

## Observational Study

## Inflammatory bowel diseases patients suffer from significant low levels and barriers to physical activity: The “BE-FIT-IBD” study

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## Abstract

### BACKGROUND

The place regular physical activity (PA) should occupy in managing patients with inflammatory bowel diseases (IBD) is unclear.

### AIM

To assess PA levels and barriers in a southern Italian IBD population.

### METHODS

IBD patients with non-severe disease activity [assessed with partial Mayo score for ulcerative colitis (UC) and Harvey-Bradshaw index for Crohn’s disease] were approached to receive an anonymous online questionnaire to assess PA levels using the International Physical Activity Questionnaire (IPAQ) and to assess disease activity as patient-reported outcomes 2 (PRO-2) and finally to assess habits, beliefs and barriers in conducting regular PA. Clinical, anthropometric and demographic data of patients were also collected. PA was expressed as continuous units of resting metabolic rate (Met) in min/wk. Three PA groups were identified: Inactive (< 700 Met min/wk), sufficiently active (700-2500 Met min/wk) and health enhancing PA (HEPA) (*i.e.*, HEPA active, > 2500 Met min/wk) patients.

### RESULTS

Included patients (219) showed overall PA levels of 834.5 Met min/wk, with a large proportion (94, 42.9%) classified as inactive while only a minority (9, 4.1%)

as health-enhancing PA. Patients without dyslipidaemia ( $P < 0.0001$ ) or on biologics therapy ( $P = 0.022$ ) showed better IPAQ scores in moderate activities. UC PRO-2 correlated negatively with IPAQ intense activities scores ( $\tau = -0.156$ ,  $P = 0.038$ ). PRO-2 did not show notable sensitivity/specificity in predicting IPAQ inactivity (AUC  $< 0.6$ ). IBD activity did not differ between active and inactive patients ( $P > 0.05$ ). Active patients expressed the need to discuss PA with their gastroenterologist. Some barriers (e.g., diagnosis of IBD and fear of flare-ups after PA) are significantly more reported by inactive patients.

## CONCLUSION

A significant rate of physical inactivity was recorded in this setting. IPAQ showed good feasibility. PA should be an element of discussion in IBD visits assessed quickly with non-invasive questionnaires.

**Key Words:** Crohn's disease; Inflammatory bowel disease; International Physical Activity Questionnaire; Physical activity; Ulcerative colitis

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**Core Tip:** The place regular physical activity (PA) should occupy in managing patients with inflammatory bowel diseases (IBD) is unclear. IBD patients were approached to receive an anonymous questionnaire to assess PA levels using the International Physical Activity Questionnaire (IPAQ), assess disease activity as patient-reported outcomes 2, and assess habits, beliefs and barriers in conducting regular PA. A large proportion of included IBD patients were classified as inactive. Patients on biologics therapy showed better IPAQ scores in moderate activities. Inactive patients report some barriers. PA should be an element of discussion in IBD gastroenterology visits.

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## INTRODUCTION

Inflammatory bowel diseases (IBD), mainly comprising Crohn's disease (CD) and ulcerative colitis (UC), underlie sustained and chronic gastrointestinal inflammation[1] associated with varying disabilities, including those in the psychological sphere[2,3], impacting patients' quality of life (QoL)[4]. Physical activity (PA) is part of and positively affects QoL [5]. A recent consensus encouraged regular PA (consistent with individual tolerance level) to ameliorate the IBD course [6]. PA is, by definition, the use of skeletal muscles with energy expenditure and can promote an anti-inflammatory phenotype in various tissues (such as muscle, adipose tissue, and heart)[7]. It is also widely framed as a modifiable risk factor for several chronic diseases, such as cardiovascular and metabolic as well as neoplastic ones and, in some, such as rheumatoid arthritis, has even shown the ability to associate with a milder disease course[8].

Moreover, low-intensity PA can positively impact mild/remission CD patients' QoL[9], and no change in CD activity nor predisposition to flare-ups had been observed[10]. Finally, a further study on the IBD population also showed how higher PA associates with better QoL, excluding sweat-inducing exercises[11].

In addition, IBD patients seem less likely to perform PA, and, despite the potential benefits of it, precise recommendations and guidelines on how to approach this subject in IBD have not yet been codified[12]. IBD patients often suffer from sarcopenia, which is, among other things, also a predictive factor for the need to incur surgery and worsening the risk of postoperative complications[13]. PA improves muscle mass and poses as an ameliorative measure of sarcopenia [14,15]. In addition, the World Health Organization recommends, generally for every age group as well as for adults with disabilities, regular PA stigmatizing its multidimensional benefits (from cardioprotective effects to beneficial psychological effects)[16].

Ultimately, the epidemiologic data regarding PA levels in IBD is severely lacking. The barriers that block patients from practising regular PA and what factors instead are facilitators of this are unknown. Even less evidence is definitive on what impact PA (splitting the data even by intensity) may have on IBD activity. Therefore, this study aimed to assess self-reported PA levels in an IBD population and to examine whether there are differences in that setting concerning clinical/demographic, patient-reported IBD activity and reported barriers to regular PA.

## MATERIALS AND METHODS

### Study design

This cross-sectional observational study was conducted at the Hepatogastroenterology Unit of the University of Campania Luigi Vanvitelli in the first half of 2023. IBD participants included were given an online questionnaire to fill out anonymously. This study was written following the “strengthening the reporting of observational studies in epidemiology” (*i.e.*, STROBE) checklist. The study was conducted in compliance with the Declaration of Helsinki and received approval from the Ethics Committee of the University of Campania Luigi Vanvitelli (protocol number 7892, 15 March 2023).

### Inclusion and exclusion criteria

Patients with an established histologic diagnosis of IBD (*i.e.*, CD or UC) were included. Patients with known psychiatric conditions and severe comorbidities, recent surgery, clinically significant infection (*e.g.*, *Clostridioides difficile*), hospitalised or who had received contraindications to performing any form and degree of PA were, instead, excluded. In addition, patients with severe disease activity assessed (within one month before the inclusion) by partial Mayo score[17] for UC patients (*i.e.*, score > 7) and by Harvey-Bradshaw index for CD patients (*i.e.*, score > 16)[18] were also excluded.

### Collected variables

Through the questionnaire, several variables were collected. First, demographic and anthropometric data were, in detail, collected, such as sex, age, weight (in Kg), height (in cm), body mass index (BMI) (in Kg/m<sup>2</sup>), level of education, employment, smoking status, alcohol consumption (the patient was defined as an alcohol user if daily consumption was ≥ 20 g in female or ≥ 30 g in the male)[19] as well as, finally, having or not having a partner. Concerning IBD, the type (*i.e.*, CD or UC), age at diagnosis of IBD, the current treatments, and previous biologic failure were collected. IBD disease activity was assessed with patient-reported outcomes 2 (PRO-2) for both CD[20] and UC[21]. Therefore, the sub-score on stool frequency (SF) and abdominal pain (AP) for patients with CD was evaluated. On the other hand, the subscore, SF and that on rectal bleeding (RB) were examined for UC patients.

Finally, patients were also asked whether they had comorbidities (such as diabetes, hypertension, nephropathies, dyslipidaemia, or pneumopathies) or extra-intestinal manifestations.

### PA Assessment

The international PA questionnaire (IPAQ) showed good validity and reliability characteristics[22,23] and was used to assess PA in this study. IPAQ evaluate the PA type and amount performed by the compiler by referring to the past 7 d. IPAQ contemplates intense activities (such as aerobic activities like running), moderate activities (such as carrying light weights) and mild activities (walking for at least 10 min). IPAQ identifies three categories of respondents based on PA levels: Type 1 (*i.e.*, inactive), type 2 (*i.e.*, minimally active), and, finally, type 3, also defined as health enhancing PA (HEPA) (*i.e.*, HEPA active).

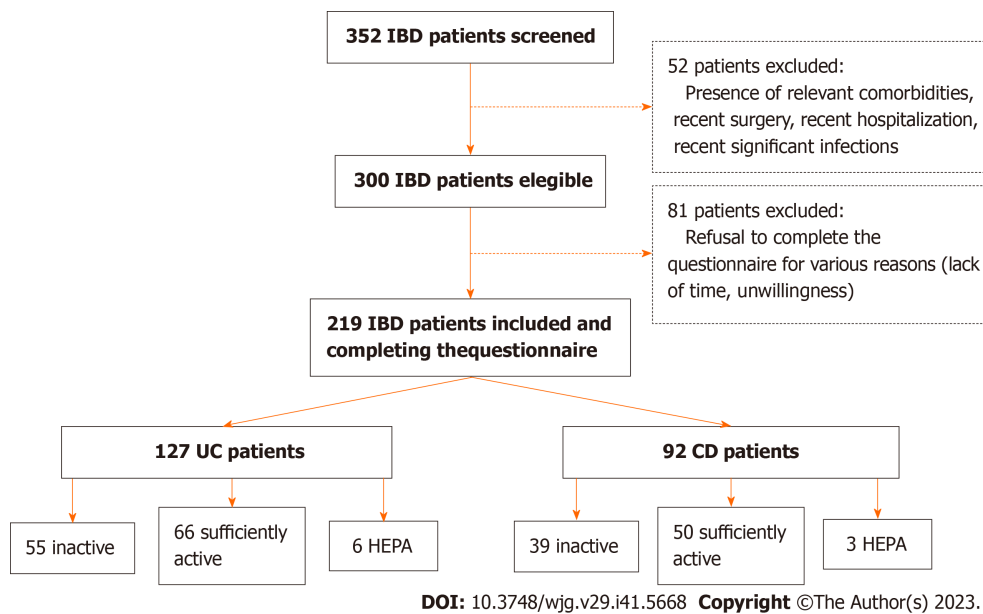
The IPAQ score was made continuous using multiples of the resting metabolic rate [*i.e.*, metabolic rate (Met)] as units. Therefore, the Met of PA was calculated by level and specifically for intense (minutes × days × 8 Met), moderate (minutes × days × 4 Met) and, finally, for mild/walking (minutes × days × X Met) activities. The value of X for the last activities is a function of a multiplier based on the steep grade. Specifically, for an intense stride that gave the compiler a marked perceived increase in respiratory rate relative to normal, the multiplier is 3.3; for a moderate stride that increased respiratory rate at a rate only moderately higher than usual, the multiplier is 3 while, finally, for a slow stride with no change in respiratory rate the multiplier is 2.5. PA levels were, therefore, ultimately expressed as Met min/wk. IPAQ has, moreover, already been employed in IBD[24]. IPAQ was scored according to the available guidelines (<http://www.ipaq.ki.se/>) using the Italian-validated IPAQ version[25]. Patients were finally considered inactive (< 700 Met min/wk), sufficiently active (700-2500 Met min/wk), or active/HEPA (> 2500 Met min/wk)[23,26].

In addition, the link provided to patients included additional questions to weigh the possible presence of barriers/facilitators to performing regular PA. These questions associate with five levels of agreement (with extremes from completely agree to disagree) responses. Finally, an 11-point Likert scale question was administered to understand how important the patient thought it was from 0 to 10 to discuss PA with their gastroenterologist during outpatient visits.

### Statistical analysis

Descriptive statistics were used for data presentation. Continuous variables are presented as a median and relative interquartile range, while categorical and ordinal variables as a percentage of the total (%) for each degree of freedom. The Kolmogorov-Smirnov test preliminarily evaluated variables distribution to choose between parametric and nonparametric analyses for data analysis according to study outcomes. The Chi-square and Fisher's exact test were used for the relationship between categorical variables. The Mann-Whitney U-test compared ordinal continuous variables with two-level categorical independent variables. In the case of ordinal variables with multiple degrees of freedom, Kruskal-Wallis's test was used instead. The strength of correlations between the variables of interest was probed with Kendall's tau-b test. If it was necessary to categorize PA levels dichotomously (active/inactive), that of 699 Met wk/min (according to IPAQ scoring) was chosen as the threshold, defining active as those who had a PA > of this threshold.

To evaluate the predictors of physical inactivity, the independent variables of the implemented logistic regression model coincided with the other continuous and/or categorical variables deemed relevant. The regression model was evaluated according to the goodness of fit according to Hosmer-Lemeshow (as well as according to Cox and Snell R<sup>2</sup> and Nagelkerke R<sup>2</sup> values) by expressing the data as an exponential value of B, *i.e.*, exp (B). The latter was presented as the



**Figure 1** Flow chart summarizing the inclusion in the study patients, divided by type of inflammatory bowel disease and resulting physical activity levels. HEPA: Health enhancing physical activity; IBD: Inflammatory bowel disease; CD: Crohn's disease.

odds ratio, and the risk measure was expressed as the OR and its 95% confidence interval (95%CI).

The receiver operating characteristic (ROC) method was used to weigh the specificity/sensitivity of any variables regarding PA levels. These assessments were performed after checking for the existence of an adequate area under the ROC curve (AUC) > 0.699, which was calculated along with its 95%CI.

To evaluate the internal reliability of the questions in our survey to assess patient barriers to PA, we analysed Cronbach's alpha coefficient, recording a value of 0.7. In addition, a statistical significance value was accepted for  $P < 0.05$  (two-tailed) values, placing an alpha error of 0.05. Statistical analyses were performed with IBM® SPSS® software, graphs with GraphPad PRISM®, and sample size calculation with G\*Power software.

## RESULTS

### Sample characteristics

Figure 1 describes the steps for the enrolment of all patients. Two hundred nineteen patients were finally included, and Table 1 summarizes their characteristics by stratifying by type of IBD. Most of the sample, 127 (58%) patients, had UC.

Some differences emerged between IBD subgroups. CD patients had a higher rate of biologics use than the UC ones (*i.e.*, 82.6% vs 61.4%,  $P = 0.001$ ) and unemployment (60.9% vs 40.2%,  $P = 0.009$ ). In addition, females had a significantly lower age than males [38 (28-50) vs 45 (31-56),  $P = 0.017$ ].

Most of the sample was on subcutaneous biologic drug therapy (113, 51.6%), while a minority were taking intravenous (24, 11%) or oral (17, 7.8%) biological treatment, while the remainder (65, 29.7%) were not taking biologics. The overall failure rate of a previous biologic was 21.5% (47/219).

### PA levels

Most of the sample (116, 53%) met the IPAQ criteria for sufficiently active, while only a minority (9, 4.1%) met the criteria for HEPA activity. On the contrary, a large sample portion was classified as inactive (94, 42.9%). The overall IPAQ total score was 834.5 (384.5 - 1424) Met min/wk. Gender did not seem particularly impactful concerning PA (Figure 2A). The other variables in Table 1 showed no variations when stratified by PA grade (Table 2). IBD type did not result in variations in PA levels (see Table 3 and Figure 2B) since both the type of PA (*i.e.*, intense, moderate, or mild) and the class of PA (*i.e.*, inactive, sufficiently or HEPA active) did not vary particularly differentially between CD and UC patients. In addition, the comorbidities most represented in our sample, hypertension ( $P = 0.095$ ), arthritis ( $P = 0.101$ ), or Hashimoto's thyroiditis ( $P = 0.540$ ), did not particularly impact IPAQ total score levels. In contrast, PA levels differed according to dyslipidaemia ( $P < 0.0001$ ). In detail, dyslipidaemia patients presented higher [956 (325 - 1622)] levels of PA than those without dyslipidaemia [811 (393.75 - 1358.77)]. However, in contrast, the moderate activity score was higher in healthy patients than in those with dyslipidaemia [176 (0-567) vs 160 (0-480),  $P < 0.0001$ ].

Patients on biological therapy showed some advantage over those on standard therapy [246 (0-642) vs 56 (0-394),  $P = 0.022$ ], as shown in Figure 2C. At bivariate analysis, neither age ( $\tau = -0.27$ ,  $P = 0.550$ ) nor BMI ( $\tau = 0.75$ ,  $P = 0.100$ ) showed correlations with IPAQ total score.

**Table 1** Sample characteristics concerning the type of inflammatory bowel disease

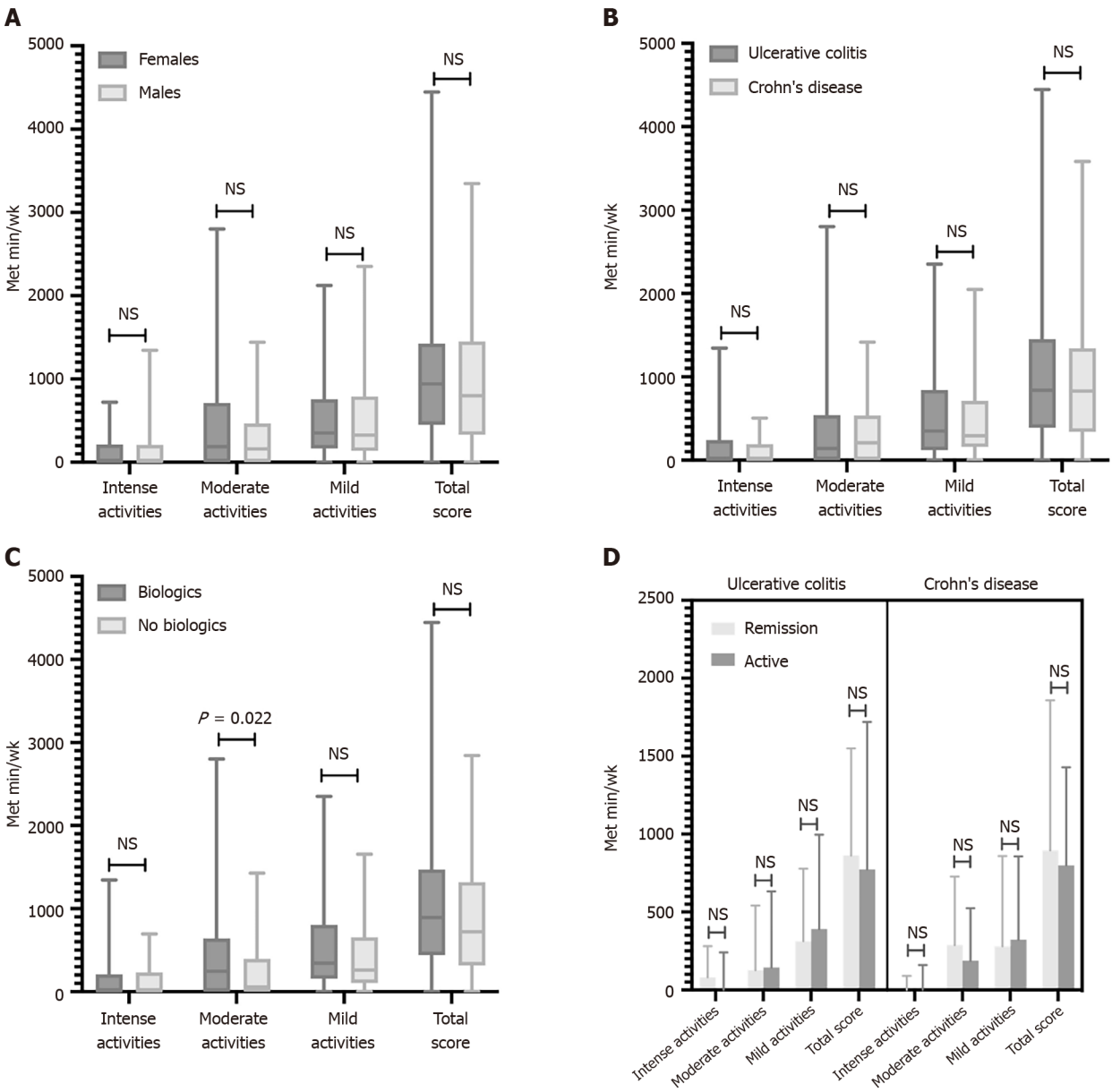
Variable	Crohn's disease (n = 92)	Ulcerative colitis (n = 127)	P value <sup>1</sup>
Age	43.5 (29-53)	41 (30-55)	0.871
BMI	23.8 (20.8-26.4)	23.8 (21.4-25.9)	0.787
<b>Gender</b>			0.157 <sup>2</sup>
Male	44 (47.8%)	73 (57.5%)	
Female	48 (52.5%)	54 (42.5%)	
<b>Education</b>			0.192
Primary school	32 (24.8%)	27 (21.3%)	
Secondary school	52 (56.5%)	78 (61.4%)	
Degree	8 (8.7%)	22 (17.3%)	
<b>Job</b>			0.009
Unemployed	56 (60.9%)	51 (40.2%)	
Employee	16 (17.4%)	38 (29.9%)	
Entrepreneur	8 (8.7%)	16 (12.6%)	
Worker	4 (4.3%)	7 (5.5%)	
Student	8 (8.7%)	15 (11.8%)	
<b>Smoking status</b>			0.003
Active smoker	16 (17.4%)	20 (15.7%)	
Past smoker	32 (34.8%)	16 (12.6%)	
Non-smoker	44 (47.8%)	91 (71.7%)	
<b>Alcohol consumer</b>			0.827 <sup>2</sup>
Yes	8 (8.7%)	10 (7.9%)	
No	84 (91.4%)	117 (92.1%)	
<b>Comorbidity</b>			0.256
Diabetes	8 (8.7%)	4 (3.1%)	
Hypertension	20 (21.7%)	10 (7.9%)	
Recurrent UTI	2 (2.2%)	4 (3.1%)	
Chronic renal failure	1 (1.1%)	2 (1.6%)	
Nephrolithiasis	3 (3.3%)	1 (0.8%)	
Asthma	3 (3.3%)	-	
COPD	2 (2.2%)	1 (0.8%)	
Previous pneumonia	1 (1.1%)	1 (0.8%)	
Dyslipidaemia	12 (13%)	35 (27.6%)	
Arthritis	32 (34.8%)	34 (26.8%)	
Hashimoto's thyroiditis	7 (7.6%)	15 (11.8%)	
<b>Partner</b>			0.322 <sup>2</sup>
Yes	68 (73.9%)	86 (67.7%)	
No	24 (26.1%)	41 (32.3%)	
<b>Biologics (yes)</b>	76 (82.6%)	78 (61.4%)	0.001 <sup>2</sup>
<b>Steroids (yes)</b>	4 (4.3%)	8 (6.3%)	0.531 <sup>2</sup>

<sup>1</sup>The P value was calculated by checking the difference in the distribution of different variables between the two identified groups (*i.e.*, Crohn's disease and

ulcerative colitis).

<sup>2</sup>The Chi-square test or Fisher's exact test was employed for evaluation.

BMI: Body mass index; COPD: Chronic obstructive pulmonary disease. Data are expressed for continuous variables as median (interquartile range) and, for categorical and ordinal variables, as numerosity (%). Significant *P* values are indicated in bold.



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**Figure 2 Physical activity levels in the main subgroups examined.** A-D: Physical activity levels observed in males and females (A), patients with ulcerative colitis and Crohn's disease (B), patients on treatment and not on biologics (C), and, finally, patients physically active or inactive concerning baseline disease activity (D). Met: Metabolic rate; NS: Not significant.

In this work, we detected a significantly higher unemployment rate in patients with CD on bivariate analysis. This finding led us to consider whether work occupation could impact PA levels. By processing the specific variable categorically over the entire sample (employed/unemployed), PA levels (as IPAQ total score) were not found to be impacted by employment rate (*P* = 0.851). This trend was also preserved when filtering by IBD type in both UC (*P* = 0.654) and CD (*P* = 0.481). Furthermore, the result was also maintained by comparing the employment and PA rates using the Chi-square test ( $\chi^2 = 0.321$ , *P* = 0.588).

**Disease activity and PA levels**

PA levels (i.e., as IPAQ total score in Met min/wk) were not different concerning PRO-2 measured IBD activity. In detail, this trend was confirmed by stratifying by PA intensity (i.e., intense, moderate and mild/walking) and total score (Figure 2D). PRO-2 data are summarized in Table 4 and related to the PA intensity.

Table 2 Sample characteristics concerning the levels of physical activity

Variable	Physically active (n = 125)	Physically inactive (n = 94)	P value <sup>1</sup>
<b>IBD</b>			0.892 <sup>2</sup>
Crohn's disease	53 (42.4%)	39 (41.5%)	
Ulcerative colitis	72 (57.6%)	55 (58.5%)	
<b>Age</b>	39 (29.5-52)	44 (29-55.25)	0.506
<b>BMI</b>	24.25 (21.47-26.28)	22.72 (20.95-25.71)	0.185
<b>Gender</b>			0.952 <sup>2</sup>
Male	67 (53.6%)	50 (53.2%)	
Female	58 (46.4%)	44 (46.8%)	
<b>Education</b>			0.903
Primary school	34 (27.2%)	25 (26.6%)	
Secondary school	75 (60%)	55 (58.5%)	
Degree	16 (12.8%)	14 (14.9%)	
<b>Job</b>			0.432
Unemployed	59 (47.2%)	48 (51.1%)	
Employee	30 (24%)	24 (25.5%)	
Entrepreneur	15 (12%)	9 (9.6%)	
Worker	6 (4.8%)	5 (5.3%)	
Student	15 (12%)	8 (8.5%)	
<b>Smoking status</b>			0.607
Active smoker	21 (16.8%)	15 (16%)	
Past smoker	29 (23.2%)	19 (20.2%)	
Non-smoker	75 (60%)	60 (63.8%)	
<b>Alcohol consumer</b>			0.892 <sup>2</sup>
Yes	10 (8%)	4 (4.3%)	
No	115 (92%)	90 (95.7%)	
<b>Comorbidity</b>			0.899
Diabetes	8 (6.4%)	4 (4.3%)	
Hypertension	20 (16%)	10 (10.6%)	
Recurrent UTI	3 (3.2%)	2 (2.1%)	
Chronic renal failure	-	1 (1.1%)	
Nephrolithiasis	3 (2.4%)	2 (2.1%)	
Asthma	2 (1.6%)	2 (2.1%)	
COPD	1 (0.8%)	1 (1.1%)	
Previous pneumonia	2 (1.6%)	-	
Dyslipidaemia	28 (22.4%)	19 (20.2%)	
Arthritis	32 (25.6%)	34 (36.2%)	
Hashimoto's Thyroiditis	12 (9.6%)	10 (10.6%)	
<b>Partner</b>			0.570 <sup>2</sup>
Yes	86 (68.8%)	68 (72.3%)	
No	39 (31.2%)	26 (27.7%)	
<b>Biologics (yes)</b>	91 (72.8%)	63 (67%)	0.354 <sup>2</sup>

<b>Steroids (yes)</b>	10 (8%)	2 (2.1%)	0.059 <sup>2</sup>
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<sup>1</sup>The *P* value was calculated by checking the difference in the distribution of different variables between the two identified groups (*i.e.*, physically active or inactive).

<sup>2</sup>The Chi-square test or Fisher's exact test was employed for evaluation.

BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; UTI: Urinary tract infections. Data are expressed for continuous variables as median (interquartile range) and, for categorical and ordinal variables, as numerosity (%).

**Table 3 Physical activity concerning the type of inflammatory bowel disease**

PA variable	Crohn's disease (n = 92)	Ulcerative colitis (n = 127)	<i>P</i> value <sup>1</sup>
<b>Intense activities</b> (Met min/wk)	0 (0-192)	0 (0-240)	0.099
<b>Moderate activities</b> (Met min/wk)	208 (0-536)	140 (0-540)	0.590
<b>Mild activities</b> (Met min/wk)	293.75 (158.12-711.6)	350 (120-840)	0.940
<b>Sitting time at work</b> (min)	210 (113-292.5)	215 (125-292)	0.719
<b>Sitting time at home</b> (min)	174 (118.75-221.75)	177 (115-229)	0.855
<b>Total score</b> (Met min/wk)	828.25 (339.37-1343.5)	839 (390-1451)	0.678
<b>PA level</b>			0.995
Inactive	39 (42.4%)	55 (43.3%)	
Sufficiently active	50 (54.3%)	66 (52%)	
HEPA active	3 (3.3%)	6 (4.7%)	

<sup>1</sup>The *P* value was calculated by checking the difference in the distribution of different variables between the two identified groups (*i.e.*, Crohn's disease and ulcerative colitis).

HEPA: Health enhancing physical activity; PA: Physical activity. Data are expressed for continuous variables as median (interquartile range) and, for categorical and ordinal variables, as numerosity (%).

**Table 4 Disease activity and physical activity levels expressed as total International Physical Activity Questionnaire score**

PA variable	n (%)	PA active (Met min/wk)	PA inactive (Met min/wk)	<i>P</i> value <sup>1</sup>
<b>PRO-2 CD</b>	<b>n = 92</b>	<b>n = 53</b>	<b>n = 39</b>	
Remission	27 (29.3%)	1353 (1026.5-2064)	210.75 (101.25-313.75)	0.303
Mild	24 (26.1%)	1213.65 (1039.52-1534.75)	346.25 (229.62-566.37)	
Moderate	41 (44.6%)	1240.75 (879.67-1950)	352.5 (45-468.75)	
<b>Overall</b>	<b>92 (100%)</b>	<b>1234 (981.75-1769.25)</b>	<b>280 (157.5-465)</b>	
<b>PRO-2 UC</b>	<b>n = 127</b>	<b>n = 72</b>	<b>n = 55</b>	
Remission	74 (58.3%)	1345.35 (1057.5-1766.75)	321.25 (204.25-535.87)	0.994
Active	53 (41.7%)	1457 (952-1964.75)	350 (0-574)	
<b>Overall</b>	<b>127 (100%)</b>	<b>1373.35 (990-1792.62)</b>	<b>325 (111.5-538.5)</b>	

<sup>1</sup>The *P* value was calculated by checking the difference in the distribution of different variables between the two identified groups (*i.e.*, active and inactive patients).

PRO: Patient reported outcome; CD: Crohn's disease; UC: Ulcerative Colitis; IPAQ: International Physical Activity Questionnaire; PA: Physical activity. Data are expressed for continuous variables as median (interquartile range) and, for categorical and ordinal variables, as numerosity (%).

Considering the whole sample, the SF of CD patients showed a median of 4.5 (2 - 8) bowel movements, while AP was reported as absent in 56 (60.9%) patients, as mild in 24 (26.1%) and finally, as moderate in 12 (13%) patients. UC patients, on the other hand, reported normal SF in most cases (92, 72.4%), increased 1-2 times in 17 (13.4%) and increased 3-4 times in 18 (14.2%) cases. Moreover, UC patients concerning RB reported no visible blood in most cases (91, 71.7%), traces in less than half of bowel movements in 27 (21.3%) cases and, finally, visible blood in most bowel movements in 9 (7.1%) cases. In general, as shown in Table 4, even in the absence of significance, CD patients in remission with regular PA had better disease activity scores than those with mild and moderate activity, while this trend was not superimposable in the



**Table 5 Beliefs about physical activity of patients included**

Question (n = 219)	Completely agree	I think it is irrelevant	Partially agree	Partially disagree	Completely disagree	P value <sup>1</sup>
I think my IBD is a block to doing regular PA	12 (5.5%)	65 (29.7%)	58 (26.5%)	28 (12.8%)	56 (25.6%)	0.957
The treatment I am taking for my IBD is a block to performing regular PA	5 (2.3%)	78 (35.6%)	15 (6.8%)	16 (7.3%)	105 (47.9%)	0.520
I believe that engaging in regular PA may reactivate my IBD or, if already active, make it worse	61 (27.9%)	43 (19.6%)	18 (8.2%)	19 (8.7%)	78 (35.6%)	<b>&lt; 0.001</b>
I believe that performing regular PA may result in complications in my IBD (e.g., fistula formation, abscesses or other)	13 (5.9%)	45 (20.5%)	21 (9.6%)	26 (11.9%)	114 (52.1%)	0.527
I believe that performing regular PA can improve my IBD	28 (12.8%)	55 (25.1%)	87 (39.7%)	6 (2.7%)	43 (19.6%)	0.942
I believe that performing regular PA can protect me from new IBD recurrence	25 (11.4%)	74 (33.8%)	87 (39.7%)	18 (8.2%)	15 (6.8%)	0.538
My family doctor adequately informed me regarding the possibility of performing regular PA	52 (23.7%)	45 (20.5%)	51 (23.3%)	18 (8.2%)	53 (24.2%)	0.936
My gastroenterologist adequately informed me regarding the possibility of performing regular PA	76 (34.7%)	26 (11.9%)	80 (36.5%)	10 (4.6%)	27 (12.3%)	0.871
People close to me (e.g., relatives and friends) have repeatedly urged me to conduct a regular PA	91 (41.6%)	22 (10%)	69 (31.5%)	18 (8.2%)	19 (8.7%)	0.795
People close to me (relatives, friends) have repeatedly advised/banned me from conducting regular PA	0 (%)	35 (16%)	29 (13.2%)	24 (11%)	131 (59.8%)	0.291
Before receiving the diagnosis of IBD, I was more inclined to perform regular PA, but now, upon receiving the diagnosis, I feel less convinced to perform PA	41 (18.7%)	45 (20.5%)	45 (20.5%)	13 (5.9%)	75 (34.2%)	<b>&lt; 0.001</b>

<sup>1</sup>The P value was calculated by checking the difference in the distribution of different variables between the two identified groups (*i.e.*, active and inactive patients).

IBD: Inflammatory bowel disease; PA: Physical activity. Data are expressed as numerosity (%). Significant P values are indicated in bold.

case of UC. At bivariate analysis, the UC PRO-2 score negatively correlated with the IPAQ intense activity subscore ( $\tau = -0.156$ ,  $P = 0.038$ ). This correlation was not met by CD patients ( $\tau = 0.114$ ,  $P = 0.160$ ). PRO-2 showed no other relationships with other IPAQ parameters ( $P > 0.05$ ). Finally, on ROC analysis, neither PRO-2 in the UC (AUC = 0.512, 95%CI 0.409-0.614) nor CD (AUC = 0.431, 95%CI 0.311-0.551) showed notable AUCs.

### IBD patient's beliefs and barriers toward PA

The sample felt, on average, essential to discuss PA with their gastroenterologist during outpatient visits, as evidenced by a median of 6 (4-8) on the 11-point Likert scale administered to patients (Figure 3A and B) and active patients tended to respond more frequently with scores at the positive extreme (*i.e.*, 9, 10,  $P = 0.044$ ). Figure 3C resumes sports practised by patients, and differences in the chosen sport between active and inactive in terms of PA were not found ( $P = 0.445$ ). In addition, several IBD-related barriers to PA were reported (Figure 3D), with some reported more frequently by inactive patients, specifically diarrhoea and evacuation urgency ( $P = 0.004$ ). Table 5 reports the central beliefs of our patients about several PA aspects. In this context, 63.8% (60/94) were wholly convinced that PA could reactivate/worsen the clinical activity of their IBD. Sixty percent (75/125) of PA active patients thoroughly reported the opposite ( $P < 0.001$ ). In addition, 46.8% (44/94) of PA inactive believed (entirely or partially) that the diagnosis of IBD was the starting point of their distrust of PA. The trend was predictably opposite in PA active patients ( $P < 0.001$ ).

A traceable element, in general, is how the patients' social network in majority urged the patient to practice regular PA. In contrast, less than half of the patients felt adequately informed by their family doctor or gastroenterologist about the possibility of performing regular PA.

Finally, a binary logistic regression analysis was conducted to investigate physical inactivity predictors among all the study variables, not recording any significant predictor (Figure 4 and Table 6).

## DISCUSSION

This study weighed patient-reported PA in a group of IBD European patients. In this study, IBD adults showed a particularly worrying rate of physical inactivity (*i.e.*, 42.9%), with only 4.1% of the sample meeting the HEPA criteria. Median overall PA levels (*i.e.*, 834.5 Met min/wk) were just above the IPAQ threshold for inactivity (*i.e.*, 700 Met min/wk).

In this experience, PA showed no relationship with IBD activity (employing the PRO-2 tool), except for a negative relationship between UC PRO-2 and moderate PA levels. Clinical PROs, as moreover measured by PRO-2, have been

**Table 6 Predictors of physical inactivity analysis among clinical and demographic variables evaluated by binary logistic regression**

Variable	Exp (B)/Odds ratio	95%CI	P value
Age (yr)	0.996	0.976-1.018	0.743
Weight (Kg)	1.017	0.992-1.041	0.180
Height (cm)	1.018	0.989-1.048	0.231
BMI (Kg/m <sup>2</sup> )	0.999	0.998-1.001	0.867
IBD (CD)	0.931	0.503-1.721	0.819
IBD (UC)	1.074	0.581-1.987	
Gender (Male)	1.196	0.642-2.225	0.573
Gender (Female)	0.836	0.449-1.556	
Partner (Yes)	1.343	0.681-2.652	0.395
Partner (No)	0.744	0.377-1.469	
Biologics (Yes)	0.816	0.430-1.549	0.534
Biologics (No)	1.225	0.646-2.325	
Arthritis (Yes)	1.710	0.892-3.278	0.106
Arthritis (No)	0.585	0.305-1.121	
Dyslipidaemia (Yes)	0.747	0.343-1.627	0.463
Dyslipidaemia (No)	1.338	0.615-2.913	
Diabetes (Yes)	1.074	0.209-5.517	0.932
Diabetes (No)	0.931	0.181-4.786	
Hypertension (Yes)	0.622	0.204-1.893	0.403
Hypertension (No)	1.608	0.528-4.893	
Hashimoto's thyroiditis (Yes)	1.121	0.462-2.717	0.800
Hashimoto's thyroiditis (No)	0.892	0.368-2.162	
Importance PA discussion (Likert 10-point scale)	0.911	0.823-1.008	0.072
Employed	0.857	0.501-1.464	0.571
Unemployed	1.167	0.683-1.994	

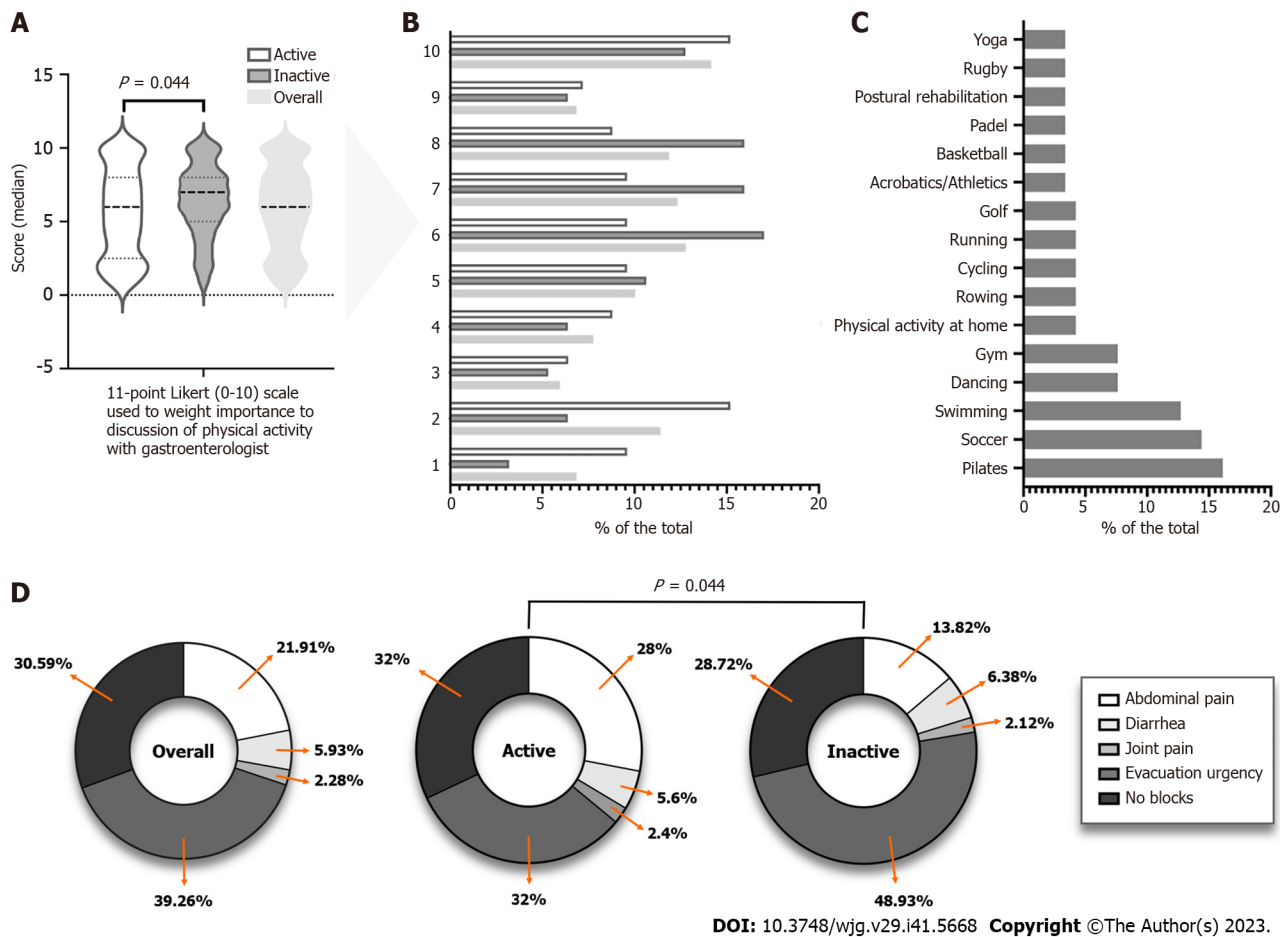
Risk is expressed as the exponential value of B, or Exp(B), presented in odds ratio with a relative 95% confidence interval and relative P value. 95%CI: 95% confidence interval; IBD: Inflammatory bowel disease; CD: Crohn's disease; UC: Ulcerative Colitis; PA: Physical activity.

shown in a recent cross-sectional study to associate with daily activities impairment compared with physician-reported ones[27]. PA and IBD relationship is still highly controversial and under study. Khalili *et al*[28], in a cohort study, showed an inverse association between PA and the risk of CD but not UC.

In contrast, another Japanese study showed an inverse association between intense-type PA and mucosal healing but not with clinical remission[29]. Much of the available evidence, albeit little, seems to suggest in IBD a moderate and, in a significant minority, mild PA intensity, and it appears that this increased PA is associated with better management of symptoms (including fatigue) as well as better psychological outcomes and QoL[30]. Despite this, there are still no detailed recommendations on the best sport to suggest, at what intensity and for how long for IBD patients.

Complicating the picture, there are vast geographical differences in conceptions of PA[31]. A previous New Zealand survey (which examined a smaller sample of 77 patients) found a higher rate of PA (*i.e.*, 66%) and PA levels (1613 *vs* 834.5 Met min/wk) than ours[32]. In each case, however, this study also found similar barriers reported by patients with IBD to PA (*i.e.*, evacuation urgency). These data were also similar to that of Tew *et al*[24].

Whether regular PA can give tangible benefits to IBD activity is still not completely clear. However, it appears that PA may increase the T-regulatory lymphocytes expression, reduce the immunoglobulins secretion by negatively regulating T helper 1 Lymphocytes, and increase the anti-inflammatory cytokine IL-10 production[8]. However, as in our study, all in all, not a strong relationship between PA and IBD activity was also obtained from another American sample of about 250 patients with an average age similar to ours (*i.e.*, 39.6 years)[33]. In contrast, in another study, more marked differences in PA had emerged between patients with active disease and in remission, postulating a negative role of disease activity [24]. These differences may be partially explained by the fact that a higher rate of patients in our study was on biologics, which have a pronounced impact on the course of the disease[34]. Not surprisingly, as written before, we observed how



**Figure 3 Importance given by patients to discuss physical activity with their gastroenterologist, major sports played by them, and barriers to physical activity related to inflammatory bowel disease.** A and B: The importance given by patients to discuss with their gastroenterologist physical activity stratified by physical activity level (A) and detailed by individual Likert scale score (B); C: Main sports stated by participants; D: Factors related to inflammatory bowel disease hinder regular physical activity.

being on biological therapy provided an advantage toward moderate PA activities ( $P = 0.022$ , Figure 2C).

This study also examined the potential impact of work employment on PA levels by leaning toward the little impact of the former on the latter. Although not detailed in IBD, this finding contrasts with what is already reported in the general population[35]. This matter is difficult to interpret in a population (i.e., IBD) already heavily impacted by unemployment [36]. Not coincidentally, our unemployment rate was high (i.e., 48.9%, 107/219), so studies including a larger sample of employed people probably need to verify a real difference in PA levels.

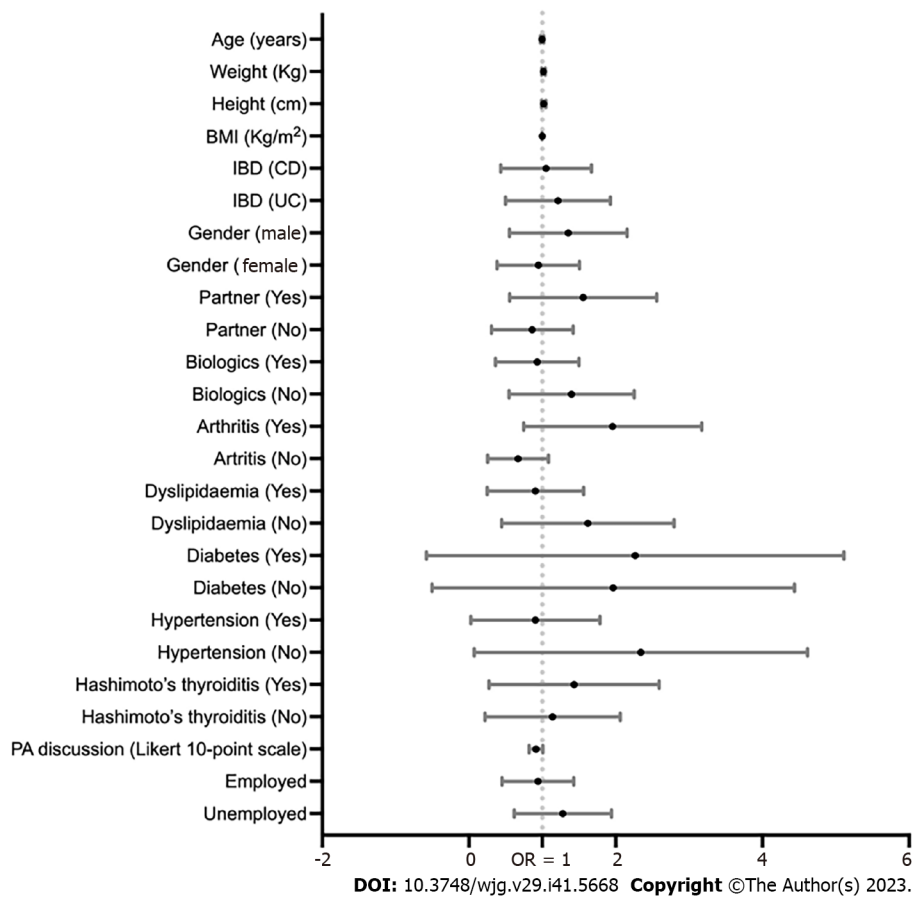
The comorbidities we noted did not have much effect on PA levels. However, to assess arthritis, we did not evaluate clinical activity because of the study design and purpose. Therefore, although having or not having this comorbidity did not impact PA levels in our setting, the limitation of not grading joint disease/disability activity must be considered. We also found better PA levels in dyslipidaemia-affected patients. However, we believe the small number of dyslipidaemia-affected patients must weigh this result compared to healthy ones, so a subgroup analysis should be considered merely exploratory. In any case, IBD patients without dyslipidaemia tolerated higher activity levels better than those with dyslipidaemia, as reported in a non-IBD setting[37].

The problem of physical inactivity in IBD is relevant because an inactive patient risks losing the potential benefits that PA can provide in several aspects already undergoing impairment in such patients (such as mood disorders[38], metabolic syndrome[39], and sarcopenia[14]).

To recover inactive patients (in terms of PA), our study offers several insights. The first point is probably, to discuss with the patient of PA during the gastroenterology visit and identify the patient's fears. Secondly, providing the patient with a cognitive intervention is necessary by discussing possible solutions to the barriers for PA (i.e., evacuation urgency, thinking that there may be disease reactivation and the like).

In view also that our inactive patients significantly identified the core of their PA-related fears at the diagnosis of IBD (Table 5,  $P < 0.001$ ) compared with active patients, this suggests that these complementary aspects should be discussed at diagnosis before patients integrate misconceptions into the management of their IBD and PA.

In addition, as exhibited in Table 5 (questions 7, 8), a not insignificant percentage of patients feel uninformed about the IBD-PA relationship by their family physician and gastroenterologist. Therefore, training courses that aim to provide general knowledge about the possibilities of practising PA in patients with chronic digestive diseases should solve this unmet patient need.



**Figure 4** Forest plot showing predictors analysis of physical inactivity among clinical and demographic variables evaluated by binary logistic regression. CD: Crohn's disease; UC: Ulcerative colitis; OR: Odds ratio.

Moreover, regular PA can pose a valuable strategy for reducing inflammatory burden, especially in diseases with inflammatory pathogenesis, such as IBD. Exercise can contribute to the promotion of an anti-inflammatory phenotype in several ways.

In fact, at the level of fatty tissue, it can downregulate several pro-inflammatory cytokines such as IL-1, IL-16 and tumour necrosis factor (TNF), and, in addition, it can promote the M2 cytotype of macrophages (*i.e.*, their anti-inflammatory cytotype) and act against oxidative stress[7]. In the context of muscle tissue, moreover, these actions are, to a large extent, repeated[7] with an increase also in peroxisome proliferator-activated receptor  $\gamma$  co-activator 1 $\alpha$ , a molecule that in knockout mice for the same, results in the promotion of IL-6 and TNF[40]. Repeated exercise also appears to induce adaptive changes in the immune system by predisposing to lower neutrophil recruitment[41]. For these reasons, exercise has been repeatedly proposed to counter chronic inflammation[42].

In addition to the above, regular PA can improve vascular endothelial balance by ameliorating oxidative stress and nitric oxide availability[43].

Although set in a research context severely lacking solid evidence already available, this study has several limitations. The data are from a single-centre experience, and future multicentre evidence would be desirable; our subgroup analyses are, by definition, exploratory; therefore, studies of larger sample sizes are desirable to confirm them. In addition, it will be preferable to confirm and strengthen our data even more a multicentre, prospective study design to bring out more differences in population subgroups.

## CONCLUSION

IBD southern Italian patients seem physically inactive and may be exposed to all the complications of not practising regular PA. This does not seem totally dependent on disease activity but is affected by patients' beliefs about PA's impact on underlining IBD. Using validated and feasible questionnaires (*e.g.*, IPAQ) could be a strategy to weigh patient-reported PA levels and get an initial idea about which patients have insufficient PA levels.

## ARTICLE HIGHLIGHTS

### Research background

Patients with inflammatory bowel diseases (IBD) often experience reduced quality of life (QoL) and disability. Regular physical activity (PA) determines QoL. Initial studies have shown that mild PA seems safe in IBD and is not associated with an increased risk of flare-ups.

### Research motivation

There are no precise guidelines on what type of PA and the intensity to recommend for patients with IBD. Epidemiological levels of PA in the IBD population are not yet fully known, nor are the barriers that block patients from practising regular PA.

### Research objectives

This study aimed to weigh PA levels with standardised instruments in an Italian IBD population to examine PA's relationship with IBD disease activity and identify barriers to PA.

### Research methods

This cross-sectional study employed the standardised International Physical Activity Questionnaire (IPAQ) to weigh PA and the patient-reported outcome 2 (PRO-2) to assess IBD disease activity. PA was expressed as multiples of resting metabolic rate (Met) in Met min/wk. This study included only patients with confirmed, excluding patients with severe or hospitalised activity.

### Research results

Two hundred nineteen patients were included. Fifty-three per cent were found to be sufficiently active, 42.9% as inactive, and only 4.1% as health-enhancing PA active. Median overall PA levels were 834.5 Met min/wk, just above the threshold for inactivity (*i.e.*, 700 Met min/wk). Ulcerative colitis PRO-2 showed a negative correlation with intense PA activities. Several barriers to PA were identified (*e.g.*, fear of IBD flare-up, fears initiated as early as IBD diagnosis).

### Research conclusions

Patients with IBD were found in this setting to be burdened by a significant rate of physical inactivity. Barriers persist on which to act to regain adherence to regular PA. As measured by the PRO-2, disease activity did not drastically affect PA. The IPAQ questionnaire showed excellent feasibility and ease of completion and interpretation.

### Research perspectives

Regular PA has multiple benefits (from cardiovascular health to psychological health), and it is necessary to make sure that patients with IBD practice it so that these benefits are not lost. It is appropriate for gastroenterologists to pay more attention to this aspect during medical visits. IPAQ can be a potential tool for recognising and monitoring physically inactive patients.

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## FOOTNOTES

**Author contributions:** Gravina AG, Pellegrino R, and Federico A designed the study; all authors participated in the acquisition and interpretation of the data and drafted the initial manuscript; Pellegrino R performed the analysis; all the authors revised the article critically for important intellectual content.

**Institutional review board statement:** The study was conducted in compliance with the Declaration of Helsinki and received approval from the Ethics Committee of the University of Campania Luigi Vanvitelli (protocol number 7892, 15 March 2023).

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** There are no conflicts of interest to report.

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**STROBE statement:** The authors have read the STROBE Statement – checklist of items, and the manuscript was prepared and revised according to the STROBE Statement – checklist of items.

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