**Daily physical activity patterns in children and adolescents with inflammatory bowel disease**

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**Consent statement**

Before beginning the study, its objectives were carefully explained to each participant and their parents/guardian. Written informed assent was obtained from the participant and consent from the parents (or guardian) by the study physician.

**Impact statement**

- There is few data on PA patterns in pediatric patients with IBD.
- Methodological issues to assess PA limit the strengths of these studies.
- Pediatric IBD patients with inactive or mildly active IBD have similar physical activity patterns compared with healthy controls, except for male patients who have reduced moderate-to-vigorous PA.
- Most patients with IBD do not fulfill the MVPA recommendations for health benefits.

## Abstract

**Background:** To assess PA patterns among children and adolescents with inflammatory bowel disease (IBD).

**Methods:** Sixty participants with IBD (42 Crohn's disease [CD], 10 ulcerative colitis [UC], and 8 IBD-unclassified [IBD-U], 30 male patients) in remission (n = 45) or with mild disease (n = 15) were compared with 60 healthy age- and sex-matched controls. Each participant wore a triaxial accelerometer during 4 consecutive days for objective daily PA quantification.

**Results:** Overall, there was no significant difference in daily PA patterns between patients with IBD and healthy controls, with 31.7% of patients with IBD and 38.3% of healthy controls fulfilling the recommendation of 60 min of moderate-to-vigorous physical activity (MVPA) daily (NS). Male patients with IBD spent significantly less time in MVPA compared with matched healthy controls (mean difference, 16.2 $\text{min}\cdot\text{day}^{-1}$; $p < 0.05$). No difference was observed for female patients with IBD. No difference in sedentary pattern between male patients with IBD and controls was found.

**Conclusions:** Children and adolescents with inactive or mildly active IBD have similar PA patterns compared with healthy controls, except for male patients who have reduced moderate-to-vigorous PA. By far, most patients with IBD do not fulfill the MVPA recommendations for health benefits.

## Introduction

Inflammatory bowel diseases (IBD) encompass Crohn's disease (CD), ulcerative colitis (UC), and IBD-unclassified (IBD-U). They represent a worldwide health-care problem with continually increasing incidence, especially in industrialized countries and among youth (1-2).

Physical activity (PA) refers to any bodily movement produced by the contraction of skeletal muscles that increase energy expenditure above a basal level (3). PA is widely recognized as an important determinant of health in youth (4). The US Department of Health and Human Services recently recommended that children and adolescents aged 6–17 years should engage in 60 minutes or more of moderate-to-vigorous physical activity (MVPA) daily (5). It has been shown that 60 min of consistent, daily MVPA reduces the risks of many chronic diseases, such as non-communicable diseases and other adverse health outcomes including bone health (6). In contrast, a sedentary lifestyle, referring to any waking behavior characterized by a low level of energy expenditure (≤1.5 metabolic equivalents of task [METs]) while sitting, reclining, or lying, is associated with adverse health consequences and increases morbidity and mortality in adulthood (7).

Several IBD symptoms, such as abdominal pain, diarrhea, and fatigue, as well as poor nutritional status and depression may reduce PA and increase sedentary status, with potential negative impacts on these children's health status (8-9). A recent systematic review showed that data on PA in children and adolescents with IBD are scarce (10). Only three studies in the past decade have assessed PA patterns in pediatric patients with IBD (11-13). However, methodological issues including limited sample size, type of accelerometer used, or use of an inappropriate epoch length to assess PA limit the strengths of their results.

Our study aim was to assess daily PA patterns measured objectively in a large sample of children and adolescents with IBD compared with healthy age- and sex-matched controls.

## Methods

### Participants

The current analyses use data from two prospective studies assessing PA, which used the same methods to assess samples of children and adolescents with IBD and healthy children and adolescents (14-15). From a total sample of 162 children and adolescents (84 patients with IBD and 78 healthy controls), 120 children and adolescents (60 patients with IBD *vs*. 60 healthy controls) could be age- and sex- matched for inclusion in these analyses.

The inclusion criteria for patients with IBD were: (*i*) IBD diagnosis (CD, UC, IBD-U) for at least 6 months (16); (*ii*) age 10–18 years; (*iii*) assent form signed by the patient and informed consent signed by parents (or legal guardian); and (*iv*) no simultaneous inclusion in another biomedical study. Exclusion criteria were: (*i*) any associated acute or chronic disease known to influence PA (*e.g.*, cardiovascular/respiratory disease, sprain, fracture, arthritis, severe skin lesions); (*ii*) any acute infection event over the past 14 days; (*iii*) no patent assent or parent/legal guardian consent; and (*iv*) (for female patients) a positive baseline blood-based pregnancy test.

The inclusion criteria for healthy control children and adolescents were: (*i*) age- (± 1 year) and sex-matched with a patient with IBD; (*ii*) informed assent signed by the participant and consent by their parents (or legal guardian); (*iii*) absence of any acute or chronic disease known to influence PA (*e.g.*, cardiovascular/respiratory disease, musculoskeletal pain); *(iv)* no acute infection over the past 14 days; and (*v*) no simultaneous inclusion in another biomedical study. Sample characteristics of patients with IBD and healthy controls are reported in Table 1.

Before beginning the study, its objectives were carefully explained to each participant and their parents/guardian. Written informed assent was obtained from the participant and consent from the parents (or guardian) by the study physician. The study was approved by the

Research Ethical Committee (Comité Protection des Personnes, Nord-Ouest IV, Lille, France) and French research competent authority (Agence Nationale de Sécurité du Médicament et des Produits de Santé, Paris, France). All procedures were performed according to the ethical standards of the 1975 Declaration of Helsinki, as revised in 2013, and the European Union's Guidelines for Good Clinical Practice. According to the General Data Protection Regulation, data collection was approved by the French personal informatics competent authority (Commission Nationale de l'Informatique et des Libertés). Studies were registered in clinicaltrials.gov (NCT02844101; NCT02341742).

Clinical assessment

Each patient and healthy control was required to pass a medical examination to exclude pathologies that would have constituted a contraindication to study participation. Body weight was measured using an electronic scale, with the participant wearing light clothing and without shoes, to the nearest 0.1 kg. Height was measured without shoes to the nearest 0.1 cm using a standard physician's scale. Body mass index (BMI) was calculated as weight divided by height squared ($kg/m^2$).

For patients with IBD, blood samples were collected by venipuncture during the physical examination by a study nurse. Hematocrit, C-reactive protein, albumin, and erythrocyte sedimentation rate were measured to assess inflammatory status and calculate disease activity. The Pediatric CD Activity Index (PCDAI) was used for patients with CD and the Pediatric Ulcerative Colitis Activity Index (PUCAI) for patients with UC (17-18). No IBD-U score was used. Remission was defined as scores <10 and mild activity as scores 10–27.5 on the PCDAI and 10–34 on the PUCAI. Values >27.5 on the PCDAI and >34 on the PUCAI indicated moderate-to-severe activity. Specific IBD drug therapy data were collected. Body composition (fat mass and fat free mass) was measured using dual-energy X-ray

absorptiometry (DEXA; Hologic Corp., Discovery Type, Software 12.6, Bedford, MA). Patients were scanned in the supine position at high resolution. Fat mass and fat free mass were determined based on whole body scan analyses.

Physical activity measurements

The methods for measuring PA have been described in detail elsewhere (19). Briefly, daily PA patterns were assessed by a triaxial accelerometer, an objective measure of PA in youth (14). This triaxial accelerometer measures 46×33×15 mm and weighs 19 g. The GT3X accelerometer has been validated for measuring PA against physiological markers of PA, such as oxygen consumption and heart rate. The epoch interval for the GT3X monitor was set at 1 s. A computer was used to initialize and synchronize the accelerometer, which was calibrated based on each patient's age, height, weight, and position for measurement using ActiLife software (version 6.13.4; ActiGraph, Pensacola, FL).

The accelerometer was worn beneath clothing on the lower back, fastened with an elastic belt and adjustable buckle. Participants were asked to follow their normal daily routine and to remove the accelerometer during sport contacts, swimming, showering, and bathing. The accelerometer recorded activity for 4 consecutive days (2 weekdays and 2 weekend days) and was removed at night. Accelerometer data were uploaded from the monitor to a computer after the completed registration period (4 days) using the same ActiLife software. Consistent with consensus recommendations for assessing PA in youth, patients who did not report at least 3 days with a minimum of 10 h of PA per day were excluded from analyses (20). Time spent in sedentary activities, light PA, moderate PA, and vigorous PA was based on cut-off points of 0–180, 181–757, 758–1112, and >1112 counts per 15 $sec^{-1}$, respectively, as previously established in laboratory conditions (21). PA patterns were analyzed according to

weekdays (Monday–Friday) and weekends. Data were averaged and expressed in counts·min$^{-1}$.

Log diary

For quality control of accelerometry in both groups, participants were asked to complete a diary during the 4-day period when they wore the accelerometer (22). Waking, going to bed, and times when the accelerometer was put on and taken off were recorded daily on a standardized, preprinted recording sheet. Participants were instructed to report why the accelerometer was removed (*e.g.*, sleeping, contact sport, water-based activities). The sport activities performed after removal of the device were classified based on the Compendium of Energy Expenditures for Youth and time spent in moderate or vigorous PA was added to the participant's record. Activities from 4–6 METs were defined as moderate PA and activities with ≥6 MET were defined as vigorous PA (23). Nonwear time each day was calculated by summing the durations noted on the log diary when the accelerometer was removed at night or for other activities.

Outcome measures

The primary outcome was the difference in time spent (in min.day$^{-1}$) in each PA level (sedentary, moderate, vigorous and MVPA) during the week, assessed by accelerometer, between IBD pediatric patients and healthy controls.

Secondary outcomes were the differences between IBD pediatric patients and healthy controls in: (*i*) time spent (min.day$^{-1}$) in each PA level (sedentary, moderate, vigorous and MVPA) during weekdays and weekend days; (*ii*) time spent in sedentary activity (min.day$^{-1}$) by accelerometer according to sex, IDB diagnosis and disease intensity; (*iii*) time spent in MVPA (min.day$^{-1}$) by accelerometer according to sex, IDB diagnosis and disease intensity.

Statistical analysis

Quantitative variables are expressed as mean (± standard deviation) in the case of normal distribution or median (range) otherwise and categorical variables are expressed as frequencies and percentages. Distribution normality was assessed using histograms and the Shapiro–Wilk test. PA parameters (*i.e.*, sedentary, moderate, vigorous, moderate-to-vigorous) assessed during all days, weekdays, and weekend days were compared between patients with IBD (cases) and their age- and sex-matched healthy controls using paired Student's t-tests. Normality of intrapair differences was checked and the magnitude of differences was assessed by calculating the mean differences (cases *vs.* controls) based on 95% confidence intervals (CIs). Initial analyses included all patients with IBD, while further analyses were based on sex, disease activity, and IBD type. Heterogeneity in case–control differences in PA parameters (measured during all days) according to the key subgroups was assessed by including the corresponding multiplicative interaction term in a linear mixed regression model with matched sets as the random effect. Two-tailed testing was conducted and an $\alpha$-level of $p < 0.05$ was considered statistically significant. Data were analyzed using SAS software (version 9.4; SAS Institute, Cary, NC).

**Results**

The participant characteristics are presented in Table 1. The mean ages of the 60 patients with IBD (30 male patients) and 60 controls were 14.3 ± 2.3 years and 13.8 ± 2.1 years, respectively. No between-group differences were observed with respect to sex, age, height, weight, or BMI. Mean disease duration was 34 months (range, 4–122). Patient data on disease activity, medical treatment, and biological markers are also presented in Table 1. According to the PCDAI and PUCAI scales, three-quarters of the patients were in remission and one-quarter had mild disease activity. There were no patients with moderate-to-severe activity. All participants wore the accelerometer during at least 3 days and had a minimum of 10 h of PA per day. No participant performed PA after removal of the accelerometer (*e.g.*, swimming, contact sports) according to their diaries. Therefore, data analyses were performed on the accelerometer data alone.

Comparisons of time spent in different PA levels between patients with IBD and healthy matched controls are presented in Table 2. There was no difference according to each intensity or during weekdays *vs.* weekend days between patients with IBD and controls. The percentage of participants fulfilling the recommended 60 min MVPA daily was 31.7% in patients with IBD and 38.3% in healthy controls ($p = 0.43$).

Figures 1 and 2 show comparisons of PA levels between patients with IBD and healthy controls. In addition, disease activity and diagnosis type (CD or UC) were considered in patients with IBD. For sedentary level, there was no significant heterogeneity according to sex, IBD diagnosis or disease activity (Figure 1). For time spent in MVPA (Figure 2), significant heterogeneity was found according to sex. Male patients with IBD spent significantly less time in MVPA compared with healthy controls (mean difference, -16.2 min·day$^{-1}$; 95% CI: −28.–−3.9) while no significant difference was observed between female patients with IBD and healthy controls (mean difference, 8.2 min·day$^{-1}$; 95% CI: −4.1–20.5).

**Discussion**

Our study shows that children and adolescents with inactive or mildly active IBD have similar sedentary and PA patterns compared with their age- and sex-matched healthy peers. The only significant difference was observed in male patients with IBD, among whom MVPA was significantly reduced compared with their healthy counterparts.

The available PA pattern data among pediatric patients with IBD can be summarized as (11-13): (*i*) children and adolescents with active IBD have lower PA than those in IBD remission (11); (*ii*) sedentary time or prevalence of TV watching and computer or video game usage (*i.e.*, all activities combined) is similar between children and adolescents with IBD and controls (12); and (*iii*) although the differences in PA duration and number of steps between pediatric patients with IBD and controls did not reach statistical significance, female patients with IBD had a significantly shorter duration of total and moderate-intensity PA (13). Methodological issues may explain some of the discrepancies between the above-mentioned studies and the present study. A primary limitation is the small sample sizes in the three abovementioned studies, N = 15, N = 22, and N = 39, respectively (11-13). A second limitation is the methodology used to assess PA patterns in patients with IBD and controls. Walker et al. used two accelerometer models (Uniaxial GT1M ActiGraph and triaxial GT3X accelerometer) within the same study (12). Mählmann et al. used the Fitbit Flex to assess PA patterns with 1 min epoch setting (11). However, a 2 or 5 s epoch is usually preferred for assessing PA in children and adolescents because most of their spontaneous activities are markedly short and do not exceed 1 min (24). In addition, the accuracy of measurement by Fitbit Flex for activity duration varies considerably by activity type and is poor for complex sets of activity, such as a run embedded within 2 walking segments (25).

In our study, male patients with IBD were significantly less active compared with healthy controls (mean difference, $-16.2$ min·day$^{-1}$ for MVPA level), while there was no difference

in sedentary time. No significant difference was found for female patients with IBD. The difference of 16 min represents 35% of the time spent in MVPA in male controls and is likely biologically relevant. Indeed, there is a dose-response association between MVPA and mortality rate in adults and metabolic syndrome in children (26-27). This may be related to low PA levels in female controls (mean difference of 35.4% between male and female controls). It is well known that PA in developed countries is lower in female patients than in male patients (28-31). In addition, the decline in PA observed with age is more important in female patients than in male patients (32).

Although only one third of patients with IBD fulfilled the recommended 60 min MVPA daily, this is not significantly different from that observed in healthy controls. Several authors have highlighted the benefits of PA for health status in patients with IBD (4,8-9). Implementing a physical education curriculum could help promote better health in patients with IBD who are in remission or have mild disease.

The current study has both strengths and limitations. Strengths include a large sample of both pediatric patients with IBD and age- and sex-matched healthy controls. However, no sample size calculation could be performed; therefore, a lack of adequate statistical power to detect significant differences, especially heterogeneity in subgroup analyses, cannot be excluded. With our sample size, a minimum effect size (standardized mean difference) of 0.43 can be detected with a paired *t*-test at a 0.05 significance level. A false positive difference regarding the multiple testing issue also cannot be excluded. Another strength is the use of a strong objective method to assess PA patterns (*i.e.*, a triaxial accelerometer with appropriate epoch length for adolescents). However, it cannot be excluded that variations in weather conditions (*e.g.*, wind, rain, sunshine) during PA assessments (not recorded) may have affected our results (33). The study is not without limitations. Parental education levels or socioeconomic status were not collected. These parameters may play a role in adolescents'

daily PA patterns and their attitudes about healthy lifestyles (34). Another limitation is that the majority of our IBD patients were either in remission or had mild disease. Therefore, they were probably more prone to have a PA higher than that of IBD patients with moderate-to-severe disease.

Overall, pediatric IBD patients in remission or with mild disease have similar PA patterns compared with their healthy counterparts. The prevalence of IBD patients fulfilling the recommended 60 min a day of MVPA is low, but not significantly different from healthy controls. It is critical that we further evaluate the health benefits of PA programs aimed at increasing PA in pediatric IBD patients in remission or with mild disease. Data are needed on PA in pediatric IBD patients with moderate-to-severe disease.

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**Figure legends**

**Figure 1.** Differences in time spent in sedentary activity (min.day$^{-1}$) between IBD patients and healthy controls, overall and according to key subgroups. Phet indicates p-value for heterogeneity across subgroups.

**Figure 2.** Differences in time spent in moderate-to-vigorous physical activity (min.day$^{-1}$) between IBD patients and healthy controls, overall and according to key subgroups. Phet indicates p-value for heterogeneity across subgroups.

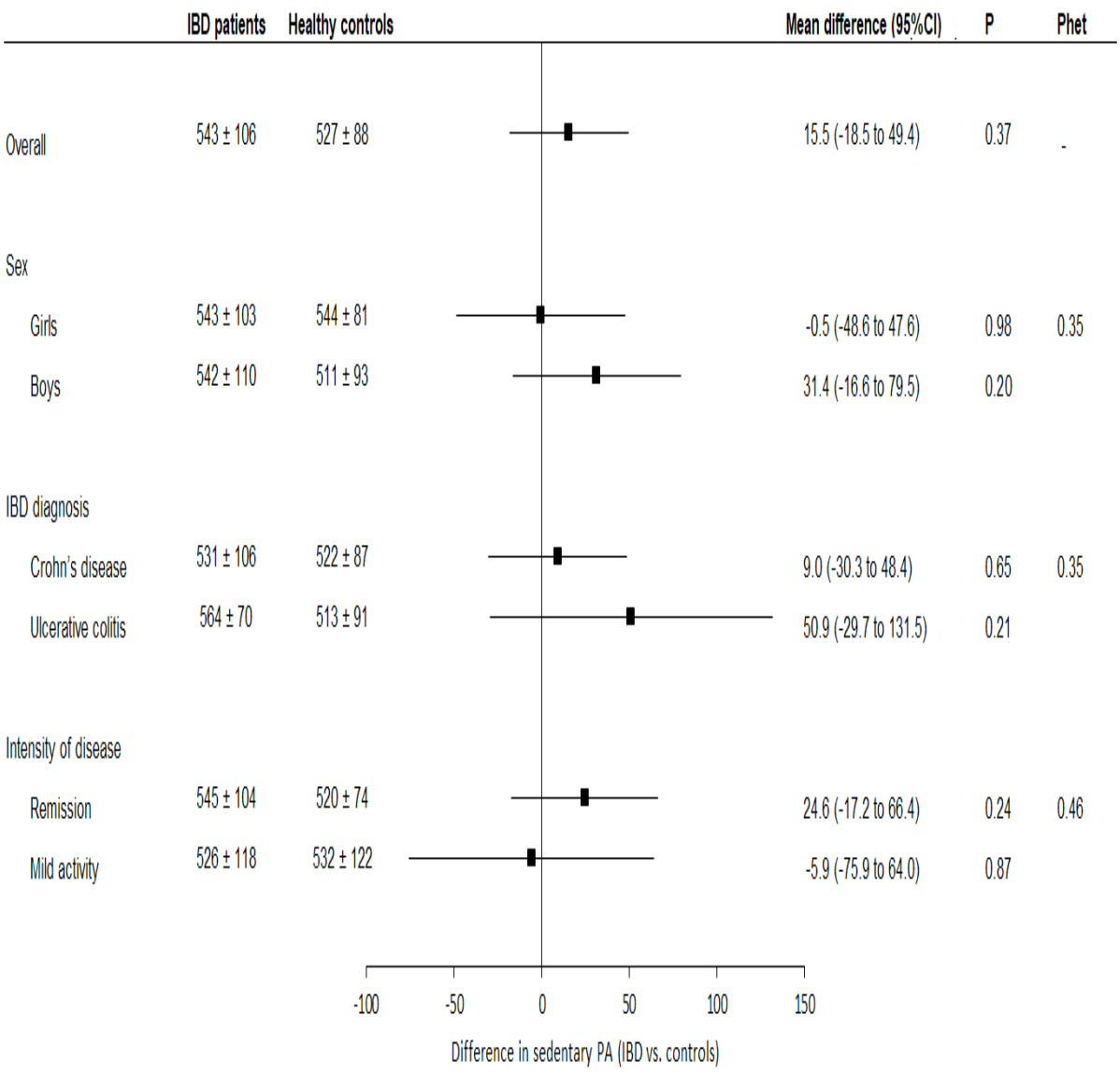
**Table 1.** Characteristics of IBD patients and healthy controls

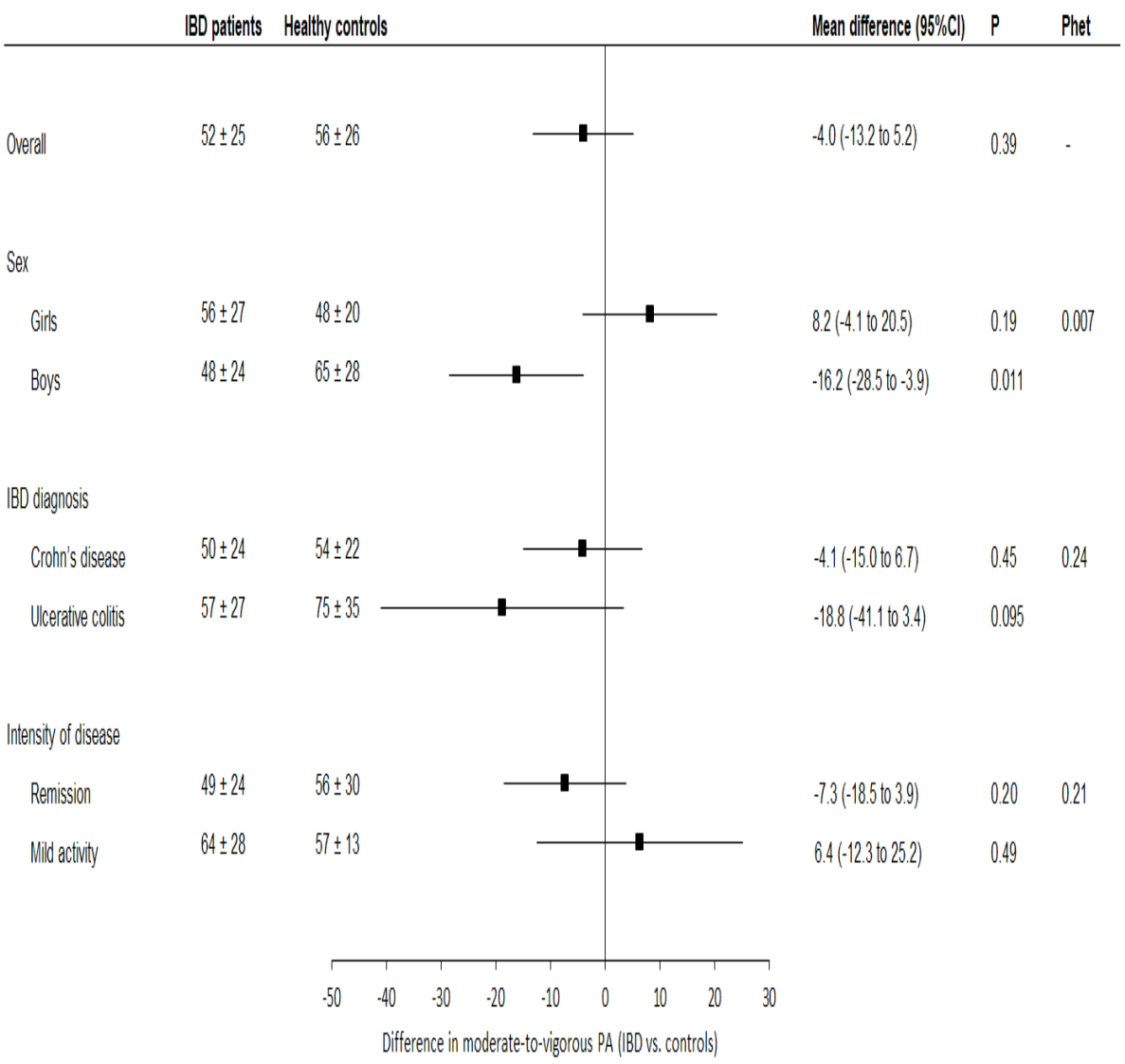
| | **IBD Patients (N=60)** | **Healthy controls (N=60)** |
|---|---|---|
| Boys/Girls | 30/30 | 30/30 |
| Age (*years*) | 14.3 ± 2.3 | 13.8 ± 2.1 |
| Height (*cm*) | 159 ± 13 | 159 ± 14 |
| Weight (*kg*) | 51 ± 15 | 49 ± 12 |
| Body mass index ($kg.m^{-2}$) | 19.8 ± 3.8 | 19.0 ± 2.8 |
| Fat Mass (*%*) | 23.2 ± 8 | |
| Fat Free Mass (*%*) | 76.8 ± 8 | |
| Age at diagnosis (*years*) | 10.8 ± 2.2 | |
| Disease duration (*months*) | 34 [range: 4-122] | |
| IBD diagnosis (*n*) | | |
| Crohn's disease | 42 (70.0%) | |
| Ulcerative colitis | 10 (16.7%) | |
| Inflammatory bowel disease-unclassified | 8 (13.3%) | |
| Blood sample parameters | | |
| C-reactive protein ($mg.L^{-1}$) | 2 [range: 0-35] | |
| Albumin ($g.L^{-1}$) | 43.8 ± 4.1 | |
| Haematocrit (*%*) | 40.3 ± 4.1 | |
| Erythrocyte sedimentation rate (*mm/h*) | 10.5 [range: 2-65] | |
| Intensity of disease (*n*) | | |
| I (Remission) | 45 (73.7%) | |
| II (Mild activity) | 15 (26.3%) | |
| III (Moderate to severe activity) | 0 (0.0%) | |
| Corticosteroids ever | 35 (58.3%) | |
| Corticosteroids lifetime | | |
| I (ever use or usage ≤3 months) | 40 (66.6%) | |
| II (usage >3 months) | 20 (33.4%) | |
| Anti-TNF therapy (*yes*) | 33 (55%) | |

**Table 2.** Comparison of physical activity levels (mean ± SD) between IBD paediatric patients and healthy controls

| | **IBD patients (N=60)** | **Healthy controls (N=60)** | **Mean difference (95%CI)** | **P** |
|---|---|---|---|---|
| **Sedentary PA** (*min.day$^{-1}$*) | | | | |
| All days | 543 ± 106 | 527 ± 88 | 15.5 (-18.5 to 49.4) | 0.37 |
| During week days | 570 ± 133 | 575 ± 101 | 5.0 (-45.9 to 35.9) | 0.81 |
| During weekend days | 516 ± 109 | 480 ± 102 | 35.9 (-4.6 to 76.4) | 0.081 |
| **Moderate PA** (*min.day$^{-1}$*) | | | | |
| All days | 33 ± 17 | 36 ± 20 | -2.9 (-9.8 to 4.0) | 0.40 |
| During week days | 36 ± 17 | 41 ± 23 | -5.6 (-13.1 to 1.9) | 0.14 |
| During weekend days | 30 ± 21 | 30 ± 24 | -0.2 (-8.3 to 8.0) | 0.96 |
| **Vigorous PA** (*min.day$^{-1}$*) | | | | |
| All days | 19 ± 12 | 20 ± 12 | -1.1 (-5.5 to 3.4) | 0.63 |
| During week days | 22 ± 16 | 25 ± 18 | -3.1 (-9.6 to 3.3) | 0.33 |
| During weekend days | 16 ± 13 | 16 ± 13 | 1.0 (-4.0 to 5.9) | 0.70 |
| **MVPA** (*min.day$^{-1}$*) | | | | |
| All days | 52 ± 25 | 56 ± 26 | -4.0 (-13.2 to 5.2) | 0.39 |
| During week days | 58 ± 29 | 67 ± 32 | -8.7 (-20.2 to 2.7) | 0.13 |
| During weekend days | 47 ± 29 | 46 ± 32 | 0.8 (-10.4 to 12.0) | 0.89 |

Abbreviations: CI=confidence interval; IBD=Inflammatory bowel disease; MVPA= Moderate-to-vigorous-physical-activity; PA=physical activity


IBD patients
Healthy controls
Mean difference (95%CI)
P
Phet
Overall
543 ± 106
527 ± 88
15.5 (-18.5 to 49.4)
0.37
-
Sex
Girls
543 ± 103
544 ± 81
-0.5 (-48.6 to 47.6)
0.98
0.35
Boys
542 ± 110
511 ± 93
31.4 (-16.6 to 79.5)
0.20
IBD diagnosis
Crohn's disease
531 ± 106
522 ± 87
9.0 (-30.3 to 48.4)
0.65
0.35
Ulcerative colitis
564 ± 70
513 ± 91
50.9 (-29.7 to 131.5)
0.21
Intensity of disease
Remission
545 ± 104
520 ± 74
24.6 (-17.2 to 66.4)
0.24
0.46
Mild activity
526 ± 118
532 ± 122
-5.9 (-75.9 to 64.0)
0.87
-100
-50
0
50
100
150
Difference in sedentary PA (IBD vs. controls)


IBD patients
Healthy controls
Mean difference (95%CI)
P
Phet
Overall
52 ± 25
56 ± 26
-4.0 (-13.2 to 5.2)
0.39
-
Sex
Girls
56 ± 27
48 ± 20
8.2 (-4.1 to 20.5)
0.19
0.007
Boys
48 ± 24
65 ± 28
-16.2 (-28.5 to -3.9)
0.011
IBD diagnosis
Crohn's disease
50 ± 24
54 ± 22
-4.1 (-15.0 to 6.7)
0.45
0.24
Ulcerative colitis
57 ± 27
75 ± 35
-18.8 (-41.1 to 3.4)
0.095
Intensity of disease
Remission
49 ± 24
56 ± 30
-7.3 (-18.5 to 3.9)
0.20
0.21
Mild activity
64 ± 28
57 ± 13
6.4 (-12.3 to 25.2)
0.49
-50
-40
-30
-20
-10
0
10
20
30
Difference in moderate-to-vigorous PA (IBD vs. controls)