Journal of Public Health
https://doi.org/10.1007/s10389-024-02278-z

REVIEW ARTICLE

Physical activity in the prevention and management of inflammatory bowel disease: a systematic review

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Received: 6 March 2024 / Accepted: 29 April 2024

Abstract

Aim This study aimed to assess the potential role of physical activity (PA) in reducing the risk of developing inflammatory bowel diseases (IBDs) and in their management.

Subject and methods A systematic review of literature was conducted up to October 2023 using the PubMed, Scopus, Web of Science and Cochrane Library databases. Observational studies, semi-experimental and experimental studies reporting PA effects were considered eligible. Data on disease status and PA characteristics, main outcomes and possible confounders were collected in a database. The Newcastle–Ottawa Quality Assessment Scale was used to assess risk of bias.

Results Of the 29 articles included, six investigated PA and risk of IBDs and four of them showed an inverse relationship. Among the others, seven reported positive effects of PA on IBD symptoms, while all showed improvements in comorbidities, complications and quality of life.

Conclusion PA seems to be effective in preventing or treating IBDs and their complications. Owing to the low quality of the majority of the studies and their heterogeneity, further research is needed to better understand which type and level of PA may be useful in the prevention and treatment of these diseases.

Keywords Physical activity · Inflammatory bowel disease · Crohn's disease · Ulcerative colitis · Exercise

Introduction

The term inflammatory bowel disease (IBD) indicates a group of chronic and lifelong diseases characterized by inflammation of the gastrointestinal tract, including Crohn's disease (CD) and ulcerative colitis (UC) (Yeshi et al. 2020). CD can affect any part of the gastrointestinal tract, but it most commonly affects the large and small intestines, while UC refers to recurring inflammation of the rectum and the colon (Gohil and Carramusa 2014). IBD is characterized by symptoms such as abdominal pain, fever, constipation or diarrhoea, and presence of blood and/or mucus in faeces (O'Reilly et al. 2023). In the early 2000s, more than 1.5 million people in North America and over 2 million people in Europe suffered from IBD (Burisch et al. 2013). It is projected that by 2030, the number of people suffering from IBD in Europe and the United States of America will exceed 7 million, or the 0.3% of the population in North America, Oceania and many countries in Europe (Hammer and Langholz 2020; Coward et al. 2019; Molodecky et al. 2012). The incidence rate of IBDs is higher than the mortality rate; although their incidence has remained constant, their prevalence is expected to increase in the next decade due to advancements in maintenance therapy (Kaplan 2015; Kaplan and Windsor 2021). However, currently there are no specific pharmaceutical treatments for IBD, given that these diseases are multifaceted disorders. Therapeutics that are used to treat IBD generally include non-specific anti-inflammatory and immunosuppressive agents and focus on the immune system, aiming to reduce inflammation and fostering mucosal healing. Beyond

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Published online: 11 May 2024

such conventional treatments, stem cell therapies, including hematopoietic stem cell transplantation and mesenchymal stem cell therapy, have been shown to improve patients' conditions (Imbrizi et al. 2023; Parigi et al. 2023). In addition, IBD is a chronic illness that can lead to frequent relapses and complications and these conditions put a significant burden on the healthcare system due to hospitalization and cost of medications, as well as on society in terms of productivity loss (Kuenzig et al. 2020; Caviglia et al. 2020, 2023).

Therefore, it is important to properly understand the risk and protective factors associated with the disease to reduce its global burden. The aetiology of IBD is unknown, but there are many factors suspected to be involved such as genetic susceptibility, environmental factors like gastrointestinal infections, an altered immune response, shifts in microbial composition, often due to antibiotic use, concomitant immune-mediated diseases, smoking, stress, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) or oral contraceptives (Axelrad et al. 2019; Ungaro et al. 2014; Torres et al. 2023; Van Der Sloot et al. 2017). In contrast to these risk factors, the dietary intake of fibre, fruits, vitamin C, breast milk and omega-3 polyunsaturated fatty acids, living in southern latitudes, possibly because of UV radiation exposure, higher vitamin D level and physical activity (PA) seem to be protective against IBD (Sahu et al. 2021; Khalili et al. 2012; Holik et al. 2019). PA in particular has been proven to also be beneficial in the course of IBDs (Parigi et al. 2023). Indeed, literature shows that PA plays a crucial role in mechanisms related to the intestinal function that involve downregulating the intestinal pro-inflammatory cell network, reducing oxidative stress and modulating the gut microbiota (Wojcik-Grzybek et al. 2022; Dorelli et al. 2021; Gallè et al. 2020). Moderate PA can have positive effects on the immune system and reduce inflammatory markers, which may be helpful for IBD patients (Nishida et al. 2023). Moreover, exercise also has psychological benefits, such as reducing stress and anxiety, which are commonly experienced by IBD patients and can trigger relapses (Ordille and Phadtare 2023). However, the role of PA in IBD prevention and treatment has not yet been defined clearly.

This systematic review was conducted to explore the evidence coming from structured PA interventions aimed at preventing IBD or at managing IBD symptoms, looking for consistent elements that could lead to future strategies.

Methods

Selection protocol and search strategy

The present systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Page et al. 2021). The protocol was registered in PROSPERO (CRD42023446860). The review question was framed using the PICO framework and the following eligibility criteria (a) Population: adult individuals of any gender; (b) Intervention: any type of PA, including exercise and sport; (c) Comparison: age-, gender- and condition-matched control group (if present); (d) Outcome: assessment of the effects of PA in prevention or treatment of IBD; (e) Study: observational studies, semi-experimental and experimental studies. The review focused on the role of PA in prevention and therapy of IBD in adults of any gender. Only studies which measured PA and its effects on human IBD development and progression were considered eligible. Four electronic databases (PubMed, Scopus, Web of Science and Cochrane Library) were interrogated using the following terms: ("physical activity" OR "exercise*") AND ("IBD" OR "Inflammatory bowel disease*" OR "gastrointestinal inflammatory disease*" OR "Crohn's disease" OR "ulcerative colitis"). The search on PubMed was carried out by title, abstract and MeSH terms; the search on Scopus, Web of Science and Cochrane Library included topic by title, abstract and keywords. The search was performed from 10 October 2023 to 31 October 2023.

Inclusion and exclusion criteria

Only those studies which specifically analysed the role of PA in prevention or treatment of IBD among adult patients of any gender were considered. Furthermore, the possible presence of confounding factors was also considered. All the studies which included individuals under the age of 18 years who were affected by any chronic conditions other than IBD or did not concern PA were excluded. Only articles presenting observational studies, semi-experimental and experimental studies were considered eligible. Reviews, meta-analysis, case studies, proceedings, qualitative studies, editorials, commentary studies and any other type were excluded. Reviews and meta-analyses were examined to identify further articles in their references that may not have been part of the baseline research results. We included only articles published in English and Italian languages. Titles and abstracts acquired from the four databases were transferred to the reference software Zotero systematic review manager for the relevance assessment process. The next step was screening the title and abstract of the potentially eligible studies, following the previously stated inclusion criteria; the screening was conducted by four authors (ADG, EM, FU, VV) independently. Then, full-texts were read independently by the same four authors (ADG, EM, FU, VV) with a later discussion about their inclusion in the review. Disagreements were mediated by the evaluation of the other three authors (CP, FV, FG) and consensus among the authors.

Data extraction process and quality assessment

The following data were extracted: author, publication year, country, sample characteristics (size, age, gender, ethnicity, socio-economic status, education, anthropometric parameters), type of control, type of IBD and disease status, PA-related information (type, frequency and duration of PA/exercise), main outcomes, confounding factors assessed and main findings. The quality assessment was performed using the Newcastle–Ottawa Quality Assessment Scale (NOS) for cohort, case–control studies and clinical trials, then adapted from cohort and case control studies to perform a quality assessment for cross-sectional studies (Wells et al. 2021). An overall rating of "poor", "fair" or "good" quality was assigned to each eligible article according to the proportion of criteria met. Four authors (ADG, EM, FU, VV) independently assigned a score to each study, and disagreements were achieved by the evaluation of the other three authors (CP, FV, FG) and consensus among the authors.

Results

The database search yielded a total of 3129 records. Of these, 1147 duplicates were removed and 1982 were screened by title and abstract. After the full-text assessment, 29 of the 68 eligible articles were included in the review (Fig. 1).

Six of them (Furuya et al. 2022; Hlavaty et al. 2013; Khalili et al. 2013; Klein et al. 1998; Lautenschlager et al. 2023; Rasmussen et al. 2021) investigated the role of PA in the development of the disease, while the others evaluated the potential beneficial effects of PA in individuals affected by IBD.

Table 1 shows the information regarding the first group. It included three cohort studies (Khalili et al. 2013; Lautenschlager et al. 2023; Rasmussen et al. 2021), two case–control studies (Furuya et al. 2022; Hlavaty et al. 2013) and a cross-sectional study (Klein et al. 1998), which were performed in Europe (Hlavaty et al. 2013; Lautenschlager et al. 2023; Rasmussen et al. 2021), Asia (Furuya et al. 2022; Klein et al. 1998) and the USA (Khalili et al. 2013). Both genders were observed in all the studies, with a sample size ranging from 232 to 57,053 individuals. Both CD and UC were considered across all the studies. With regard to quality assessment, three studies were considered "poor", two "fair" and one "good". As for the results, four studies (Hlavaty et al. 2013; Khalili et al. 2013; Klein et al. 1998; Lautenschlager et al. 2023) showed an inverse association between PA and onset of IBDs or at least of CD. The study by Rasmussen et al. did not find any association between PA and risk of developing IBDs (Rasmussen et al. 2021). However, in the same study, a higher time spent in do-it-yourself work appeared to be associated with IBD onset. The study by Furuya et al. registered a positive association between occupational PA level and UC risk (Furuya et al. 2022).

The data from the selected studies which investigated the role of PA in IBD treatment are reported in Table 2. As for the design of the study, nine of the selected articles described randomized controlled trials (Cronin et al. 2019; Elsenbruch et al. 2005; Jones et al. 2020; Klare et al. 2015; Lamers et al. 2021a, b; Lamers et al. 2022; Ng et al. 2007; Robinson et al. 1998; Watters et al. 2001), while the others reported observational studies. Seventeen studies were performed in Europe (Cronin et al. 2019; Elsenbruch et al. 2005; D'Incà et al. 1999; Henderson et al. 2022; Holik et al. 2019; Jones et al. 2020; Klare et al. 2015; Lamers et al. 2021a, b; Lamers et al. 2021a, b; Lamers et al. 2022; Ratajczak-Pawłowska et al. 2023; Spijkerman et al. 2021; Tew et al. 2016; Wiestler et al. 2019; Ng et al. 2007; Robinson et al. 1998; Watters et al. 2001), four in the Americas (Jones et al. 2015; Lo et al. 2021; Mack et al. 2011; Taylor et al. 2018) and two in Asia (Kim et al. 2021; Watanabe et al. 2021). The sample size varied across the selected studies from 20 to 117 for RCTs and from 12 to 289,658 individuals for observational studies. Both genders were represented in all the studies but one which involved only men (D'Incà et al. 1999) and two which did not report this information (Watters et al. 2001; Jones et al. 2015). Of the 16 studies which reported the status of the disease for participants, all but three (Cronin et al. 2019; D'Incà et al. 1999; Jones et al. 2015) included participants with different clinical conditions. As for quality, 12 of these studies were considered "poor", ten "fair" and one "good".

The results differ across the selected studies. As for RCTs, the study by Cronin et al. showed a significant reduction in body fat percentage among patients who underwent 8 weeks of aerobic and resistance training, together with improvements in IBD-related sarcopenia and obesity-related metabolic disorders (Cronin et al. 2019). The study by Elsenbruch et al. reported a significant improvement in mental health, but this resulted from a multicomponent intervention, including stress management training, moderate exercise, Mediterranean diet, behavioural techniques and self-care strategies (Elsenbruch et al. 2005). Jones K et al. found significant improvements in bone mineral density and muscular function among IBD patients who underwent the 26-week exercise programme and not among those who did not exercise; quality of life and fatigue improvements were also registered in this study (Jones et al. 2020). Even Klare et al. registered an improvement in quality of life among patients who practiced moderate-intensity running (Klare et al. 2015). Lamers et al. observed an exercise-related increase in cytokine production among IBD-walkers and non-walkers and no changes in faecal calprotectin concentration; a significant increase in disease activity was registered among CD and not in UC walkers (Lamers et al. 2021a, b). In the subsequent RCT by Lamers et al., significant improvements

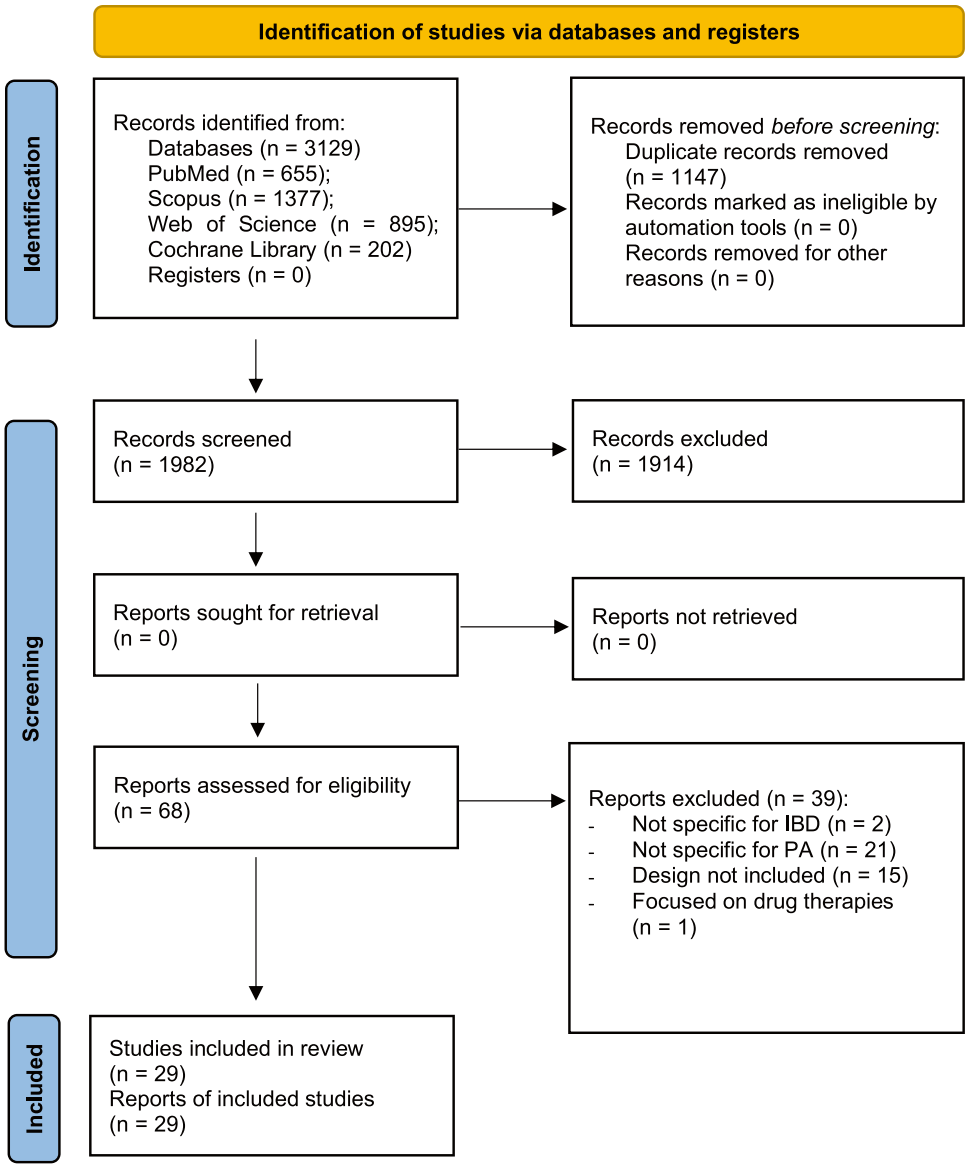

Fig. 1 PRISMA flow diagram for the article selection

in impact of disease in daily life and fatigue were obtained after a multidisciplinary intervention, but they were related to changes in diet and not to PA level, which remained the same (Lamers et al. 2022). Ng et al. reported a significantly higher improvement in quality of life and symptoms in patients involved in walking with respect to controls (Ng et al. 2007). The 12-month exercise intervention implemented by Robinson et al. led to significant improvements in bone mineral density among participants, which were not observed in controls Robinson et al. 1998. Instead, the resistance training intervention applied by Watters et al. showed a positive relationship between exercise and wellbeing in IBD patients (Watters et al. 2001).

As for the observational studies, the study by D'Incà et al. showed a post-exercise increase in orocaecal transit time and neutrophils which did not differ from that observed in healthy controls (D'Incà et al. 1999). Henderson et al. registered similar changes among IBD patients and healthy controls in breath volatile organic compounds and cytokines production after repeated prolonged moderate exercise (Henderson et al. 2022). Holik et al. found a significant relationship between daily PA and disease activity, which was independent by intensity level and type of IBD (Holik et al. 2019). Even in the study by Jones P et al., higher exercise level was associated with decreased risk of relapse or active disease for IBD patients (Jones et al. 2015). Kim et al. found an association between weekly PA level and quality of life (Kim et al. 2021). Lamers et al. found a significant association between disease activity and PA in CD but not in UC patients, and an improvement in general fitness, quality of life and self-image was reported by the majority of participants (Lamers et al. 2021a, b). The findings of Lo et al.

Table 1 Data from the studies regarding the possible role of physical activity in IBD development

Author year Country, study design, quality	Sample size; Characteristics of the sample (mean age ± SD, age range), gender n (%), type of IBD	Controls	Type, frequency and duration of physical activity	Confounding factors	Main findings
Furuya et al. 2021 Japan, case–control, poor (4)	2650: 564 cases and 2086 controls; 51.7 ± 8.3 years; 1639 men (61.9%) and 1011 women (38.1%), 172 CD, 392 UC	Patients hospitalised for reasons unrelated to IBD and who did not have a history of IBD	1050 Low OPA, 1022 Intermediate OPA, 279 High OPA	Age, sex, admission year, alcohol consumption, smoking status	The risk for UC was higher among sales workers and carrying, cleaning and packing workers (OR 2.62; OR 2.52). There was no association between occupation type and CD risk. Higher OPA level decreased CD risk (OR 0.5) and increased UC risk (OR 1.53)
Hlavaty et al. 2013 Slovakia, case–control, good (7)	693: 338 cases and 355 controls; 31 years (16–80); 298 men (43%) and 395 women (57%), 190 CD, 148 UC	355 healthy volunteers age- and sex-matched with the patient group	Sporting activity in childhood; times/week	Smoking status, socio-economic status, age, gender, comorbidities, breastfeeding duration	Both CD and UC were associated with less than two weekly sessions of sporting activities in childhood
Khalili et al. 2013 USA, cohort, poor (4)	194.711: 647 cases; 42.2 ± 10.9 years; 0 men (0%) and 194.711 women (100%), 284 CD, 363 UC	-	Cumulative average PA in MET h/wk: lowest 2.6 ± 1.5, highest 41.4 ± 29.9	Age, smoking status, BMI	Increased PA was associated with a lower risk of developing CD but not of UC
Klein et al. 1998 Israel, cross-sectional, poor (4)	232: 88 cases and 144 controls; 29.5 ± 1.2 years; 140 men (60%) and 92 women (40%), 33 CD, 55 UC	Clinic control and population selected by Israel Population Registry	Low, moderate and high PA level	Age, education, weight, BMI	During the preillness period more patients had low levels of PA as compared to controls, while more controls engaged in moderate or high levels of PA. Patients spent fewer hours in strenuous PA
Lautenschlager et al. 2023 Switzerland, cohort, fair (6)	1443: 1070 cases and 365 controls; 49.2 ± 14.8 years; 503 men (22%) and 575 women (25%); BMI 24 ± 3.7, 610 CD, 468 UC	365 patients' childhood friends, who grew up in a similar environment	Endurance sport; regular practice	-	PA is a protective factor for IBD

Table 1 (continued)

Author year Country, study design, quality	Sample size; Characteristics of the sample (mean age ± SD, age range), gender n (%), type of IBD	Controls	Type, frequency and duration of physical activity	Confounding factors	Main findings
Rasmussen et al. 2021 Denmark, cohort, fair (6)	57.053; 50–64 years; 27.178 men (48%) and 29.875 women (52%), 106 CD, 423 UC	-	LTPA: walking, housework, gardening, do-it-yourself work, cycling and sports; active ≥ 3 MET hours/week or spending > 0 h/week on each type of activity	Occupational PA, smoking status, intake of fibre, fermented dairy products, red and processed meat, alcohol, hormon replacement therapy (for women), non-steroidal anti-inflammatory drugs, comorbidity, age and gender	No association between PA and risk of IBD when comparing physically active with inactive participants, neither any dose–response effect when comparing quartile groups of MET hours/week with the lowest quartile as reference. Do-it-yourself work appeared to be associated with a higher risk of IBD when comparing the third quartile with the second quartile of h/week

CD, Crohn's disease; *UC*, ulcerative cholitis; *IBD*, inflammatory bowel disease; *PA*, physical activity; *OPA*, occupational physical activity; *LTPA*, leisure-time physical activity; *MET*, metabolic equivalent of task; *BMI*, body mass index

indicated a lower mortality rate related to PA in IBD patients (Lo et al. 2021). In the study by Mack et al., LTPA has been associated with reduced risk of onset and management of IBD comorbidities such as osteoporosis and colon cancer (Mack et al. 2011). In the study by Ratajczak-Pawłowska et al., vigorous, moderate and total PA were found to be positively related to bone mineral density and body mass among IBD patients, while only moderate PA was related to BMD in controls (Ratajczak-Pawłowska et al. 2023). Spijkerman et al. found an apparent suppression of the proinflammatory response in IBD patients after three consecutive days of walking (Spijkerman et al. 2021). In the study by Taylor et al., MVPA and walking were associated with physical and mental health-related quality of life (Taylor et al. 2018). Tew et al. found that PA was negatively and independently associated with depression, disease activity and perceived barriers to exercise in people with CD, and with depression and age in people with UC (Tew et al. 2016). Watanabe et al. showed that strenuous activity is significantly inversely associated with mucosal healing but not with clinical remission (Watanabe et al. 2021). The study by Wiestler et al. reported that disease activity and quality of life were significantly correlated with the duration of strenuous PA per day (Wiestler et al. 2019).

Adverse events were reported in four studies (Lamers et al. 2022; Ratajczak-Pawłowska et al. 2023; Spijkerman et al. 2021; Wiestler et al. 2019). Apart from one fall, they consisted of limitations to PA related to the disease.

Discussion

IBDs pose a major public health concern due to increasing prevalence, deaths and disability-adjusted life-years and, thus, require specific preventive and management policies (Wang et al. 2019). Considering that PA positively influences all physiologic systems and it can be used as a "medicine" towards several conditions and diseases (Anderson and Durstine 2019), the present systematic review was performed to examine the beneficial role of PA in counteracting the development of IBDs and/or managing these diseases after their occurrence (Holik et al. 2019).

The first finding of this systematic review is that the preventive role of PA towards IBD is considered to a lesser extent than the therapeutic one. In fact, only six articles evaluate PA for this purpose (Furuya et al. 2022; Hlavaty et al. 2013; Khalili et al. 2013; Klein et al. 1998; Lautenschlager et al. 2023; Rasmussen et al. 2021). Four of these found positive and encouraging results (Hlavaty et al. 2013; Khalili et al. 2013; Klein et al. 1998; Lautenschlager et al. 2023). Conversely, an included study found no association (Rasmussen et al. 2021), while another one found a direct

Table 2 Data from the studies regarding the possible role of physical activity in IBD management

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Cronin et al. 2019 Ireland, RCT, poor (4)	20: 13 cases and 7 controls; 25 ± 6.5 years; 15 men (75%) and 5 women (25%); BMI 28.9 ± 3.8, 7 CD and 13 UC; clinical remission	Controls instructed to maintain usual levels of PA (none or low) for the 8-week period	Combined aerobic and resistance training program performed three times per week for 8 weeks	Body composition change (body fat and total lean tissue mass), disease activity, quality of life and mood scores, pro-inflammatory cytokines	–	Combined short-term aerobic and resistance training achieves favorable changes in body composition in IBD patients such as a median decrease in intervention of 2.1% body fat compared with controls ($p = 0.022$)
D'Incà et al. 1999 Italy, case–control, poor (3)	12: 6 cases and 6 controls; 12 men (100%) and 0 women (0%), 6 CD; in remission	Healthy participants	1 h Session of moderate physical exercise: stepwise incremental graded exercise on an electrically braked cycle ergometer	Orocaecal transit time (breath test to lactulose), intestinal permeability, antioxidant trace elements	–	Orocaecal transit time increased after exercise in Crohn's disease patients (72 min ± 30 vs 100 min ± 34) with no significant difference from controls (77 min ± 20 vs 83 min ± 23). The variations in intestinal permeability were not significant, while neutrophils in CD patients showed an increase post exercise ($p = 0.008$) similar to controls ($p = 0.221$), as well as urinary zinc ($p = 0.031$)
Elsenbruch et al. 2005 Switzerland, RCT, poor (3)	30: 15 cases and 15 controls; 42.7 ± 10 years; 10 men (33%) and 20 women (67%); UC; 17 in remission, 4 acute exacerbation, 6 chronically active, 3 indeterminate	Controls continued usual medical care and only came to the clinic for a total of two study visits at the clinic, once before and after the end of the waiting period	Moderate exercise; Structured 60-h training program over a 10-week period (6 h on one day per week for 10 weeks)	Clinical disease activity, quality of life, perceived stress, leukocytes and lymphocyte subsets in peripheral blood, levels of cortisol, prolactin, growth hormone and catecholamine, beta-adrenergic modulation of TNF-alpha production		The intervention group showed significantly greater improvement in the SF-36 scale Mental Health (Cohen's $d = 0.84$, $p = 0.01$). No difference between intervention and controls in the disease activity (CAI score), serum hormones, leukocyte and lymphocyte subset and modulation of TNF-alpha

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Henderson et al. 2022 the Netherlands, cohort, poor (4)	37: 18 cases and 19 controls; 54 ± 12.5 years; 15 men (40.5%) and 22 women (59.5%); BMI 25.9 ± 4.15, CD, UC	Non-IBD participants	Walking per 3 consecutive days (30/40/50 km)	Breath volatile organic compounds (VOCs) and inflammation markers in blood samples (IL-6, IL-8, IL-10, IL-1β, and TNF-α)	–	Exercise accounted for 15% of the explained variance in the breath VOC profile, whilst the IBD condition contributed for 3%. Most breath VOCs increased in concentration in relation to exercise, only isoprene showed a decrease. Repeated prolonged moderate-intensity exercise affects exhaled butanoic acid and IL-6 of participants with or without IBD in the same manner
Holik et al. 2019 Croatia, cross-sectional, good (7)	312; 49.9 ± 15.0 years; 166 men (53.2%) and 146 women (46.8%), 114 CD, 198 UC; Active disease 79 (40.0%) and inactive disease 119 (60.0%)	–	Walk, bicycle ride, gardening, hard manual work, sports; low (30-min walk), moderate (bicycle ride, gardening), and intensive (hard manual work, sports)	Disease activity	Family medical history for IBD	A significant difference in disease activity was found between patients practicing low PA and those that did not practice daily ($p < 0.001$). Daily PA was significantly connected to the inactive stage of IBD ($p < 0.001$), regardless of the intensity of daily PA and type of IBD, even for participants not on medication

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Jones et al. 2020 UK, RCT, fair (6)	47: 23 cases and 24 controls; 49.3 ± 13.0 years; 15 men (32%) and 32 women (68%); BMI 26.6 ± 4.3, 47 CD: 31 quiescent (66%) and 16 mildly active disease (34%)	Two controls groups: 23 cases who did not exercise and follow usual therapy and 33 healthy controls	Marching on the spot, squat and punch, big arm circles, forward and backward leg swings; 60 min exercise sessions on non-consecutive days each week for 26 consecutive weeks	BMD of the hip and lumbar spine and muscle function at 6 months. Resting heart rate values, HRQoL, fatigue	Age, gender, smoking status	At 6 months, the BMD values for the exercise group were superior to those for the control group with statistical significance at lumbar spine ($p < 0.001$), but not at femoral neck ($p = 0.059$) or greater trochanter ($p = 0.415$); the intervention was also associated with improvements in generic HRQoL and fatigue. Muscle function was superior ($p < 0.001$) and resting heart rate was lower ($p = 0.032$) in the exercise group at both 6 and 3 months
Jones et al. 2015 USA, cohort, fair (6)	1857; median age 42 years; BMI 24 (22–28), 1308 CD, 549 UC; in clinical remission	–	Exercise with intensity and frequency divided by Godin index (AI) in low activity level Godin and high activity level	Presence of active disease at 6 months, defined as sCDAI > 150 for CD or SCCAI > 2 for UC/IC	Steroid therapy	Among those with CD, 20% of those in low-exercise category experienced relapse or developed active disease at 6 months with a sCDAI > 150, compared with 15% of those in the high-exercise category ($p < 0.01$). Higher exercise level was associated with decreased risk of active disease for CD with a sCDAI < 150 and UC/IC with SCCAI < 2

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Kim et al. 2021 Korea, cross-sectional, poor (4)	158; 45.96 ± 17.58 years; 97 men (61.4%) and 61 women (38.6%); BMI 21 ± 3, 62 CD, 73 UC, and 23 IB disease; 139 clinical remission, 18 mild, 1 moderate–severe	–	Total PA divided into mild, moderate and strenuous based on total MET h/week values and min/week	Quality of life (QoL)	–	Increased PA levels were associated with improved QoL. More leisure activity and non-sweat-inducing exercise were associated with improved QoL
Klare et al. 2015 Germany, RCT, fair (5)	30: 15 cases and 15 controls; 41 ± 14 years; 8 men (27%) and 22 women (27%); BMI 22.8 ± 4.1, 19 CD, 11 UC; mild to moderate IBD	IBD patients without exercise prescription	Moderate-intensity running thrice a week for 10 weeks	Health-related quality of life, (IBDQ total score)	–	IBDQ total score improved by 19% in the intervention group and 8% in the control group
Lamers et al. 2021a the Netherlands, RCT, fair (6)	56: 18 cases and 38 controls; 54 ± 12 years; 23 men (41%) and 33 women (59%) BMI 26.0 ± 3.8; 16 CD, 21 UC; flare-ups in past 12 months	19 non-IBD walkers and 19 IBD non-walkers	30, 40 or 50 km walking exercise on 4 consecutive days	Effects of repeated prolonged moderate-intensity exercise on objective inflammatory markers (cytokine concentrations and faecal calprotectin) in IBD patients	–	Changes in cytokine concentrations were similar for IBD walkers and non-IBD walkers, with a temporary significant increase in IL-6 and IL-10 from baseline to post-exercise day 1. Faecal calprotectin was not affected by exercise. Clinical disease activity did not change in the IBD walkers with UC ($p = 0.92$) but did increase in the CD walkers ($p = 0.024$)

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Lamers et al. 2021b the Netherlands, cross-sectional, fair (5)	338; 48.8 ± 15 years; 113 men (33.4%) and 225 women (66.6%); BMI 24.9 ± 4.2, 176 CD, 162 UC; 237 in remission (70%), 67 mild (20%) and 34 moderate (10%)	–	Dutch physical activity guidelines of 150 min of moderate to high intensity exercise per week spread over several days; Total min per week: CD 1907 ± 1031, CU 2143 ± 1016	Disease activity	Age, gender, BMI and education level, and additionally age at diagnosis, medication use and previous IBD-related surgery	In CD, the total PA score was inversely associated with disease activity, even after adjustment for confounders ($\beta = -0.375$; $p = 0.013$). No association between PA and disease activity was found in UC. Of the interviewees, 86% experienced beneficial effects of PA, such as improved general fitness, quality of life and self-image
Lamers et al. 2022 the Netherlands, RCT, poor (4)	26; 36 years; 11 men (42%) and 15 women (58%); BMI 26.4 ± 3.8; 12 CD, 14 UC in remission or with mildly active disease	–	Walking, running, cycling, swimming and resistance exercise at moderate intensity for 30 min per day at least 5 days per week	Effects on impact of disease on daily life, clinical disease activity, fecal calprotectin, fatigue and health-related quality of life (HRQoL)	Healthy diet	Over time, a significant decrease was found in impact of disease on daily life ($p < 0.009$) and fatigue ($p < 0.001$), while no significant change was observed in clinical disease activity, HRQoL, and fecal calprotectin. Physical activity was not associated with any of the outcomes
Lo et al. 2021 USA, cohort, poor (4)	289.658; 32–65 years, 51.529 men (18%) and 238.129 women (82%), CD, UC	–	Vigorous PA equivalent to two hours per week of jogging, running, biking, swimming or playing tennis; 2 h/week	Reduced mortality	Mediterranean diet, maintenance of normal BMI, light alcohol consumption, non-smoking	For PA, compared with the first quintile, IBD patients in the third, fourth, and fifth quintiles had lower mortality risk, with the HRs ranging from 0.31 to 0.55

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Mack et al. 2011 Canada, cross-sectional, poor (3)	114.801: 1.116 self-reported cases and 113.685 controls; age > 18 years; 409 men (36.6%) and 707 women (63.4%); 479 CD, 637 UC	Individuals aged ≥ 18 years who did not self-report a diagnosis of IBD	LTPA; inactive (1.50 kcal/kg/day), moderately active (1.50–2.99 kcal/kg/day), or active (3.00 kcal/kg/day)	Comorbidities	–	LTPA has been associated with lowered risk of onset and management of osteoporosis and colon cancer both known comorbidities associated with a diagnosis of CD/UC
Ng et al. 2007 UK, RCT, fair (6)	32: 16 cases and 16 controls; 14 men (44%) and 18 women (56%), CD; in remission or mildly active disease	Non-exercise group which was asked to maintain the habitual PA level	Walking session lasting 30 min, 3 times per week and the study lasted 3 months	Inflammatory Bowel Disease Questionnaire, inflammatory Bowel Disease Stress Index, Harvey–Bradshaw Simple Index	–	Controls showed a statistically significant worsening of symptoms whereas the exercise group showed a statistically significant reduction in symptoms. Exercise group experienced a statistically significant improvement in QoL with no detrimental effects on disease activity
Ratajczak-Pawłowska et al. 2023 Poland, case–control, poor (3)	78: 54 cases and 24 controls; 18–50 years; 38 men (49%) and 40 women (51%), 28 CD, 26 UC	Healthy adults	PA	BMI, bone mineral density and T- and Z-scores of the lumbar spine (L1–L4) and femoral neck (FN) assessed using dual-energy X-ray absorptiometry method, diet index	Healthy diet	A positive correlation between moderate PA and BMD and the T-score of the femoral neck ($p < 0.01$ and $p = 0.02$) was found in controls. In the IBD group, vigorous PA correlated with BMD ($p = 0.03$), T- ($p = 0.049$) and Z-scores ($p = 0.04$) of L1–L4. A positive correlation between total PA and BMD ($p = 0.04$) and Z-score ($p = 0.045$) of L1–L4 was found

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Robinson et al. 1998 UK, RCT, fair (5)	117; 60 cases and 57 controls; 18—65 years; 48 men (41%) and 69 women (59%); mean BMI 23.4, CD	Healthy participants who maintained their habitual physical activity patterns	5-min warm-up, stretching of muscles, 12 core floor-based low-impact exercises at least twice a week, with a minimum of 10 sessions per month, for 12 months	Change in BMD of in femoral neck, lumbar spine, trochanter, ward's triangle and dietary intake	Steroid intake, body weight, diet	Non-significant gains in BMD occurred at the hip and spine in the exercise group compared with controls ($p > 0.05$). In fully compliant patients, BMD increased by 3.54% at the femoral neck, 2.97% at the spine, 4.1% at Ward's triangle, and 7.77% at the greater trochanter. Compared with controls, gain in BMD at the greater trochanter was statistically significant ($p = 0.02$)
Spijkerman et al. 2021 the Netherlands, case–control, poor (4)	38: 19 cases and 19 controls; 54 ± 12 years; 16 men (42%) and 22 women (58%)	Age- and gender-matched healthy controls who underwent the same repeated exercise bouts	30, 40, or 50 km per day on 3 consecutive days at a self-selected pace	BMI, blood analysis, heart rate, flow cytometry analysis, responsiveness of neutrophils, eosinophils, and monocytes to N-Formylmethionine-leucyl-phenylalanine (fMLF)	–	Smaller increased responsiveness to fMLF was shown after 3 days of prolonged exercise in IBD walkers compared with non-IBD walkers in the expression of CD11b, CD35 in neutrophils ($p = 0.01$; $p = 0.03$) and monocytes ($p = 0.001$; $p = 0.008$), and CD10 ($p = 0.005$) in neutrophils, even though a lower expression of CD10 was shown in the neutrophils of IBD walkers compared with non-IBD walkers ($p = 0.01$) at day 0

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Taylor et al. 2018 USA, cross-sectional, poor (2)	328; 39.6 ± 14.3 years; 48 men (20%) and 194 women (80%); 96 CD, 145 UC, 1 undetermined diagnosis; 60.3% in remission and 39.7% in a disease flare	–	Vigorous PA, moderate PA, walking	Mental and physical HRQOL (health-related quality of life)	Demographic variables, resilience, and time spent sitting	Both walking and MVPA were independently associated with physical ($\beta = 0.21$ and $\beta = 0.26$, respectively; $p \leq 0.001$) but not mental HRQOL ($p > 0.05$). Higher volumes of MVPA were significantly associated with physical HRQOL ($p < 0.001$) while higher volumes of walking were associated with both physical and mental HRQOL ($p \leq 0.01$)
Tew et al. 2016 UK, cross-sectional, poor (3)	859; age > 18 years; 213 men (25%) and 646 women (75%), CD, UC	–	Cycling, running/jogging, gym/exercise classes, walking, weight lifting, swimming, other	Psychological symptoms (Hospital Anxiety and Depression Scale), fatigue (IBD fatigue scale), disease activity	–	PA was negatively and independently associated with depression, disease activity, and perceived barriers to exercise in people with CD, and with depression and age in people with UC (all $p \leq 0.038$)
Watanabe et al. 2021 Japan, cross-sectional, fair (6)	327; 48 years; 190 men (58%) and 137 women (42%), UC	–	Sedentary, standing, walking, and strenuous activity; daily total METs	Mucosal healing (MH), complete MH	–	Plentiful strenuous activity was significantly inversely associated with MH and complete MH. A very high daily MET total was significantly inversely associated with complete MH. No association between PA and clinical remission was found

Table 2 (continued)

Author year country, study design, quality	Sample size and participants' characteristics [mean age ± SD, age range, gender n (%), type and status of IBD]	Controls	Type, frequency and duration of physical activity	Outcomes	Confounding factors	Main findings
Watters et al. 2001 UK, RCT, fair (6)	107: 54 cases and 53 controls; 41 years, CD	Healthy participants who maintained their habitual PA patterns	12 core floor-based, low-impact, resistance-type exercises at least twice a week, with 10 sessions per month for 12 months	Hospital anxiety, depression, acceptance of illness and satisfaction (via interview scales)	–	High wellbeing promotes exercising which, in turn, enhances wellbeing and, by contrast, low wellbeing (e.g. depression) reduces exercising which further compromises wellbeing
Wiestler et al. 2019 Germany, cross-sectional, fair (6)	91; age > 18 years; 49 men (54%) and 42 women (46%), CD, UC	–	Weekly PA level assessed through accelerometer	Inflammatory Bowel Disease Questionnaire (IBDQ)	–	The IBDQ was significantly correlated with the duration of strenuous PA per day ($p=0.029178$)

CD, Crohn's disease; *UC*, ulcerative cholitis; *IBD*, inflammatory bowel disease; *PA*, physical activity; *MVPA*, moderate-vigorous physical activity; *LTPA*, leisure-time physical activity; *MET*, metabolic equivalent of task; *HRQoL*, health-related quality of life; *BMI*, body mass index

association between PA and UC and an inverse association with CD (Furuya et al. 2022).

In this respect, it is well demonstrated that regular PA is a protective factor for several noncommunicable diseases (NCDs) such as cardiovascular diseases, diabetes and several cancers (Anderson and Durstine 2019). With regard to the IBDs, it should be considered that PA can influence several features of the immune system and the development of autoimmune diseases (Sharif et al. 2018). Indeed, it has been proved that the lack of PA can cause an altered Th1/Th2 balance. Th1 and Th2 influence, respectively, the secretion of pro-inflammatory and anti-inflammatory cytokines; thus, the shift of T1/T2 cells ratio determines and alteration of the balance between pro-inflammatory and anti-inflammatory mechanisms, responsible for the immune responses developed by the patients (Steensberg et al. 2001; Huang and Chen 2016). This explanation is supported by the evidence that the incidence of other autoimmune diseases, such as rheumatoid arthritis, multiple sclerosis or psoriasis is higher in participants less engaged in PA (Lautenschlager et al. 2023; Sharif et al. 2018). In addition to the effects associated directly with PA on the immune system, lack of PA is related to a major threat of overweight and obesity, known risk factors for chronic low-grade inflammation (Winer et al. 2016) and for the development of IBDs (Lautenschlager et al. 2023; Kugathasan et al. 2007).

As for the role of PA on IBDs management, seven studies (Holik et al. 2019; Ng et al. 2007; Lamers et al. 2021a, b; Tew et al. 2016; Jones et al. 2015; Watanabe et al. 2021) reported positive effects of PA/exercise on disease symptoms and activity, while three (Elsenbruch et al. 2005; D'Incà et al. 1999; Henderson et al. 2022) did not observe significant improvements with respect to controls and one (Lamers et al. 2021a, b) showed negative effects. These contrasting results can be due to the type and the intensity level of PA practiced by the studied populations; additionally, the different periods of life in which PA was carried out, the characteristics of the population included in the study, the stage of the disease and the presence of complications, as well as the methodological quality of the study, can also affect the evidence of an association between PA and the development and/or the course of IBDs.

Another important finding of the present systematic review is related to the preventive role of PA towards the complications associated with IBDs, mainly bone loss, osteoporosis and metabolic bone diseases (Robinson et al. 1998; Lee et al. 2005). The effect of PA on bone health can be explained considering that exercise, increasing muscle mass, can determine osteogenic effects through muscle pull on the bones, whereas activities promoting high-impact weight-bearing such as running or step aerobics can produce positive changes in bone strength and can reduce fracture risk (Lee et al. 2005). In addition, PA can aid in

the prevention of cardiovascular disease outcomes in IBDs (Jaiswal et al. 2023). Indeed, even if the potential biological pathways of PA effects on cardiovascular diseases still need to be clarified, the inverse relationship between PA and cardiovascular diseases has been amply demonstrated (Zhuo et al. 2021; Carnethon 2009) and the mechanisms involved seem to be related to a healthier metabolic milieu with a reduction of systemic chronic inflammation and to antiatherogenic effects, myocardial regeneration and cardioprotection (Valenzuela et al. 2023).

Moreover, with the exception of the study by Lamers et al., all the studies included in this review which examined the possible consequences of PA on IBD comorbidities or mental health reported positive effects (Cronin et al. 2019; Elsenbruch et al. 2005; Jones et al. 2020; Lamers et al. 2022; Robinson et al. 1998; Lamers et al. 2021a, b; Ratajczak-Pawłowska et al. 2023; Tew et al. 2016; Lo et al. 2021; Mack et al. 2011). This result is in line with the scientific evidence reporting that PA can contribute to decreasing the frequency of mental disorders, in particular depression and anxiety, by reducing health disparities and mental health symptoms (Schuch & Vancampfort 2021). Furthermore, nine of the selected studies investigated the effects of PA or exercise on patients' quality of life (Jones et al. 2020; Klare et al. 2015; Lamers et al. 2022; Ng et al. 2007; Watters et al. 2001; Lamers et al. 2021a, b; Wiestler et al. 2019; Taylor et al. 2018; Kim et al. 2021). With the exception of the findings of Lamers et al. (Lamers et al. 2021a, b), the other studies reported an improvement in quality of life among active patients affected by IBDs.

Notwithstanding the differences in the design of the studies and in the aspects examined, the majority of the articles highlighted the possible benefits that could derive from PA in patients with IBDs. However, the question of whether or not these patients are able to engage in PA must be considered. In fact, although data support the assumption that PA is feasible in IBDs patients (Klare et al. 2015; Lamers et al. 2021a, b), PA may not always be easy to practice due to abdominal pain (Coates et al. 2023). De Filippis et al. found that nearly 40% of the respondents felt that IBD limited their exercise for various reasons, most commonly fatigue, joint pain, embarrassment, weakness and abdominal pain, while some reported a subjective increase in symptoms immediately following exercise (De Filippis et al. 2016). These limitations may result in lower PA levels after the diagnosis of IBDs than before, with a reduction in the percentage of patients participating in sports activities at amateur, semi-professional and professional levels (Gatt et al. 2019; van Langenberg and Gibson 2010), including and most notably in relation to the stage of disease as assessed in some studies (Tew et al. 2016; Wiestler et al. 2019; Mack et al. 2011).

Some limitations should be considered when interpreting these results. First, the examined studies differed in design, type and level of PA/exercise, outcomes investigated and assessment methods, and this did not allow us to perform a meta-analysis of the results nor to obtain more consistent results. Moreover, it should be noted that the results were not controlled for possible confounding factors in all the selected studies, which contributed to their generally low quality. As mentioned earlier, the insufficient number of papers concerning the preventive aspect of PA does not allow us to state its effectiveness for public health purposes.

Conclusions

The results of the present systematic review suggest that PA could be considered a useful factor both for preventing and managing IBDs. In particular, the available literature shows that PA may represent a preventive factor towards the development of these diseases. In fact, even if the biological process is not yet elucidated, it seems that the lack of PA can determine a shift of the balance between pro-inflammatory and anti-inflammatory mechanisms responsible for the alteration of immune responses developed by the patients. In addition, evidence shows that in patients affected by IBDs, PA can prevent the complications such as bone loss, osteoporosis, metabolic bone diseases and cardiovascular diseases, and it can be used for managing associated comorbidities and mental disorders and for improving the patients' quality of life.

However, further research on this topic is needed to develop individualized and customized exercise plans according to individual risk and type of IBD.

Author contributions Conceptualization: Carmela Protano, Federica Valeriani and Francesca Gallè; literature search and data analysis: Veronica Volpini, Andrea De Giorgi, Elisa Mazzeo and Francesca Ubaldi; Writing—original draft preparation: Carmela Protano, Francesca Gallè, Veronica Volpini, Andrea De Giorgi, Elisa Mazzeo and Francesca Ubaldi; Writing—review and editing: Carmela Protano, Federica Valeriani and Francesca Gallè; Critical review: Vincenzo Romano Spica; Matteo Vitali.

Funding Open access funding provided by Università Parthenope di Napoli within the CRUI-CARE Agreement.

Data availability All the data are reported in the manuscript.

Declarations

Ethics approval Not applicable.

Informed consent Not applicable.

Conflicts of interest The authors declare that they have no conflicts of interest.

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