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## **Research Article**





# Device-Measured Walking and Standing are Associated with Improved Quality of Life, Mental Health, and Biochemical Markers in Patients with Ulcerative Colitis: A Pilot Study

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#### Abstract

**Background:** Device-measured daily steps/step cadence and other prominent behaviours occurring throughout the 24-hour day (i.e., sitting, lying, standing) have not been examined in patients with ulcerative colitis (UC). The degree to which these behaviours are associated with mental health, quality of life and clinical outcomes in this population is unknown. Aims: To explore the associations between device-based walking, step cadence, and sedentary time and clinical outcomes among UC patients. **Methods:** Patients with UC wore an activPAL<sup>TM</sup> accelerometer for 7 days to measure daily steps, step cadence, lying, standing, and sitting time. Outcomes included total Mayo score (TMS), risk of depression (PHQ-8), risk of anxiety (GAD-7), and health-related quality of life [HRQoL (SF-12)] which included mental composite scores (MCS) and physical composite scores (PCS). Blood and stool samples were used to measure C-reactive protein (CRP) and fecal calprotectin (FCP). **Results:** Of 30 participants, thirteen (43.3%) had moderate to severe UC symptoms. The percentage of patients with moderate to severe depression and anxiety symptoms were 25.0% and 57.1%, respectively. Average daily steps were 7,869  $\pm$  3339. Step cadence  $\geq$  100 steps/min was positively associated with mental HRQoL and TMS, and inversely associated with FCP. Faster walking was negatively correlated with CRP. **Conclusion:** This study identifies potential associations between device-measured brisk walking/running and periods of standing with HRQoL, mental health, and clinical outcomes. This study should be replicated in a larger sample to determine if these associations remain.

**Keywords:** Ulcerative Colitis; Physical Activity; Behaviour; Mental Health (or mental well-being); Quality of life; Accelerometer

#### Introduction

Inflammatory Bowel Disease (IBD) is a chronic and relapsing, remitting inflammatory disorder affecting the gastrointestinal tract. The two major phenotypes of IBD, Ulcerative Colitis (UC) and Crohn's Disease, affect young adults in their productive years, imposing a significant challenge to an individual's well-being and a significant burden on the healthcare system [1,2]. Along with disease-related symptoms, IBD is also associated with a higher prevalence of anxiety and depression [3], and decreased quality of life (QoL) [4,5]. Depression and anxiety in those with IBD have been linked to increased mortality [6], decreased quality of life [7], higher likelihood of clinical recurrence, increased hospitalization rates, and decreased treatment compliance [8].

There is inconclusive evidence of the impact physical activity has on IBD disease activity [9,10]. Physical activity is defined as any bodily movement that substantially increases energy expenditure [11]. Some studies have suggested higher levels of physical activity may be associated with more favorable psychological health outcomes in those with IBD [12,13]. A recent narrative review described how greater time spent in physical activity may also be associated with decreased IBD prevalence, decreased IBD symptoms [14], and possibly, maintenance of disease remission [15]. There is evidence that suggests individuals with IBD (both active and in remission) are less physically active than healthy controls [9], with some patients noticing physical activity causing positive changes in disease activity while others say the opposite [10]. One study reported prolonged moderateintensity walking did not have any harmful effects on inflammatory markers in those with IBD [16].

The impact time spent sitting, sleeping, or standing has on IBD disease activity has not been evaluated. However, in adults with type 2 diabetes, accelerometer-measured sedentary time was associated with increased levels of CRP in women but not men  $(\beta = 0.24, p = 0.04, \beta = 0.05, p = 0.54, respectively)$  [17]. Most studies completed in patients with IBD use self-report assessments of physical activity [18-21]. Self-report measures are more likely to be biased due to recall bias and measurement error. One systematic review looked at 148 studies and found low-moderate correlations (mean r = 0.37, SD = 0.25) between self-reported and objectively measured PA [22]. These self-report studies generally only assess leisure-time physical activity rather than total daily movement, sedentary and sleeping time [23]. To date, only one abstract has reported objective (i.e., device-based) walking and sleep time measurements in 39 patients with IBD [24]. Despite the importance of considering all behaviours occurring throughout

a 24-hour day, to our knowledge, none have investigated sitting, lying down, steps, step cadence, or standing time in the context of IBD.

Accelerometers are devices patients can wear that use acceleration and motion to provide a precise, valid, and reliable estimate of daily movement patterns. Different accelerometers can capture a variety of different variables such as total activity, activity intensity, steps, sitting, standing, and lying down [25]. Previous work in individuals with UC has focused mostly on investigating the effect of moderate (i.e., brisk walking) to vigorous physical activity (i.e., running) [15]. However, additional behaviours occurring throughout the day such as steps (and step cadence), sitting, standing, lying down, and their association with mental health, patient reported outcomes, disease course, or inflammatory markers have not been studied.

The objectives of this exploratory study were to examine whether accelerometer measured step count, step cadence, sitting time, time spent lying down, and standing time associated with a) mental health (i.e., depression and anxiety risk), b) health-related quality of life (HRQoL), and c) clinical outcomes (total Mayo score [TMS], fecal calprotectin [FCP] and C-reactive protein [CRP]) in individuals with UC.

#### Methods

#### Participants

Thirty individuals aged 18 years or older were recruited from IBD outpatient clinics at the Foothills Medical Centre in Calgary, Alberta, Canada between May 2017, and November 2020. To be eligible, patients required a diagnosis of UC, managed with conventional medical therapies (oral and/or topical 5-ASA, either alone, in combination with biologic and/or immunosuppressant therapies and with or without oral corticosteroid therapy). Exclusion criteria included major medical comorbidities (diabetes, active malignancy within past 5 years, active infection, severe respiratory or cardiac disease, or acute or chronic kidney disease), a history of previous bowel surgery, or was a current smoker. The study protocol was approved by the University of Calgary Conjoint Health Research Ethics Board and all participants provided informed written consent prior to participating in the study.

#### Physical activity measurement

Time spent lying down, sitting, standing, step count, and step cadence were measured using the activPAL<sup>TM</sup> accelerometer (PAL Technologies, Glasgow, Scotland). Participants were instructed to adhere the activPAL<sup>TM</sup> device to the front-midline portion of the thigh with stretch tape that was provided. Participants wore the activPAL<sup>TM</sup> at all times (except when showering or swimming), for seven days. Time spent sitting, lying down, and step count were calculated using activPAL<sup>TM</sup> algorithms (PAL Software version

8). We were also able to calculate the number of steps taken at a higher stepping cadence ( $\geq 100$  steps/min) which was reflective of moderate (100+ steps/min) to vigorous (130+ steps/min) intensity physical activity [26, 27].

#### Mental health and HRQoL

This study used the Patient Health Questionnaire-8 (PHQ-8) [28] which measures the presence and severity of depression based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria [29]. The PHQ-8 consists of eight items measuring symptoms from the past two weeks with a response scale ranging from "0" (not at all) to "3" (nearly every day) and does not ask the question about suicidal ideation included in the PHQ-9. A PHQ-8 score  $\geq$  10 is used to characterize moderatesevere depression risk in clinical practice and has a sensitivity and specificity of 70% and 98% respectively [28]. The Generalized Anxiety Disorder-7 (GAD-7) [30] is a seven-item clinical tool used to measure severity of generalised anxiety disorder risk and symptoms from the past two weeks. The response scale ranges from "0" (not at all) to "3" (nearly every day). A GAD-7  $\geq 10$ characterizes moderate to severe anxiety risk (sensitivity of 89%, specificity of 82%) [30].

HRQoL was measured using the 12-Item Short-Form Health Survey (SF-12) version 1 [31]. The SF-12 is a self-report tool that assesses the impact of mental and physical health on everyday life. The SF-12 measures eight physical, psychological and psychosocial health domains to tabulate a physical (PCS, based on 4 items) and mental health composite score (MCS, based on 4 items). We used PCS and MCS scores > 50 as a cut-off where a score above 50 represents an above average score and a score of 50 or less represents a below average score [31].

#### UC clinical outcomes

TMS was calculated for participants by the treating physician. Surveys completed at baseline were used to collect information regarding medication use including immunosuppressants, probiotics, antibiotics, steroids, amino salicylates, and biologic therapies. Stool samples were collected at home by the patient to measure FCP levels, and serum samples were taken to measure CRP levels. TMS, FCP, and CRP variables were dichotomized at clinically relevant cut-offs where TMS  $\leq$  5 indicated mild disease or clinical remission,  $FCP \le 250 \text{ mg/g}$ , and CRP < 8 mg/L (biomarker thresholds represent objective markers of remission).

#### **Statistical Analyses**

Proportions, means, and standard deviations were calculated for all relevant sociodemographic, clinical and accelerometer characteristics. To analyze relationships between activPAL<sup>TM</sup> variables and mental health, HRQoL and clinical outcomes we used both independent sample t-tests and analysis of variance (ANOVA) for categorical cutoffs (n  $\geq$  7 in each group), and Pearson's correlations for continuous variables. Due to the small sample size, large variability in physical activity data, and exploratory nature of this study, the significance value was set at p < 0.20.

#### Categorical data analyses

When a significant independent t-test was present (p < 0.20), an analysis of variance (ANOVA) was used to further evaluate the relationship between activPAL<sup>TM</sup> variables and mental health, HRQoL and clinical outcomes, controlling for relevant covariates (i.e., age, gender, steroids, BMI, and valid days activPAL<sup>TM</sup> worn).

#### Continuous data analyses

Pearson correlation coefficients were calculated to identify associations between continuous activPAL<sup>TM</sup> variables and mental health, HRQoL and clinical outcomes. When a significant correlation was observed (p < 0.20), multivariable linear regression analyses evaluated associations controlling for relevant covariates. Model covariates included activPAL<sup>TM</sup> wear time, age, gender, body mass index (BMI), corticosteroid use, TMS, and FCP.

#### Results

Baseline sociodemographic characteristics and clinical outcomes are presented in (Table 1). Participants (N=30) had a mean age of  $38.6 \pm 12.1$  years and a mean BMI of  $26.1 \pm 3.2$  kg/m<sup>2</sup>, with 63.3% overweight or obese (i.e., BMI  $\ge 25$  kg/m<sup>2</sup>). TMS scores indicated 56.7% (n=17) of participants were in clinical remission or had mild clinical disease activity (TMS  $\le 5$ ). The mean TMS score was  $4.5 \pm 3.7$ . Thirteen patients (43.3%) had an FCP > 250 mg/g. The mean FCP score was  $928.2 \pm 1410.2$  mg/g. Only one patient (3.3%) had a CRP at or above 8 mg/L and the mean CRP score was  $2.1 \pm 2.5$  mg/L.

Characteristic	No. of respondents	%	Mean (SD)
Demographic		•	•
Males	16	53.3	
Females	14	46.7	
Age (years)	30		38.6 (12.1)
Clinical			
Body mass index (kg/m <sup>2</sup> )	30		26.1 (3.2)
Normal weight (< 25 kg/m <sup>2</sup> )	11	36.7	
Overweight/obese ( $\geq 25 \text{ kg/m}^2$ )	19	63.3	
Total Mayo score	30		4.5 (3.7)
Clinical remission/mild (TMS $\leq$ 5)	17	56.7	
Moderate-severe UC symptoms (TMS > 5)	13	43.3	
Fecal calprotectin (mg/g)	30		982 (1410.2)
C-reactive protein (mg/L)	30		2.1 (2.5)
Medications	30		
5-ASA	20	66.7	
Corticosteroids	12	40.0	
Anti-TNF agent	8	26.7	
Immunosuppressants	5	16.7	
Any (incl. above)	29	96.7	
Antibiotics	5	16.7	

 Table 1: Sociodemographic characteristics and clinical outcomes.

#### Physical activity characteristics

Accelerometer data are presented in (Table 2)

activPAL <sup>TM</sup>	Mean (SD)	Mean PHQ	Mean PHQ	Mean GAD	Mean GAD	MCS (n=28)	PCS (n=28)
variables	Mean (SD)	< 10 (n=21)	≥10 (n=7)	<10 (n=12)	≥10 (n=16)	WICS (II-20)	r CS (ll-28)
Valid days	5.57 (1.01)						
Total steps	7869 (3339)	8130 (3179)	7295 (4398)	7586 (2853)	8173 (3916)	7869 (3339)	7869 (3339)
Steps at a cadence of ≥100 steps/min	2319 (1734)	2102 (1709)	2764 (1974)	2007 (1918)	2454 (1677)	2319 (1734)	2319 (1734)
Time spent upright (hours)	5.64 (1.73)	5.90 (1.90)	4.97 (1.26)	6.02 (2.10)	5.41 (1.53)	5.64 (1.73)	5.64 (1.73)
Time spent standing (hours)	3.96 (1.41)	4.13 (1.63)	3.46 (0.56)	4.36 (1.88)	3.67 (1.00)	3.96 (1.41)	3.96 (1.41)
Time spent lying down (hours)	8.50 (2.43)	8.42 (1.94)	8.75 (3.94)	8.03 (1.95)	8.86 (2.86)	8.50 (2.43)	8.50 (2.43)
Time spent sitting (hours)	8.71 (2.75)	8.48 (2.44)	9.11 (3.93)	8.78 (2.98)	8.52 (2.78)	8.71 (2.75)	8.71 (2.75)

**Table 2:** Descriptive statistics for activPAL<sup>TM</sup> measured 24-hour activities (N=28); MCS and PCS cutoffs not included due to n < 7 for the cutoff groups.

For the total sample, mean sitting time was  $8.7 \pm 2.8$  hours per day with a mean standing time of  $4.0 \pm 1.4$  hours per day. Mean time spent lying down was  $8.5 \pm 2.4$  hours per day. Participants had an average of  $7,869 \pm 3,339$  steps per day. The mean number of steps patients took at a cadence  $\geq 100$  steps per minute was  $2,319 \pm 1,734$  while the amount of time spent walking at this pace was  $20.59 \pm 14.82$  minutes per day.

#### **Clinical outcomes**

Independent sample t-tests demonstrated a positive association between TMS and standing time (t = 1.04, p = 0.154), step count at a cadence of  $\ge 100$  steps/min (t = 1.31, p = 0.100), and time spent walking at a cadence of  $\ge 100$  steps/min (t = 1.13, p = 0.135) (Table 3). There was an inverse association between FCP and step count (t = -1.14, p = 0.133), standing time (t = -1.46, p = 0.077), step count at a cadence of  $\ge 100$  steps/min (t = -1.05, p = 0.151), and time spent walking at a cadence of  $\ge 100$  steps/min (t = -1.18, p = 0.123). No associations were found between FCP and the activPAL<sup>TM</sup> variables. We did not run a t-test for CRP as there was only one patient who was above the pre-specified cutoff (CRP  $\ge 8$ mg/L) for analysis.

activPAL <sup>TM</sup> variables	TMS	FCP
Step count (t-test)	0.292	-1.136*
Sitting time	0.669	0.123
Standing time	1.038*	-1.464*
Time spent lying down	-0.865	0.766
Number of steps at cadence $\geq 100$ steps/min	1.311*	-1.050*
Time stepping at 100 steps/min	1.127*	-1.184*

**Table 3:** Associations between clinical outcomes and activPAL<sup>TM</sup> variables (analysis of CRP not completed due to n < 7 patients above cutoff) p < 0.200; p < 0.200; p < 0.100.

After the t-tests, an ANOVA was conducted on relationships that were significant in the t-tests and covariates were added. In the ANOVA, no significant associations between the clinical outcomes and activPAL<sup>TM</sup> variables remained (Table 4).

Relationship	ANOVA <i>p</i> -value	Difference between high and low cutoffs
TMS/time standing	0.797	0.188 hours
TMS/number of steps at 100 steps per minute	0.236	-989 steps
TMS/time stepping at 100 steps per minute	0.332	-0.117 hours
FCP/step count	0.252	-1,537 steps
FCP/time standing	0.425	-0.315 hours
FCP/number of steps at 100 steps per minute	0.455	-519 steps
FCP/time stepping at 100 steps per minute	0.331	-0.098 hours

**Table 4:** ANOVA tests for significant associations between clinical outcome cutoffs and activPAL<sup>TM</sup> variables. Model covariates: age, gender, steroids, BMI, valid days accelerometer worn.

CRP was negatively correlated with the number of steps taken at a cadence  $\geq 100$  step/min (r = -0.336, p < 0.070) and time spent stepping at this faster cadence (r = -0.343, p = 0.063) (Table 5). There were no significant correlations present between TMS or FCP and activPAL<sup>TM</sup> variables.

activPAL <sup>TM</sup> variables	TMS	FCP (mg/g)	CRP (mg/L)
Step count	-0.104	0.174	-0.031
Sitting time	0.058	0.026	0.114
Standing time	-0.248	-0.230	-0.227
Time spent lying down	0.082	0.090	0.112

Number of steps at cadence $\geq 100$ steps/min	-0.273	-0.150	-0.336*
Time spent stepping at cadence $\geq 100$ steps/min	-0.245	-0.166	-0.343*

**Table 5:** Pearson correlations between clinical outcomes and activPAL<sup>TM</sup> variables; \*p < 0.100

#### Mental Health and HRQoL

Overall, 25% (n = 7) of the sample had moderate to severe depression symptoms (PHQ-8  $\ge$  10). The mean PHQ-8 score was 6.6  $\pm$  5.2. Meanwhile, 57.1% (n = 16) had moderate to severe anxiety symptoms (GAD-7  $\ge$  10). The mean GAD-7 score was 12.0  $\pm$  4.4. Eight patients (28.6%) had both moderate to severe depression and anxiety. Mean MCS scores were 44.2  $\pm$  3.3 and mean PCS scores were 42.7  $\pm$  4.1.

Based on the t-tests, both the PHQ-8 and GAD-7  $\ge$  10 were inversely associated with standing time (t = -1.06, p = 0.15, t = -1.26, p = 0.11 respectively; (Table 6).

activPAL <sup>TM</sup> variables	PHQ-8	GAD-7
Step Count (t-test value)	-0.46	0.44
Sitting Time	0.51	-0.24
Standing Time	-1.06*	-1.26*
Time spent lying down	0.29	0.86*
Number of steps at cadence > 100 steps/min	0.86	0.67
Time spent stepping at cadence > 100 steps/min	0.66	0.68

**Table 6:** The association between mental health cutoffs and activPAL<sup>TM</sup> variables (MCS and PCS removed due to insufficient patients above cutoff); p < 0.200; \*\*p < 0.100

GAD- $7 \ge 10$  scores were also positively associated with greater time spent lying down (t = 0.861, p = 0.198). The ANOVA on the t-test's significant relationships did not demonstrate any significant associations after including covariates (Table 7). T-tests and ANOVAs were not performed on the MCS or PCS scores as there were insufficient patients above the cutoff of 50 (zero and one patient, respectively).

Relationship	ANOVA <i>p</i> -value	Delta
PHQ-8/Time standing	0.23	- 0.76 hours
GAD-7/Time standing	1.00	0.00 hours
GAD-7/Time lying down	0.89	0.19 hours

Table 7: ANOVA tests for significant associations between mental health cutoffs and activPAL<sup>TM</sup> variables.

Both MCS and PCS were positively correlated with step count (r = 0.471, p = 0.011; r = 0.265, p = 0.173, respectively), steps at a cadence  $\geq 100$  steps/min (r = 0.439, p = 0.038; r = 0.336, p = 0.081, respectively), and time spent walking at this faster cadence (r = 0.439, p = 0.019; r = 0.348, p = 0.070, respectively) (Table 8). After controlling for covariates, average daily steps were significantly associated with better MCS ( $\beta = 0.700$ , p = 0.001) (Table 9). No significant correlations were identified between risk of depression and anxiety (PHQ-8 & GAD-7) and the activPAL<sup>TM</sup> variables (Table 8). Daily steps at a cadence  $\geq 100$  steps per minute, and total minutes walking at this higher cadence, were significantly associated with better MCS scores ( $\beta = 0.503$ , p = 0.044 and  $\beta = 0.563$ , p = 0.019, respectively).

activPAL <sup>TM</sup> variables	MCS	PCS	PHQ-8	GAD-7
Step count	0.471***	0.265*	-0.13	0.017
Sitting time	-0.161	0.007	-0.14	-0.042
Standing time	0.008	0.006	-0.055	-0.154

Upright time	0.182	0.100	-0.099	-0.138
Time spent lying down	0.143	-0.002	0.102	0.120
Number of steps at cadence $\geq 100$ steps per minute	0.394***	0.336**	-0.014	0.230
Time spent stepping at cadence $\geq 100$ steps per minute	0.439***	0.348**	-0.055	0.193

**Table 8**: Correlations between patient reported outcomes and activPAL<sup>TM</sup> variables. \*p < 0.20;

\*\**p* < 0.10; \*\*\* *p* < 0.05.

Relationship	Standardized b-weight
MCS/step count	0.700**
MCS/time at 100 steps per minute	0.503**
MCS/number of steps at 100 steps per minute	0.563**
PCS/time at 100 steps per minute	0.304
PCS/number of steps at 100 steps per minute	0.284
CRP/time at 100 steps per minute	-0.336*
CRP/number of steps at 100 steps per minute	-0.340*

**Table 9:** Relationships between MCS and PCS scores and activPAL<sup>TM</sup> variables; controlling for age, gender, steroids, BMI, total mayo score, baseline FCP, valid days; \*p < 0.100; \*\*p < 0.05.

#### Discussion

This study examined the average amount of time individuals with UC spent sitting, standing, lying down, step cadence and number of steps taken over a 24-hour period. We also examined associations between activPAL<sup>TM</sup> variables and mental health, HRQoL, and clinical outcomes. These results provide preliminary evidence that in patients with UC, the amount of time spent standing and stepping at a cadence  $\geq 100$  steps/min (i.e., brisk walking or running) are associated with improved mental health, lower FCP, and increased TMS. Furthermore, there is a positive association between stepping at a cadence  $\geq 100$  steps/min and HRQoL, and an inverse association with CRP.

Previous studies have described positive effects of mild, moderate, and vigorous intensity physical activity in patients with UC on HRQoL, depression, and anxiety [32-36]. A review of five studies (N = 505 patients with IBD) identified an increase in leisuretime physical activity levels (measured via device or self-report) were associated with improved QoL (measured using EuroQOL or SF-36) [32]. Another study in IBD patients found higher average daily leisure activity levels (measured via Godin leisure activity questionnaire) had a relationship with higher PCS scores (p =0.05), but not MCS scores [33]. Fewer studies have examined the effect of habitual walking and/or stepping cadence on mental and physical HRQoL in patients living with IBD. Similar to our study, a European study identified positive correlations between PCS score and walking (r = 0.30, p < 0.05) although, this was selfreported time spent walking via the International Physical Activity Questionnaire whereas we measured step count (which could have included walking or running) [34].

The European study did not identify a significant correlation between MCS score and walking (r = 0.265, p = 0.173) [34], which is inconsistent with our findings. Another cross-sectional study of 2,052 patients with UC found leisure-time physical activity (measured using the self-report Godin-Shephard Leisure Time Activity Index) was inversely associated with depression and anxiety ( $\beta = -0.025$ , p = 0.001,  $\beta = -0.025$ , p = 0.001, respectively) while being positively associated with QoL ( $\beta = 0.005$ , p < 0.001) [35]. It is important to highlight these previously cited studies assessed self-reported leisure-time physical activity, which is different than measuring daily step count and number of steps at a cadence  $\geq 100$  steps/min (i.e. brisk walking or running).

No other study to our knowledge has evaluated the relationship between steps and step cadence (i.e. brisk walking  $\geq 100$  steps/min or running) with depression, anxiety, or TMS in patients with IBD even though associations between daily step counts (regardless of the cadence) and reduced symptoms of depression ( $\beta = -0.60$ , p = 0.03) have been identified in a healthy population of military veterans over 24 weeks [36].

A positive association between time spent lying down and increased anxiety risk (t = 0.861, p = 0.198) but not depression risk was identified. This association has not been reported in patients

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with IBD or in the general population therefore, we are unable to explain this association. Our study did not identify any significant associations between sitting time or time spent lying down, and depression, or HRQoL (Table 2 & 3). The lack of associations between time spent sitting/lying down and mental health outcomes (other than time spent lying down and anxiety) is inconsistent with recently published research that reported patients with depression and/or anxiety symptoms were more likely to be sedentary (p < 0.05), based on the Godin Exercise Score [21].

However, our study measured the time spent sitting/lying down whereas the mentioned study looked at the absence of leisure-time physical activity. To our knowledge, there are no other studies that explore associations between time spent sitting or lying down and HRQoL in patients with IBD. While our study did not identify an association between time spent sitting or lying down and mental health (depression and anxiety risk), it did demonstrate an inverse association between standing time and both depression and anxiety. Standing could be a way to break up long periods of sedentary time [37]. Limiting sedentary time to 30 minutes bouts or less over one year correlated with lower scores on the depression subscale of the Profile of Mood States ( $\beta = 0.23$ , p = 0.02) [37]. Standing may have interrupted long periods of sedentary time, a potential mechanism for its effectiveness.

No other study, to our knowledge, has evaluated the association between steps and step cadence and clinical outcomes such as TMS, FCP, or CRP. Our findings demonstrate a *positive* association between stepping at a cadence  $\geq 100$  steps/min (i.e. brisk walking or jogging) and Total Mayo Score (TMS). One narrative review explained how the inflammatory response to physical activity in patients with IBD is intensity-dependent [38]. High intensity activity could lead to immune system suppression while lower intensity exercise could lead to anti-inflammatory effects [38]. Our results, in combination with the narrative review [38], demonstrate the importance of having a personalized approach to using physical activity as a therapy for IBD patients to achieve the highest intensity of physical activity without risking increased UC symptoms.

Our study identified a negative correlation between stepping at a cadence  $\geq 100$  steps/min and CRP. While no study has looked at step cadence and CRP, there was a review of 17 studies that reported regular leisure-time physical activity was associated with lower average CRP levels in a healthy population [39]. Steps at a cadence > 100 steps/min would be considered moderate-vigorous physical activity therefore, our negative correlation seems concordant to the present literature in the general population [39].

This pilot study's results may serve as a foundation for further novel discovery exploring physical activity interventions and management of mental health, QoL, and clinical outcomes of patients with UC. Strengths of this study include the use of activPAL<sup>TM</sup> accelerometers to measure daily movement patterns, the heterogeneous UC sample, and using reliable and valid measures of HRQoL, depression and anxiety. This study was also one of the first to investigate the relationships between activPAL<sup>TM</sup> variables and UC clinical outcomes including FCP, CRP, and TMS. The primary limitation of the study includes the small sample size combined with the large variability observed in activPAL<sup>TM</sup> variables, both contributing to a high likelihood of type-2 errors. As this study was exploratory and descriptive in nature, significance criteria were set at p < 0.20 to decrease the risk for type 2 errors.

To our knowledge this is the first study in patients with UC to report on device-based estimates of step count, stepping cadence, sitting time, standing time, and time spent lying down. Standing time, step cadence and time spent at a cadence  $\geq 100$  steps/min appeared to be consistently related to mental health and clinical outcomes in this study; however, may increase GI symptoms [21]. This warrants further study of the associations between devicemeasured daily movement, mental health, HRQoL, and clinical outcomes in a larger number of patients with UC.

#### Disclosure

#### **Author Contributions**

Conceptualization: Maitreyi Raman, Jeff K. Vallance; Methodology: Maitreyi Raman, Jeff K. Vallance; Formal analysis and investigation: Brandon A. Chiew, Munazza Yousuf, Lorian M. Taylor, Maitreyi Raman, Jeff K. Vallance; Writing - original draft preparation: Brandon A. Chiew, Andreina Bruno, Maitreyi Raman, Jeff K. Vallance; Writing - review and editing: Brandon A. Chiew, Kate A. Lyden, Alana Schick, Sandeep Kaur, Munazza Yousuf, Andreina Bruno, Lorian Taylor, Maitreyi Raman, Jeff K. Vallance; Funding acquisition: Maitreyi Raman,; Resources: Maitreyi Raman; Supervision: Jeff K. Vallance, Lorian M. Taylor, Maitreyi Raman

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#### **Institutional Review Board Statement**

The study protocol was approved by the University of Calgary Conjoint Health Research Ethics Board and all participants provided informed written consent prior to participating in the study.

#### Data Availability Statement

Data supporting the study results can be provided followed by request sent to the corresponding author's e-mail.

#### **Conflicts of Interest**

None.

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