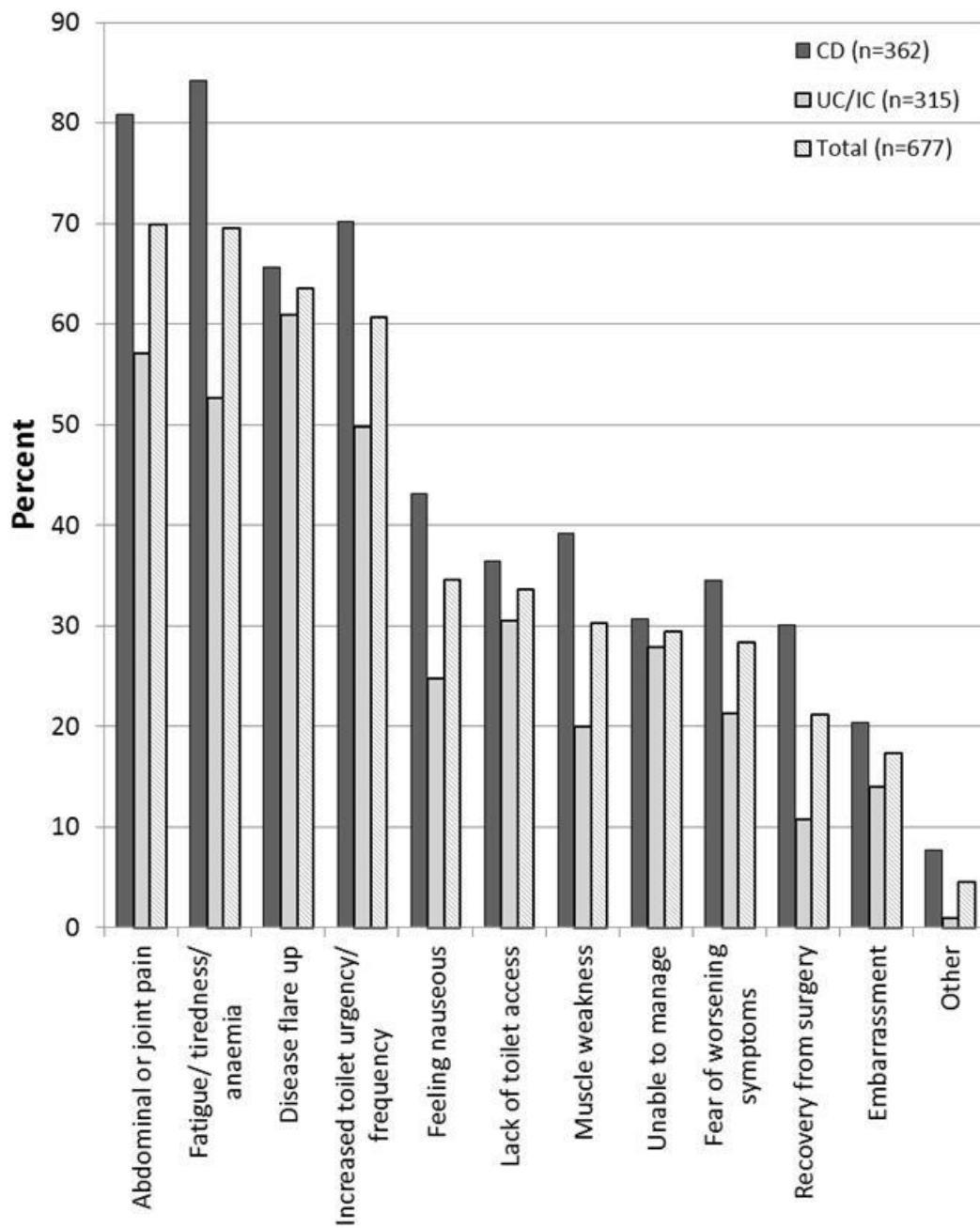


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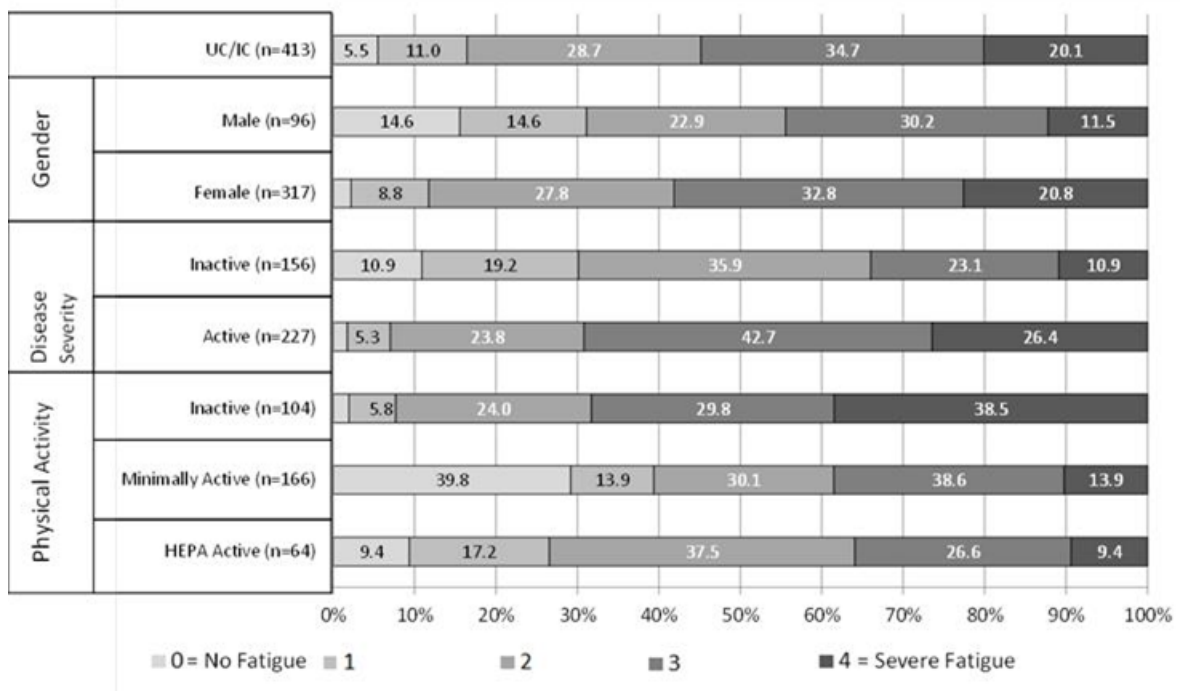
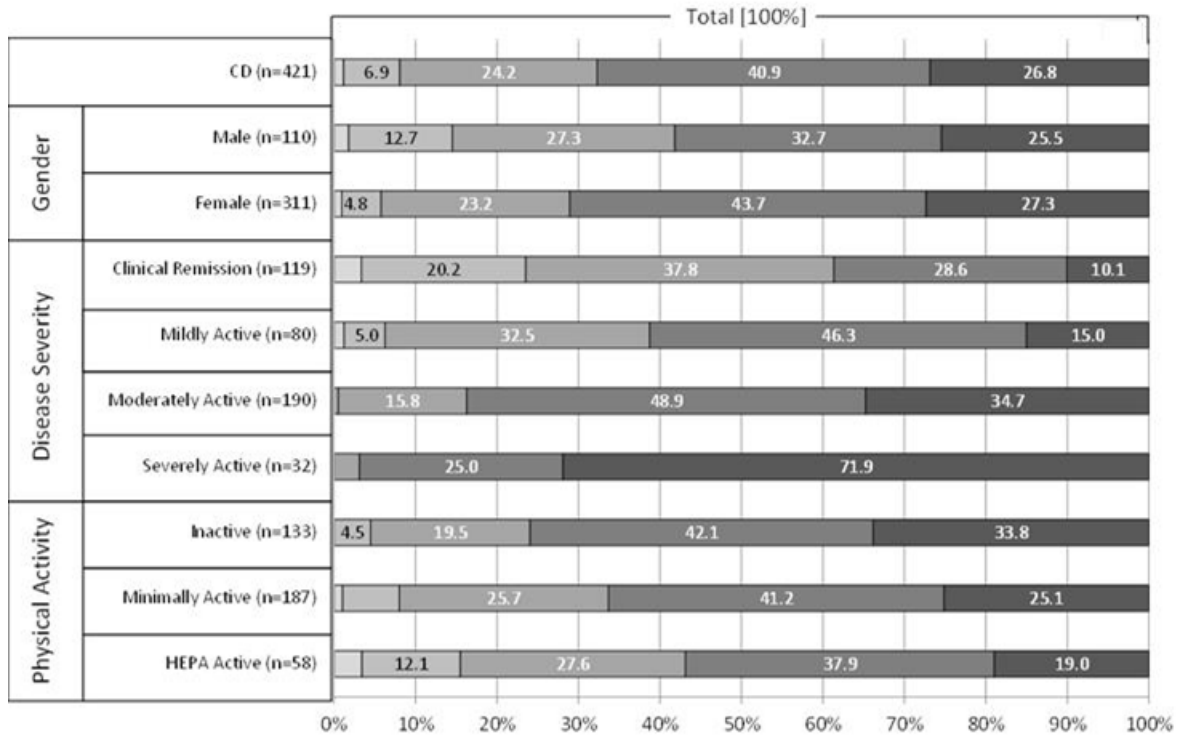
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452 **Table 1** Demographic and disease-related characteristics

	CD (n = 446)	UC/IC (n = 413)	Total (n = 859)
Age, mean (SD), years	36.9 (11.5)	37.7 (11.6)	37.3 (11.6)
Female, n (%)	329 (73.8)	317 (76.8)	646 (75.2)
Male, n (%)	117 (26.2)	96 (23.2)	213 (24.8)
Employment status, n (%)			
Employed Full Time	192 (43.0)	232 (56.2)	424 (49.4)
Employed Part Time	70 (15.7)	60 (14.5)	130 (15.1)
Unemployed- Unable	83 (18.6)	39 (9.4)	122 (14.2)
Unemployed- Other	32 (7.2)	25 (6.1)	57 (6.6)
Student	55 (12.3)	36 (8.7)	91 (10.6)
Retired	11 (2.6)	17 (4.1)	28 (3.3)
Don't know/ Prefer not to say	3 (0.7)	4 (1.0)	7 (0.8)
Smoking Status, n (%)			
Yes	75 (16.8)	33 (8.0)	108 (12.6)
No	278 (62.3)	293 (70.9)	571 (66.5)
Not anymore	92 (20.6)	86 (20.8)	178 (20.7)
Don't Know/ Prefer not to say	1 (0.2)	1 (0.2)	2 (0.2)
Time since diagnosis, median (IQR), months <sup>a</sup>	102 (36-188)	74.5 (36-168)	87 (36-178)
Disease activity, n (%) <sup>a</sup>			
PRO3: Clinical Remission	119 (28.3)		
PRO3: Mildly Active	80 (19.0)		
PRO3: Moderately Active	190 (45.1)		
PRO3: Severely Active	32 (7.6)		

P-SCCAI: Inactive 156 (40.7)

P-SCCAI: Active 227 (59.3)

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453 CD, Crohn's Disease; UC, Ulcerative Colitis; IC, Indeterminate Colitis; PRO3, 3-item Patient Reported

454 Outcome (CD only); P-SCCAI, Patient-based Simple Clinical Colitis Activity Index (UC/IC only)

455 <sup>a</sup>5.6% (n = 25) CD respondents and 7.3% (n = 30) UC/IC respondents did not complete

456

457 **Table 2** Clinical characteristics

	CD (n = 421)	UC/IC (n = 383)	Total (n = 804)
<b>Current Treatment (%)<sup>a</sup></b>			
Oral 5-Aminosalicylates	95 (23.3)	196 (54.0)	291 (37.9)
Corticosteroids	83 (20.4)	79 (21.7)	162 (21.0)
Immunosuppressants	262 (63.7)	147 (38.6)	409 (51.7)
Antibiotics	23 (5.5)	17 (4.4)	40 (4.9)
Anti-Diarrheals	83 (19.7)	71 (18.5)	154 (19.2)
Pain Relief	163 (38.7)	99 (26.1)	262 (32.7)
Iron Supplements	85 (20.2)	67 (17.5)	152 (18.9)
Vitamin B-12 Injections	111 (26.4)	N/A	111 (13.8)
Calcium Supplements	94 (22.3)	N/A	94 (11.7)
Vitamin D Supplements	139 (33.0)	N/A	139 (17.3)
Nutrition Therapy	15 (3.6)	N/A	15 (1.9)
No Medication Required	20 (4.8)	27 (7.3)	47 (6.0)
Don't Know/ Prefer not to say	3 (0.7)	5 (1.3)	8 (1.0)
Other	66 (15.7)	62 (16.2)	128 (15.9)
<b>Surgical History (%)<sup>a</sup></b>			
Permanent Ileostomy	27 (6.4)	27 (7.0)	54 (6.7)
Temporary Ileostomy	38 (9.0)	43 (11.2)	81 (10.1)
Permanent Colostomy	13 (3.1)	29 (7.6)	42 (5.2)
Temporary Colostomy	7 (1.7)	3 (0.8)	10 (1.2)
Strictureplasty	24 (5.7)	N/A	24 (3.0)
Resection	111 (26.4)	N/A	111 (13.8)

Ileocaecal Resection	49 (11.6)	N/A	49 (6.1)
Limited Right Hemicolectomy	32 (7.6)	N/A	32 (4.0)
Proctocolectomy	15 (3.6)	N/A	15 (1.9)
Ileo-Anal Pouch	N/A	54 (14.1)	54 (6.7)
I have not had surgery	203 (48.2)	283 (73.9)	486 (60.4)
Don't know/ Prefer not to say	2 (0.5)	1 (0.3)	3 (0.4)
Other	62 (14.7)	21 (5.5)	83 (10.3)
Time Since Last Surgery, median (IQR), months	36 (16-96)	36 (12-84)	36 (13-84)

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458 CD, Crohn's Disease; UC, Ulcerative Colitis; IC, Indeterminate Colitis

459 <sup>a</sup>5.6% (n = 25) CD respondents and 7.3% (n = 30) UC/IC respondents did not complete

**Table 3** Physical activity, depression and anxiety data by disease type and activity

	Total	CD				UC/IC	
	(n = 834)	(n = 421)				(n = 413)	
		Clinical remission	Mildly active	Moderately active	Severely active	Inactive	Active
IPAQ Category (%) <sup>a</sup>							
HEPA active	17.1	21.5	23.2	10.4	3.4	21.2	17.8
Minimally active	49.6	51.4	55.1	48.6	34.5	57.6	44.1
Inactive	33.3	27.1	21.7	41.0	62.1	21.2	38.1
IPAQ MVPA, median (IQR),	360	960	720	0	0	820	120
MET·min/week <sup>a</sup>	(0-1875)	(0-2120)	(0-2040)	(0-1380)	(0-410)	(0-2160)	(0-1440)
IPAQ Total PA, median (IQR),	1866	2222	2730	1386	600	2355	1386
MET·min/week <sup>ab</sup>	(594-4040)	(1205-4584)	(1158-4986)	(996-3412)	(60-2079)	(983-4650)	(446-3465)
IPAQ Sitting, mean (SD), min/day <sup>a</sup>	429 (225)	369 (177)	416 (220)	444 (254)	561 (317)	410 (202)	445 (214)
EBBS Barriers Score, mean (SD) <sup>c</sup>	31.6 (6.6)	29.8 (7.0)	31.5 (6.6)	33.4 (5.4)	34.2 (7.0)	30.2 (6.4)	31.7 (6.8)
EBBS Benefits Score, mean (SD) <sup>c</sup>	84.9 (15.3)	87.8 (14.3)	83.0 (20.3)	81.2 (13.6)	80.1 (15.8)	88.0 (15.0)	86.4 (14.9)

HADS Anxiety, mean (SD)	9.1 (4.5)	7.3 (4.1)	8.9 (4.3)	11.4 (4.1)	12.4 (3.7)	6.8 (4.1)	9.6 (4.3)
HADS Depression, mean (SD)	7.0 (4.3)	4.8 (3.4)	6.7 (4.2)	9.2 (4.1)	11.3 (3.7)	4.5 (3.5)	7.8 (4.1)

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CD, Crohn's Disease; UC, Ulcerative Colitis; IC, Indeterminate Colitis; IPAQ, International Physical Activity Questionnaire; EBBS, Exercise Benefits/Barriers

Scale; HADS, Hospital Anxiety and Depression Scale; MVPA, Moderate-to-Vigorous Physical Activity

<sup>a</sup>10.2% (n = 43) CD respondents and 19% (n = 79) UC/IC respondents did not complete

<sup>b</sup>Total physical activity computed as the sum of Walking + Moderate + Vigorous MET·min/week scores

<sup>c</sup>14% (n = 59) CD respondents and 23.7% (n = 98) UC/IC respondents did not complete

**Table 4** Correlation matrix between physical activity and fatigue (composite) scores and various demographic, clinical and psychological factors

	Physical activity <sup>a</sup>		Fatigue	
	CD	UC/IC	CD	UC/IC
Age	-0.098	-0.158**	0.036	-0.070
Time since diagnosis	-0.042	-0.064	0.110*	0.017
Disease activity	-0.228**	-0.123*	0.479**	0.393**
Depression	-0.287**	-0.240**	0.538**	0.572**
Anxiety	-0.120*	0.049	0.465**	0.453**
Physical activity	-	-	-0.127*	-0.181**
Fatigue	-0.127*	-0.181**	-	-
Exercise benefits	0.244**	0.171**	N/A	N/A
Exercise barriers	-0.292**	-0.112	N/A	N/A

CD, Crohn's disease; IC, Indeterminate Colitis; UC, Ulcerative Colitis

<sup>a</sup>Total physical activity computed as the sum of Walking + Moderate + Vigorous MET·min/week scores (logarithmic transformed)

\*Correlation is significant at the 0.05 level

\*\*Correlation is significant at the 0.01 level

**Table 5** Regression model results for total physical activity (logarithmic transformed)

	Crohn's Disease						Ulcerative and Indeterminate Colitis					
	B	Std. Error	Beta	t	P-value	Adjusted R <sup>2</sup>	B	Std. Error	Beta	t	P-value	Adjusted R <sup>2</sup>
First Model <sup>a</sup>												
(Constant)	8.015	0.862		9.299	<0.001	0.132	7.685	0.609		12.611	<0.001	0.076
Age	N/A	N/A	N/A	N/A	N/A		-0.016	0.006	-0.146	-2.566	0.011	
Gender	0.216	0.155	0.074	1.393	0.165		0.000	0.168	0.097	1.676	0.095	
Disease activity	-0.010	0.005	-0.130	-2.083	0.038		-0.053	0.027	-0.001	-0.010	0.992	
Depression	-0.077	0.024	-0.251	-3.199	0.002		-0.053	0.024	-0.177	-2.252	0.025	
Anxiety	0.034	0.021	0.114	1.576	0.116		N/A	N/A	N/A	N/A	N/A	
Fatigue	0.024	0.018	0.086	1.294	0.197		-0.013	0.019	-0.049	-0.671	0.503	
Exercise benefits	0.007	0.006	0.081	1.238	0.216		0.005	0.005	0.062	0.993	0.321	
Exercise barriers	-0.035	0.013	-0.171	-2.655	0.008		N/A	N/A	N/A	N/A	N/A	
Second Model <sup>b</sup>												
(Constant)	9.437	0.342		27.563	<0.001	0.123	8.505	0.247		34.439	<0.001	0.073



Age	N/A	N/A	N/A	N/A	N/A	-0.015	0.006	-0.145	-2.636	0.009
Disease activity	-0.009	0.005	-0.109	-1.873	0.062	N/A	N/A	N/A	N/A	N/A
Depression	-0.048	0.019	-0.157	-2.563	0.011	-0.069	0.016	-0.232	-4.216	<0.001
Exercise barriers	-0.043	0.011	-0.212	-3.847	<0.001	N/A	N/A	N/A	N/A	N/A

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<sup>a</sup>Including only those variables that were significantly correlated with physical activity in the initial exploratory work (correlation matrices)

<sup>b</sup>Including only those variables that were statistically significant in the First Model

**Table 6** Regression model results for fatigue (composite score)

	Crohn's Disease						Ulcerative and Indeterminate Colitis					
	B	Std. Error	Beta	t	P-value	Adjusted R <sup>2</sup>	B	Std. Error	Beta	t	P-value	Adjusted R <sup>2</sup>
First Model <sup>a</sup>												
(Constant)	0.380	1.549		0.245	0.806	0.367	4.512	1.547		2.917	0.004	0.373
Gender	-0.649	0.473	-0.062	-1.373	0.171		-1.360	0.495	-0.125	-2.744	0.006	
Time since diagnosis	0.005	0.002	0.112	2.550	0.011		N/A	N/A	N/A	N/A	N/A	
Disease activity	0.083	0.014	0.287	5.772	<0.001		0.152	0.081	0.098	1.884	0.061	
Depression	0.278	0.070	0.251	3.982	<0.001		0.454	0.070	0.408	6.455	<0.001	
Anxiety	0.226	0.063	0.211	3.554	<0.001		0.180	0.061	0.172	2.969	0.003	
Physical activity	0.163	0.163	0.045	0.996	0.320		-0.253	0.180	-0.068	-1.405	0.161	
Second Model <sup>b</sup>												
(Constant)	1.172	0.503		2.328	0.020	0.370	3.320	0.727		4.565	<0.001	0.360
Gender	N/A	N/A	N/A	N/A	N/A		-1.476	0.455	-0.133	-3.242	0.001	

Time since diagnosis	0.003	0.002	0.083	2.111	0.035	N/A	N/A	N/A	N/A	N/A
Disease activity	0.076	0.013	0.270	6.102	<0.001	N/A	N/A	N/A	N/A	N/A
Depression	0.324	0.060	0.295	5.375	<0.001	0.517	0.057	0.465	9.148	<0.001
Anxiety	0.183	0.056	0.170	3.237	0.001	0.178	0.054	0.168	3.312	0.001

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<sup>a</sup>Including only those variables that were significantly correlated with fatigue in the initial exploratory work (correlation matrices)

<sup>b</sup>Including only those variables that were statistically significant in the First Model