

World Journal of *Gastroenterology*

World J Gastroenterol 2023 October 14; 29(38): 5361-5434



MINIREVIEWS

- 5361 Intraductal papillary neoplasm of the bile duct: The new frontier of biliary pathology
Mocchegiani F, Vincenzi P, Conte G, Nicolini D, Rossi R, Cacciaguerra AB, Vivarelli M

ORIGINAL ARTICLE**Basic Study**

- 5374 Expression and functional study of cholecystokinin-A receptors on the interstitial Cajal-like cells of the guinea pig common bile duct
Xu D, Ma SL, Huang ML, Zhang H

Retrospective Study

- 5383 Impressive recompensation in transjugular intrahepatic portosystemic shunt-treated individuals with complications of decompensated cirrhosis based on Baveno VII criteria
Gao L, Li MB, Li JY, Liu Y, Ren C, Feng DP

Observational Study

- 5395 Hepatitis D virus dual-infection among Chinese hepatitis B patient related to hepatitis B surface antigen, hepatitis B virus DNA and age
Zi J, Li YH, Wang XM, Xu HQ, Liu WH, Cui JY, Niu JQ, Chi XM

SYSTEMATIC REVIEWS

- 5406 Scoping review on health-related physical fitness in patients with inflammatory bowel disease: Assessment, interventions, and future directions
Demers K, Bak MTJ, Bongers BC, de Vries AC, Jonkers DMAE, Pierik MJ, Stassen LPS

CASE REPORT

- 5428 Dose escalation of adalimumab as a strategy to overcome anti-drug antibodies: A case report of infantile-onset inflammatory bowel disease
Ancona S, Signa S, Longo C, Cangemi G, Carfora R, Drago E, La Rosa A, Crocco M, Chiaro A, Gandullia P, Arrigo S

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Emilio De Raffe, MD, PhD, Assistant Professor, Consultant Surgeon, Dipartimento Medico Chirurgico delle Malattie Digestive, Epatiche ed Endocrinometaboliche, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Via Albertoni 15, Bologna 40138, Italy.

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now abstracted and indexed in Science Citation Index Expanded (SCIE), MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJG* as 4.3; Quartile category: Q2. The *WJG*'s CiteScore for 2021 is 8.3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xu Guo*; Editorial Office Director: *Jia-Ru Fan*.

NAME OF JOURNAL

World Journal of Gastroenterology

ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE

October 1, 1995

FREQUENCY

Weekly

EDITORS-IN-CHIEF

Andrzej S Tarnawski

EXECUTIVE ASSOCIATE EDITORS-IN-CHIEF

Xian-Jun Yu (Pancreatic Oncology), Jian-Gao Fan (Chronic Liver Disease), Hou-Bao Liu (Biliary Tract Disease), Naohisa Yoshida (Gastrointestinal Endoscopy)

EDITORIAL BOARD MEMBERS

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

PUBLICATION DATE

October 14, 2023

COPYRIGHT

© 2023 Baishideng Publishing Group Inc

PUBLISHING PARTNER

Shanghai Pancreatic Cancer Institute and Pancreatic Cancer Institute, Fudan University
Biliary Tract Disease Institute, Fudan University

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/gerinfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/gerinfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

POLICY OF CO-AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/310>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/gerinfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

PUBLISHING PARTNER'S OFFICIAL WEBSITE

<https://www.shca.org.cn>
<https://www.zs-hospital.sh.cn>

Scoping review on health-related physical fitness in patients with inflammatory bowel disease: Assessment, interventions, and future directions

Karlijn Demers, Michiel T J Bak, Bart C Bongers, Annemarie C de Vries, Daisy M A E Jonkers, Marieke J Pierik, Laurents P S Stassen

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Shalaby MN, Egypt; Stogov MV, Russia

Received: July 28, 2023

Peer-review started: July 28, 2023

First decision: August 25, 2023

Revised: September 6, 2023

Accepted: September 12, 2023

Article in press: September 12, 2023

Published online: October 14, 2023



Karlijn Demers, Laurents P S Stassen, Department of Surgery, Maastricht University Medical Center+, Maastricht 6229 HX, Netherlands

Karlijn Demers, Marieke J Pierik, Department of Internal Medicine, Division of Gastroenterology-Hepatology, Maastricht University Medical Center+, Maastricht 6229 HX, Netherlands

Karlijn Demers, Daisy M A E Jonkers, Marieke J Pierik, Department of Internal Medicine, Division of Gastroenterology-Hepatology, School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht 6229 ER, Netherlands

Karlijn Demers, Bart C Bongers, Laurents P S Stassen, Department of Surgery, School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht 6229 ER, Netherlands

Michiel T J Bak, Annemarie C de Vries, Department of Gastroenterology and Hepatology, Erasmus University Medical Center Rotterdam, Rotterdam 3015 GD, Netherlands

Bart C Bongers, Department of Nutrition and Movement Sciences, School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht 6229 ER, Netherlands

Corresponding author: Karlijn Demers, MD, MSc, Department of Surgery, Maastricht University Medical Center+, Maastricht 6229 HX, Netherlands.
k.demers@maastrichtuniversity.nl

Abstract

BACKGROUND

Reaching the Selecting Therapeutic Targets in Inflammatory Bowel Disease-II (STRIDE-II) therapeutic targets for inflammatory bowel disease (IBD) requires an interdisciplinary approach. Lifestyle interventions focusing on enhancing and preserving health-related physical fitness (HRPF) may aid in improving subjective health, decreasing disability, or even controlling inflammation. However, ambiguity remains about the status and impact of HRPF (*i.e.* body composition, cardiorespiratory fitness, muscular strength, muscular endurance, and flexibility) in IBD patients, hindering the development of physical activity and physical exercise training guidelines.

AIM

To review HRPF components in IBD patients and the impact of physical activity and physical exercise training interventions on HRPF.

METHODS

A systematic search in multiple databases was conducted for original studies that included patients with IBD, assessed one or more HRPF components, and/or evaluated physical activity or physical exercise training interventions.

RESULTS

Sixty-eight articles were included. No study examined the complete concept of HRPF, and considerable heterogeneity existed in assessment methods, with frequent use of non-validated tests. According to studies that used gold standard tests, cardiorespiratory fitness seemed to be reduced, but findings on muscular strength and endurance were inconsistent. A limited number of studies that evaluated physical activity or physical exercise training interventions reported effects on HRPF, overall showing a positive impact.

CONCLUSION

We performed a scoping review using a systematic and iterative approach to identify and synthesize an emerging body of literature on health-related physical fitness in patients with IBD, highlighting several research gaps and opportunities for future research. Findings of this review revealed a gap in the literature regarding the accurate assessment of HRPF in patients with IBD and highlighted important methodological limitations of studies that evaluated physical activity or physical exercise training interventions. This scoping review is a step towards performing studies and systematic reviews in the future, which was not possible at present given the heterogeneity in endpoints and designs of the available studies on this topic. Future well-designed studies are required to determine the optimal training paradigm for improving HRPF in patients with IBD before guidelines can be developed and integrated into the therapeutic strategy.

Key Words: Inflammatory bowel disease; Physical fitness; Assessment; Intervention; Physical activity; Exercise

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Lifestyle interventions focusing on enhancing and preserving health-related physical fitness (HRPF) may aid in improving subjective health, decreasing disability, or even controlling inflammation in patients with inflammatory bowel disease (IBD). This scoping review encompassed a comprehensive exploration of the available literature on the assessment of HRPF components in patients with IBD, summarized the effects of physical activity and physical exercise training interventions on these components in this specific patient population, and provided valuable recommendations for future research directions.

Citation: Demers K, Bak MTJ, Bongers BC, de Vries AC, Jonkers DMAE, Pierik MJ, Stassen LPS. Scoping review on health-related physical fitness in patients with inflammatory bowel disease: Assessment, interventions, and future directions. *World J Gastroenterol* 2023; 29(38): 5406-5427

URL: <https://www.wjgnet.com/1007-9327/full/v29/i38/5406.htm>

DOI: <https://dx.doi.org/10.3748/wjg.v29.i38.5406>

INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory diseases of the gastrointestinal tract[1,2]. The disease course is characterized by recurrent episodes of mucosal inflammation. Besides a genetic predisposition, an altered immune response and intestinal microbiota perturbations as well as psychosocial and lifestyle factors underlie the recurrent inflammation of IBD. As a result, substantial variation exists between patients for disease course and treatment outcomes. Since the disease course is unfavorable for many patients and a significant proportion requires surgery to manage the disease or its complications[3], novel drugs have been introduced and tight control of mucosal inflammation has been added to the traditional treatment goal of steroid-free clinical remission[4,5]. In addition to intestinal symptoms caused by mucosal inflammation or intestinal complications, patients frequently experience impaired subjective well-being due to symptoms such as fatigue, or impaired social functioning or emotional health[6-8]. This often persists even in the absence of mucosal inflammation and contributes to a high physical and psychological disease burden with a significant impact on quality of life.

The treat-to-target strategy for IBD, according to the Selecting Therapeutic Targets in Inflammatory Bowel Disease-II (STRIDE-II) recommendations, aims for endoscopic healing, absence of disability, and optimal subjective health, and

warrants a multidisciplinary treatment approach[9]. Lifestyle interventions involving physical activity or physical exercise training to improve or preserve physical fitness might improve the outcome of IBD. In general, such interventions are key factors in health promotion and disease prevention programs[10,11]. Beneficial effects include a reduced risk of all-cause mortality, reduced risk of developing noncommunicable diseases (*e.g.* cardiovascular diseases, diabetes, cancer, neurodegenerative diseases) and postoperative complications, and better mental health and subjective well-being[12-16]. In addition, the anti-inflammatory benefits of regular physical activity and physical exercise training (*e.g.* the release of myokines, reduction in visceral fat, and subsequent decrease of adipokine release) are well documented [17,18].

The use of standardized nomenclature is necessary to understand and optimally target the concepts of physical fitness, physical activity, physical exercise training, and their interrelationships. Physical fitness can be considered an integrated measure of bodily functions involved in daily physical activity. The physical fitness components that have a relationship with health are referred to as health-related physical fitness (HRPF), which includes body composition, cardiorespiratory fitness, muscular strength, muscular endurance, and flexibility[19-21]. Physical activity and physical exercise training are often used interchangeably but are physiologically different, resulting in unique local and systemic responses[19,22-24]. While physical activity is defined as any bodily movement produced by skeletal muscles that requires energy expenditure, physical exercise training is considered a subcategory of physical activity that is planned, structured, and repetitive with the final or intermediate purpose of maintaining or improving one or more physical fitness components.

To date, the status of several components of HRPF and their impact on inflammation and subjective health in IBD is not clear, which hinders the development of (inter)national guidelines regarding physical activity and physical exercise training for this population. Due to a sedentary lifestyle in general, lack of physical activity as a consequence of illness as well as corticosteroid use is likely to cause patients with IBD to suffer from an impaired HRPF[25-27]. Furthermore, malnutrition and the direct effect of proinflammatory cytokines can negatively influence muscle quality and function[28, 29]. The need for such guidelines to improve HRPF is further highlighted by a potential link between impaired components of HRPF in patients with IBD and subjective well-being in terms of fatigue and health-related quality of life [30,31].

Accurate assessment of HRPF components is necessary to obtain more insight into the state of HRPF in patients with IBD as well as to clearly define endpoints in intervention studies to determine whether physical activity or physical exercise training can improve HRPF components in these patients. Therefore, the first objective of this scoping review was to provide an overview of studies on the assessment of HRPF components in patients with IBD using a systematic and iterative approach. As the literature on body composition in patients with IBD was recently reviewed systematically [32-34], the current review focused on the remaining components of HRPF (*i.e.* cardiorespiratory fitness, muscular strength, muscular endurance, and flexibility). The second objective was to review the effects of physical activity and physical exercise training interventions on HRPF in patients with IBD. The ultimate goal of this scoping review was to identify and synthesize an emerging body of literature on health-related physical fitness in patients with IBD, highlighting several research gaps and opportunities for future research.

MATERIALS AND METHODS

This scoping review was performed and reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews guideline[35].

Search strategy

A comprehensive search was performed in MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, Web of Science, and PEDro for articles published through November 5, 2022. The literature search was performed in collaboration with the medical librarian of Maastricht University. An overview of the search strategy is presented in [Supplementary material](#).

Study selection

Eligible studies were those that fulfilled the following criteria: (1) Inclusion of children and/or adults diagnosed with IBD; and (2) Addressing at least one of the following two elements: Assessing one or more of the four HRPF components (*i.e.* cardiorespiratory fitness, muscular strength, muscular endurance, and flexibility); and/or Assessing the effects of any frequency, intensity, time, and type of physical activity or physical exercise training interventions.

All original studies performed in humans from any geographical setting were eligible for inclusion. Letters, case reports, study protocols, animal studies, reviews, (conference) abstracts, and studies written in languages other than Dutch or English were excluded. In cases where the full-text article was not available, the corresponding authors were contacted. After the removal of duplicates, all unique studies were screened by title and abstract based on the predefined inclusion criteria by two reviewers (Demers K and Bak MTJ). Subsequently, these reviewers independently evaluated the full texts of all potentially relevant records to determine eligibility. Any disagreements between the reviewers were solved through discussion until a consensus was reached. Reasons for exclusion at this stage were documented. Furthermore, a snowball method was administered for the included studies to identify other relevant studies that were not identified within the search strategy.

Data extraction

The two independent reviewers extracted data in duplicate. For each study, the following data were collected (if

applicable) using a standardized registration form: First author; year of publication; study design; study location; population (number of participants, sex, age, disease entity, disease duration, disease location, disease activity, IBD medication, previous IBD-related surgery); control group or reference values; assessment methods (*e.g.* tests, test protocols) and corresponding outcomes; and physical activity intervention or physical exercise training intervention and comparator intervention (*e.g.* frequency, intensity, time, type, compliance, adverse events) and the reported effects.

Data synthesis

First, an overview was provided of the assessment methods used to assess HRPF in the included studies, classified according to the four different components of HRPF. A distinction was made between gold standard tests (*i.e.* laboratory-based tests) and practical field tests. Then, studies that used gold standard tests to assess HRPF were selected and considered key publications and used to report HRPF outcomes of patients with IBD in comparison with healthy control subjects or reference values, if applicable. Finally, the effects of physical activity interventions and physical exercise training interventions on HRPF components were reviewed.

Gold standard tests

The objective assessment of maximal oxygen uptake (VO_{2max}) or oxygen uptake at peak exercise (VO_{2peak}) using the cardiopulmonary exercise test (CPET), at which the patient performs a maximal effort, is considered the gold standard measurement method for assessing cardiorespiratory fitness[11,36]. If no true VO_{2max} (*i.e.* leveling-off of oxygen uptake despite further increases in exercise intensity) is achieved, the VO_{2peak} is often recorded. In that case, a respiratory exchange ratio at peak exercise, which represents the ratio of carbon dioxide production and oxygen uptake, ≥ 1.10 is indicative of a maximal or near-maximal effort. Isokinetic (*i.e.* dynamic) and isometric (*i.e.* static) peak torque measurements performed on an electromechanical dynamometer (*e.g.* Cybex, Biodex) are considered the most accurate and the gold standard tests for muscular strength and endurance examination[37-39]. The assessment of a single joint-specific range of motion using goniometers or fleximeters is considered the gold standard test for testing flexibility. However, publications describing compound flexibility measures, which involve the assessment of more than one joint, were also considered key publications[40,41].

RESULTS

Search results

The search yielded 7323 records. After removing duplicates, screening for eligibility, and snowballing, 68 studies were included in the review (Figure 1) with 4412 unique patients. The median sample size of the included studies was 42 [interquartile range (IQR): 24-77]. In total, 53 studies were conducted in adults and 15 studies in children or adolescents. Most studies ($n = 32$) evaluated patients with CD, followed by studies that included both patients with CD and UC ($n = 30$) and studies that included only patients with UC ($n = 6$). In total, 59 studies (86.8%) reported on disease activity. Although definitions varied across studies, 2410 unique patients were considered to be in remission, and 1147 patients were considered to have active disease, according to 48 studies that reported the number of patients in each group.

In total, 56 studies assessed one or more of the four HRPF components (*i.e.* cardiorespiratory fitness, muscular strength, muscular endurance, and flexibility) in a total number of 3949 unique patients with IBD. Physical activity or physical exercise interventions were evaluated in 22 studies, including 740 unique patients with IBD. Only 10 of these 22 studies (45.5%) reported the effects of the intervention on one or more HRPF component. The sample size distribution of the studies included is shown in Figure 2. The median sample size of the studies that assessed HRPF components in patients with IBD (*i.e.* assessment studies) was 42 (IQR: 24-75). The median sample size of the studies examining physical activity or physical exercise training interventions in patients with IBD (*i.e.* intervention studies) was 34 (IQR: 21-58).

Assessment of HRPF

Of all studies that assessed HRPF ($n = 56$), none assessed all components of HRPF within its IBD study population, and no single study assessed flexibility. Most studies ($n = 42$) examined only one component, including cardiorespiratory fitness ($n = 13$), muscular strength ($n = 28$), and muscular endurance ($n = 1$). Two or more components were assessed in 14 studies. Of these, 13 studies assessed two components of HRPF [muscular strength and muscular endurance ($n = 8$) and cardiorespiratory fitness and muscular strength ($n = 5$)]. One study assessed three components of HRPF (cardiorespiratory fitness, muscular strength, and muscular endurance). In total, cardiorespiratory fitness was assessed in 19 studies, muscular strength in 42 studies, and muscular endurance in 10 studies.

Methods used to assess HRPF

Table 1 shows an overview of the assessment methods used to assess HRPF components in patients with IBD, distinguishing between gold standard tests and practical field tests. Significant heterogeneity was observed in the assessment methodologies applied for the various components of HRPF, with frequent use of non-validated practical field tests such as a cycle ergometer test or a 6-min walk test for cardiorespiratory fitness, handgrip strength or jumping mechanography for muscular strength, and handgrip endurance or the chair-stand-test for muscular endurance. Overall, gold standard tests were used in 19 studies (33.9%). Cardiorespiratory fitness was assessed by CPET performance in eight out of nineteen studies (42.1%). However, only seven studies reported the gold standard VO_{2max}/VO_{2peak} . Muscular strength was examined by the gold standard peak torque measurement performed on a dynamometer in 12 out of 42 studies

Table 1 Overview of methods used to assess health-related physical fitness components in patients with inflammatory bowel disease

Health-related physical fitness component	Gold standard or practical field test	Assessment method	Outcome	Number of studies
Cardiorespiratory fitness	Gold standard test	CPET on a cycle ergometer	VO ₂ max/VO ₂ peak	7[28,43-45,57,59,61]
			WRpeak	1[71]
	Practical field test	Incremental cycle ergometer test	Submaximal heart rate	2[42,72]
			WRpeak	1[73]
		6-min walk test	Distance	2[28,53]
			Speed	1[74]
		Incremental shuttle walk test	Distance	2[75,76]
		CAFT step test	Estimated VO ₂ max	1[60]
		Bruce treadmill stress test	Duration of exercise and heart rate recovery index	1[77]
		Rockport 1-mile walk test	Estimated VO ₂ max	1[56]
Duke activity status index	Points	1[78]		
Muscular strength	Gold standard test	Isometric dynamometry	Peak torque	7[30,42,46-49,72]
		Isokinetic dynamometry	Peak torque	5[28,50-52,79]
	Practical field test	Handgrip strength	Peak torque	31[42,49,51,55,58,72,74-76,80-101]
		Jumping mechanography	P _{max} , F _{max} , jump height	4[99,102-104]
		Finger pinching strength	Peak torque	2[42,72]
		Isometric leg-press strength	Peak torque	1[98]
		Isometric HHD	Peak torque	1[58]
		Respiratory muscle strength	MIP, MEP	1[76]
Peak expiratory flow	1[93]			
Muscular endurance	Gold standard test	Isometric dynamometry	Slope of median muscle activation frequency	1[48]
			Decrement in peak torque	1[30]
	Practical field test	Handgrip endurance	Decrement in peak torque	2[86,87]
			Mean peak torque	1[98]
		Chair-stand test/sit-to-stand test	Repetitions	1[51]
			Time	4[49,51,55,74,98]
		3-meter walk test	Speed	1[55]
		Leg-press endurance	Mean force	1[98]
		Arm-curl test	Repetitions	1[51]
		Sit-ups	Repetitions	1[54]
		Back extensions	Repetitions	1[54]
		Push-ups	Repetitions	1[54]
		Squats	Repetitions	1[54]
Plank position	Time	1[54]		
Flexibility	N/A	N/A	N/A	0

CAFT: Canadian aerobic fitness test; CPET: Cardiopulmonary exercise testing; F_{max}: Maximum force; HHD: Hand-held dynamometry; MEP: Maximal expiratory pressure; MIP: Maximal inspiratory pressure; N/A: Not available; P_{max}: Maximum power; VO₂max: Maximal oxygen uptake; VO₂peak: Oxygen uptake at peak exercise; WRpeak: Work rate at peak exercise.

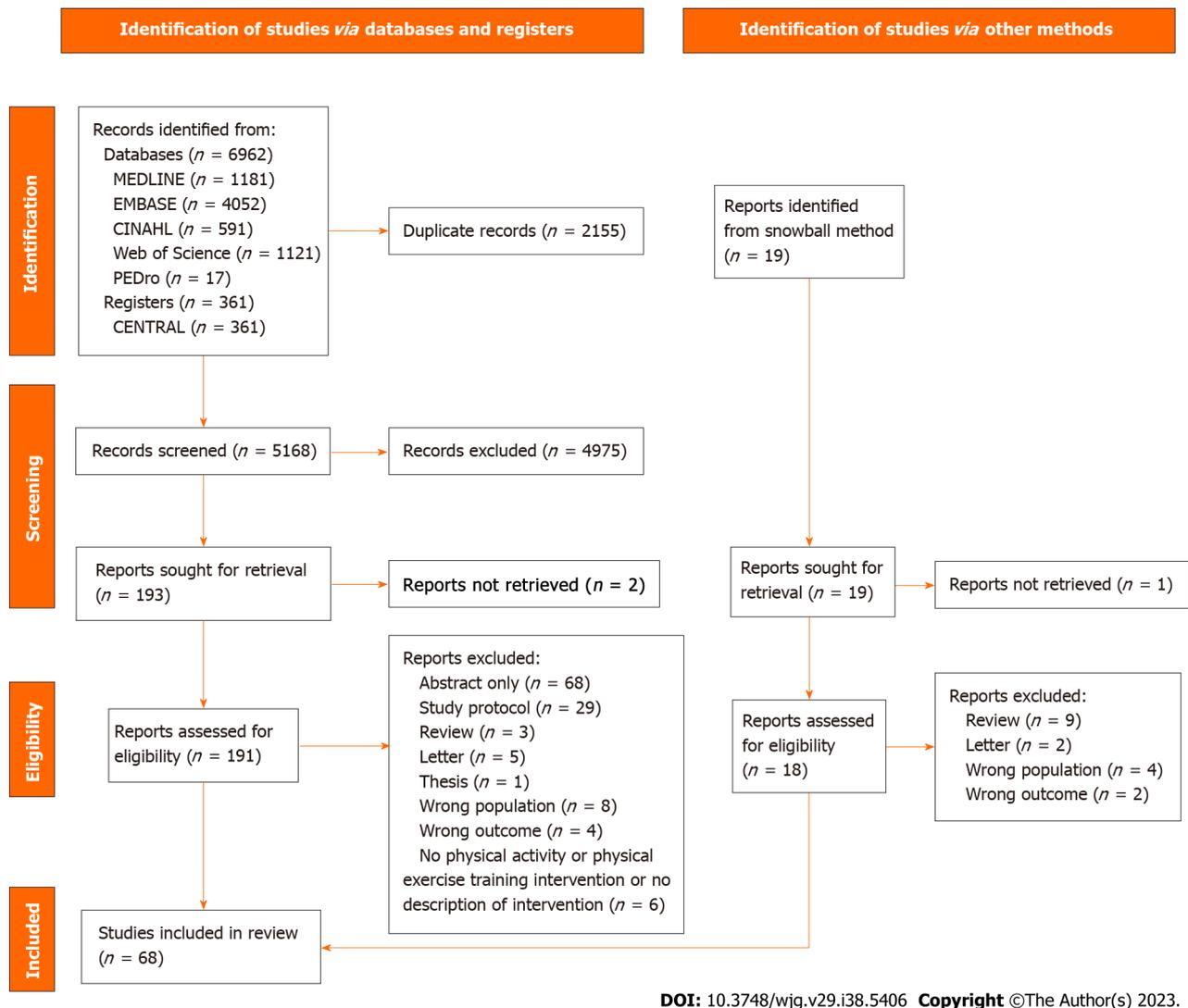


Figure 1 Preferred reporting items for systematic reviews and meta-analyses flow diagram of the literature search and selection process.

(28.6%). However, in one study, muscular strength was reported as a composite outcome combining dynamometry peak torque and practical field test results[42]. Muscular endurance was assessed by the gold standard method in two out of ten studies (20.0%).

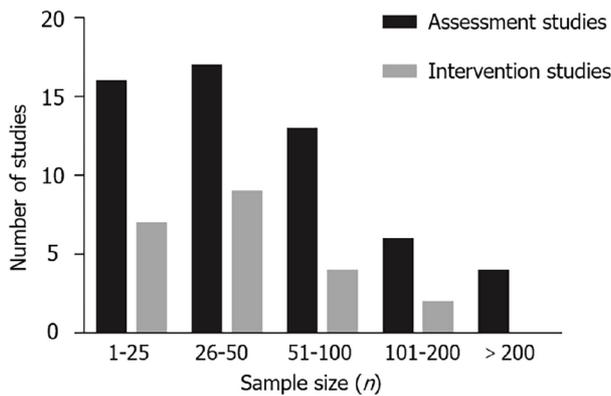
HRPF outcomes

Comprehensive descriptions and main outcomes of the included studies assessing cardiorespiratory fitness, muscular strength, and muscular endurance with the gold standard as well as practical field tests are presented in [Supplementary Tables 1-3](#).

Cardiorespiratory fitness: The seven studies that assessed cardiorespiratory fitness by $VO_2\text{max}/VO_2\text{peak}$ measurement during CPET performance are summarized in [Table 2](#). A true $VO_2\text{max}$ was reported in one study, while six studies reported $VO_2\text{peak}$. However, the achieved respiratory exchange ratio at peak exercise was only reported in two studies, indicating maximal achieved performance at the group level in both studies[28,43]. Four studies compared the cardiorespiratory fitness of patients with IBD to a healthy control group or reference values. All studies showed a diminished VO_2 peak in children or adolescents with CD and UC in remission or with mildly active disease[43,44], in adult patients with CD and UC in remission[28], and in patients with CD and UC awaiting colorectal surgery[45].

Muscular strength: The 11 studies that assessed muscular strength by isokinetic or isometric peak torque measurements performed on a dynamometer are listed in [Table 3](#). Nine studies compared the muscular strength of patients with IBD to a healthy control group or reference values, with inconsistent results. However, it is crucial to note that testing methodologies and population characteristics varied throughout these studies, making comparison challenging. Two studies assessed muscular strength in pediatric and adolescent patients with CD, and seven evaluated adult patients with CD and/or UC.

Regarding pediatric and adolescent patients, reduced strength of the ankle dorsiflexion muscles was found in a prospective cohort of CD patients with low bone density in remission or with active disease and in a cross-sectional



DOI: 10.3748/wjg.v29.i38.5406 Copyright ©The Author(s) 2023.

Figure 2 Distribution of sample sizes of the studies that assessed health-related physical fitness components ($n = 56$) and that investigated physical activity or physical exercise training interventions ($n = 22$).

cohort of patients with new-onset CD experiencing moderate-to-severe disease activity[46,47]. However, reduced strength of the ankle dorsiflexion muscles was not observed in patients with new-onset CD experiencing mild disease activity in the cross-sectional cohort[47].

Of the seven studies that assessed muscular strength in adult patients with CD and/or UC, three studies showed reduced muscular strength of the lower limbs, two studies found both decreased and equivalent strength with regard to different muscle groups, and two studies found an equal strength of the lower limbs as compared to healthy control groups. The three studies that showed reduced muscular strength of the lower limbs were conducted in CD patients in remission with prior small bowel resection and musculoskeletal pain or weakness[48], in a cohort of fatigued and non-fatigued CD and UC patients in remission[28], and in sedentary female patients with UC and varying disease activity severity[49]. Both a decreased and equivalent strength in different muscle groups was demonstrated by Geerling *et al*[50] and Jones *et al*[51]. Geerling *et al*[50] showed a diminished strength of the knee flexor muscles but not the knee extensor muscles in a cohort of patients with longstanding CD, and Jones *et al*[51] demonstrated a reduced strength of the knee extensor muscles but no difference in elbow flexor strength in a group of CD patients in remission and with active disease. An equivalent strength of the lower limb muscles compared to healthy control groups was observed in recently diagnosed patients with CD and UC and in patients with CD in remission or with active disease[30,52].

Muscular endurance: Two studies assessed muscular endurance of the lower limbs by isometric endurance measurements on a dynamometer in patients with CD as compared to healthy control groups (Table 3), also with conflicting results. Salacinski *et al*[48] showed significantly better endurance of the rectus femoris muscle and an equivalent endurance of the vastus lateralis muscle in patients with CD in remission with prior small bowel resection and musculoskeletal pain or weakness as compared to healthy control subjects. van Langenberg *et al*[30] demonstrated worse endurance of the knee extensor muscles in patients with CD in remission or with active disease in comparison with a healthy control group.

Physical activity and physical exercise training interventions

Different types of physical activity and physical exercise training interventions have been published (*e.g.*, walking, running, cycling, resistance exercises, video gameplay, yoga) ranging from low-intensity to high-intensity. Detailed tables with the study characteristics and main findings of all interventions are presented in Supplementary Table 4. In total, 10 studies investigated the effect of a physical activity or physical exercise training intervention on one or more HRPF components (Table 4), of which the majority used non-validated practical field tests. The remaining studies examined other outcomes, such as feasibility, acceptability, or safety of the interventions as well as their effects on other health outcomes concerning disease activity and subjective well-being (*e.g.* quality of life, fatigue, depression, anxiety, sleep, stress).

Two studies focused on pediatric patients with IBD, and both demonstrated beneficial effects of their intervention on HRPF components[53,54]. Mählmann *et al*[53] demonstrated that an 8-wk aerobic exercise training intervention with active video gameplay increased the distance reached on the 6-min walk test, a practical field test for assessing cardiorespiratory fitness, in children with IBD in remission and with active disease. The effects of a home-based resistance exercise training program for 6 mo on HRPF components in children and adolescents with IBD in remission were investigated by Trivić *et al*[54]. Lean body mass significantly improved, whereas lean body mass age-based and sex-based z-scores did not. Furthermore, they found a significant improvement in muscular endurance as measured by using various practical field tests.

Eight studies examined the effect of a physical activity or physical exercise training intervention on HRPF components in adult patients with IBD – three were randomized controlled trials[51,55,56], four were pilot studies[57-60], and one involved a secondary analysis[61]. Seven studies included patients in remission or with mildly active disease activity, and one study included patients in remission as well as patients with mild to severely active disease. Two pilot studies and a secondary analysis investigated the effects of aerobic exercise and showed favorable effects on cardiorespiratory fitness

Table 2 Description and main findings of studies examining cardiorespiratory fitness by objective maximal oxygen uptake or oxygen uptake at peak exercise assessment in patients with inflammatory bowel disease

Ref.	Study design, country	Sample size (n)	Sample features	CD, UC, IBD-U (n)	Female sex, (%)	Age in yr, mean (SD)	Disease activity	Control group	Test protocol	Main findings, mean (SD), or median (IQR)
Ploeger <i>et al</i> [43], 2011	Cross-sectional study, Canada	29	N/A	19, 0	41%	13.7 (2.3)	Remission (n = N/A) or mildly active disease (n = N/A)	Healthy age-matched and sex-matched youth	Incremental ramp cycle ergometer test: Height-based increase of work rate every 2 min until exhaustion (pedaling frequency < 50 rpm)	VO ₂ peak: CD, 34.9 (6.5) mL/kg/min; UC, 37.8 (7.7) mL/kg/min; Total, 36.0 (7.0) mL/kg/min; VO ₂ peak CD, UC, total < VO ₂ peak ref (P < 0.05, P < 0.001)
Nguyen <i>et al</i> [44], 2013	Cross-sectional study, Canada	7	N/A	7, 0	N/A	15.2 (2.3)	Remission (n = 7)	Healthy age-matched and sex-matched CG (n = 7)	Incremental ramp cycle ergometer test: Height-based increase of work rate every 2 min until exhaustion (pedaling frequency < 50 rpm)	VO ₂ peak: CD, 43.1 (6.5) mL/kg/min; CG, 53.5 (4.6) mL/kg/min; VO ₂ peak CD < VO ₂ peak CG (P < 0.01)
Otto <i>et al</i> [45], 2012	Retrospective study, United Kingdom	100	Patients awaiting colorectal surgery	54, 46, 0	N/A	41.1 (14.9)	Active disease requiring surgery (n = 100)	Reference values[105]	Incremental ramp cycle ergometer test (8-12 min): Work rate increments based on prediction quotation and PA until exhaustion (pedaling frequency < 40 rpm)	VO ₂ peak: CD, 20.0 (7.9) mL/kg/min; UC, 21.9 (7.1) mL/kg/min; Total, 20.9 (7.6) mL/kg/min; VO ₂ peak total; VO ₂ peak ref (P < 0.0001)
Vogelaar <i>et al</i> [28], 2015	Cross-sectional study, The Netherlands	20	With fatigue (n = 10), without fatigue (n = 10)	15, 5, 0	50%	37.3 (11.4)	Remission (n = 20)	Reference values[106]	Incremental ramp cycle ergometer test (8-12 min): Work rate starting at 20 W, which increased by 15-20 W/min until exhaustion (pedaling frequency < 60 rpm)	VO ₂ peak: IBD with fatigue, 1.99 (0.44) L/min; IBD without fatigue, 2.43 (0.75) L/min; VO ₂ peak IBD < VO ₂ peak ref (P = N/A)
Tew <i>et al</i> [59], 2019	Pilot RCT, United Kingdom	36	N/A	36, 0	53%	36.9 (11.2)	Remission (n = 32) or mildly active disease (n = 4)	N/A	Incremental ramp cycle ergometer test: Work rate starting at 0 W, which increased by 15-20 W/min until exhaustion (pedaling frequency < 60 rpm)[107]	VO ₂ peak ¹ : CD, 28.2 (8.6) mL/kg/min
Bottoms <i>et al</i> [61], 2019	Secondary analysis of Tew <i>et al</i> [59], United Kingdom	25	HIIT group (n = 12), MICT group (n = 13)	25, 0	60%	N/A for total sample	Remission (n = 32) or mildly active disease (n = 4)	N/A	Incremental ramp cycle ergometer test: Work rate starting at 0 W, which increased by 15-20 W/min until exhaustion (pedaling frequency < 60 rpm)[107]	VO ₂ peak ¹ : N/A for total sample; CD HIIT group, 27.3 (7.7) mL/kg/min; CD MICT group, 28.7 (8.6) mL/kg/min
van Erp <i>et al</i> [57], 2021	Pilot study, The Netherlands	25	With severe fatigue	21, 3, 1	40%	45 (2.6)	Remission (n = 25)	N/A	Incremental ramp cycle ergometer test: Protocol N/A	VO ₂ max ¹ : IBD, 28 (25-31) mL/kg/min

¹Baseline values are shown.

CD: Crohn's disease; CG: Control group; HIIT: High-intensity interval training; IBD: Inflammatory bowel disease; IBD-U: Inflammatory bowel disease unclassified; IQR: Interquartile range; MICT: Moderate-intensity continuous training; N/A: Not available; PA: Physical activity; RCT: Randomized controlled trial; ref: Reference; SD: Standard deviation; UC: Ulcerative colitis; VO₂max: Maximal oxygen uptake; VO₂peak: Oxygen uptake at peak exercise.

Table 3 Description and main findings of studies examining muscular strength and muscular endurance by isokinetic or isometric strength or endurance assessment on a dynamometer in patients with inflammatory bowel disease

Ref.	Study design, country	Sample size (n)	Sample features	CD, UC (n)	Female sex, (%)	Age in yr, mean (SD), mean (95%CI), or median (IQR)	Disease activity	Control group	Test protocol	Main findings, mean (SD), mean (95%CI), or median (IQR)
Lee <i>et al</i> [47], 2015	Cross-sectional study, United States	64	Recently diagnosed	64, 0	41%	12.8 (2.7)	Remission to mild active disease (n = 26), moderate-to-severe active disease (n = 38)	Healthy subjects (n = 264)	Isometric muscular strength dynamometry (Biodex): AD peak torque (20° plantar flexion)	AD peak torque: CD, 14.7 (10.1-18.8) ft/lbs; CG, 17.9 (11.2-24.8) ft/lbs; AD peak torque CD (remission-mild activity) = AD peak torque CG (P = 0.72); AD peak torque CD (moderate-to-severe activity) < AD peak torque CG (P = 0.05)
Lee <i>et al</i> [46], 2018	Prospective study, United States	138	With low bone density	138, 0	52%	14.2 (2.8)	Remission (n = 85), or mild (n = 46), or moderate-to-severe (n = 7) active disease	Healthy subjects (n = 264)	Isometric muscular strength dynamometry (Biodex): AD peak torque (20° plantar flexion)	AD peak torque Z-score ¹ (relative to age, sex, race, adjusted for tibia length): CD, -0.43 (0.90); AD peak torque CD < AD peak torque ref (P < 0.0001)
Geerling <i>et al</i> [50], 1998	Cross-sectional study, The Netherlands	32	With longstanding disease	32, 0	56%	40.0 (34.3-54.0)	Remission (n = 17) or active disease (n = 15)	Healthy age-matched and sex-matched CG (n = 32)	Isokinetic muscular strength dynamometry (Cybex II): KE and KF peak torque (60°/s, 180°/s)	KE peak torque: CD 60°/s, 123.1 (27.4) Nm; CD 180°/s, 81.5 (18.5) Nm; CG 60°/s, 136.5 (53.8) Nm; CG 180°/s, 88.7 (39.7) Nm; KE peak torque CD = KE peak torque CG (P = N/A); KF peak torque: CD 60°/s, 71.6 (22.3) Nm; CD 180°/s, 45.6 (15.2) Nm; CG 60°/s, 87.6 (33.4) Nm; CG 180°/s, 59.3 (31.9) Nm; KF peak torque CD (60°, 180°/s) < KF peak torque CG (P < 0.02, P < 0.05)
Geerling <i>et al</i> [52], 2000	Cross-sectional study, The Netherlands	69	Recently diagnosed	23, 46	52%	35.4 (13.6)	Remission (n = 61) or active disease (n = 8)	Healthy age-matched and sex-matched CG (n = 69)	Isokinetic muscular strength dynamometry (Cybex II): KE and KF peak torque (60°/s, 180°/s)	KE peak torque: N/A for total sample; CD 60°/s, 127.5 (33.4) Nm; CD 180°/s, 81.5 (25.7) Nm; CG for CD 60°/s, 142.4 (33.2) Nm; CG for CD 180°/s, 93.2 (37.2) Nm; UC 60°/s, 148.8 (44.6)

										Nm; UC 180°/s, 96.1 (30.7) Nm; CG for UC 60°/s, 155.7 (50.0) Nm; CG for UC 180°/s, 100.5 (38.4) Nm; KE peak torque CD and UC = KE peak torque CG (<i>P</i> = N/A); KF peak torque: N/A for total sample; CD 60°/s, 74.9 (23.5) Nm; CD 180°/s, 46.8 (25.3) Nm; CG for CD 60°/s, 86.8 (19.8) Nm; CG for CD 180°/s, 57.8 (22.0) Nm; UC 60°/s, 89.7 (31.9) Nm; UC 180°/s, 58.6 (21.3) Nm; CG for UC 60°/s, 98.5 (37.3) Nm; CG for UC 180°/s, 64.8 (30.4) Nm; KF peak torque CD and UC = KF peak torque CG (<i>P</i> = N/A)
Jensen <i>et al</i> [72], 2002	Follow-up study of Kissmeyer-Nielsen <i>et al</i> [42], Denmark	20	Patients who accepted follow-up 4-6 yr after J-pouch surgery	0, 20	60%	38 (9)	N/A	N/A	Isometric muscular strength dynamometry (Metitur): KE peak torque (60° knee flexion), AF peak torque (90° elbow flexion)	KE peak torque: UC preoperative, 475 (187) N; UC 4-6 yr postoperative, 532 (179) N (<i>P</i> = 0.080); AF peak torque: UC preoperative, 258 (93) N; UC 4-6 yr postoperative, 275 (83) N (<i>P</i> = 0.017)
Salacinski <i>et al</i> [48], 2013	Cross-sectional study, United States	19	≥ 1 small bowel resection and idiopathic musculoskeletal pain or weakness	19, 0	53%	44.2 (10.3)	Remission (<i>n</i> = 19)	Healthy age-matched and sex-matched CG (<i>n</i> = 19)	Isometric muscular strength dynamometry (customized): KE and KF peak torque (45° knee flexion)	KE peak torque/KE peak torque normalized to BW: CD, 75.2 (45.4) Nm/kg; CG, 105.6 (40.7) Nm/0.07 (0.03) Nm/kg; KE peak torque CD < KE peak torque CG (<i>P</i> = 0.013, normalized to BW <i>P</i> = 0.039); KF peak torque/KF peak torque normalized to BW: CD, 27.2 (10.7) Nm/0.02 (0.01) Nm/kg, CG, 53.7 (27.3) Nm/0.09 (0.02) Nm/kg; KF peak torque CD < KF peak torque CG (<i>P</i> = 0.001, normalized to BW <i>P</i> = 0.022)
								Isometric muscular endurance dynamometry (customized): Slope of median VL and RF muscle activation frequency measured with EMG during 60-s submaximal (60% of maximum) contraction (45° knee flexion)	RF fatigue rate: CD, -0.069 (0.06) Hz/s; CG, -0.142 (0.09) Hz/s; RF fatigue rate CD < RF fatigue rate CG (<i>P</i> = 0.015); VL fatigue rate: CD, -0.028 (0.042) Hz/s; CG, -0.027 (0.085) Hz/s; VL fatigue rate CD = VL fatigue rate CG (<i>P</i> = 0.969)	

van Langenberg <i>et al</i> [30], 2014	Cross-sectional study, Australia	27	N/A	27, 0	56%	43 (38, 48)	Remission (<i>n</i> = 19) or active disease (<i>n</i> = 8)	Healthy age-matched and sex-matched CG (<i>n</i> = 22)	Isometric muscular strength dynamometry (Biodex): KE peak torque (60° knee flexion)	KE peak torque: CD 60°, 148.8 (130, 168) Nm; CG 60°, 133.6 (111, 156) Nm; KE peak torque CD = KE peak torque CG (<i>P</i> = 0.29)
									Isometric muscular endurance dynamometry (Biodex): Fatigue rate as decrement of KE peak torque from maximal peak torque (repetition 2 or 3) to peak torque at the end of 30 maximal contractions (at 60° knee flexion)	KE fatigue rate: CD, -5.2 (-8.2, -2.2) Nm/min; CG, -1.3 (-3.9, 1.4) Nm/min; KE fatigue rate CD > KE fatigue rate CG (<i>P</i> = 0.047)
Zaltman <i>et al</i> [49], 2014	Case-control study, Brazil	23	Sedentary	0, 23	100%	43.9 (10.0)	Remission (<i>n</i> = 8), mild (<i>n</i> = 9), or moderate (<i>n</i> = 5), or severe (<i>n</i> = 1) active disease	Healthy age-matched, sex-matched, and BMI-matched CG (<i>n</i> = 23)	Isometric muscular strength dynamometry (IsoTeste): KE peak torque (angle N/A)	KE peak torque: UC, 38.6 (4.4) Kgf; CG, 41.0 (1.1) Kgf; KE peak torque UC < KE peak torque CG (<i>P</i> = 0.012)
Subramaniam <i>et al</i> [79], 2015	Prospective study, Australia	19	Starting with IFX	19, 0	42%	33.2 (10.7)	Active disease (<i>n</i> = 19)	N/A	Isokinetic muscular strength dynamometry (Cybex/HUMAC Norm): KE peak torque (30°/s, 60°/s, 90°/s)	KE peak torque ¹ : CD 30°/s left leg, 166.5 (93.4) Nm, right leg 184.8 (96.6) Nm; CD 60°/s left leg, 172.8 (103.5) Nm, right leg 183.5 (116.4) Nm; CD 90°/s left leg, 128.5 (55.9) Nm, right leg 139.4 (54.4) Nm
Vogelaar <i>et al</i> [28], 2015	Cross-sectional study, The Netherlands	20	With fatigue (<i>n</i> = 10), without fatigue (<i>n</i> = 10)	15, 5	50%	37.3 (11.4)	Remission	Reference values	Isokinetic muscular strength dynamometry (Biodex): KE and KF peak torque (60°/s, 180°/s)	KE peak torque: N/A for total sample; IBD with fatigue 60°/s, 107.1 (25.4) Nm; IBD with fatigue 180°/s, 60.7 (12.3) Nm; IBD without fatigue 60°/s, 123.7 (38.0) Nm; IBD without fatigue 180°/s, 73.5 (21.4) Nm; KE peak torque IBD with and without fatigue < KE peak torque ref (<i>P</i> = N/A); KF peak torque: N/A for total sample; IBD with fatigue 60°/s, 51.7 (14.3) Nm; IBD with fatigue 180°/s, 31.1 (8.0) Nm; IBD without fatigue 60°/s, 63.0 (20.1) Nm; IBD without fatigue 180°/s, 38.9 (14.2) Nm; KF peak torque IBD with and without fatigue < KF peak torque ref (<i>P</i> = N/A)
Jones <i>et al</i> [51], 2020	RCT, United Kingdom	47	N/A	47, 0	68%	49.3 (13.0)	Remission (<i>n</i> = 31) or	Healthy age-	Isokinetic muscular strength	KE peak torque ¹ : CD 60°/s, 72.6

mild active disease (<i>n</i> = 16)	matched, sex-matched, PA-matched, BMI-matched, and ethnicity-matched CG (<i>n</i> = 33)	dynamometry (Biodex): KE peak torque (60°/s, 180°/s), EF peak torque (60°/s, 120°/s)	(33.3) Nm; CD 180°/s, 46.2 (23.0) Nm; CG 60°/s, 94.6 (46.6) Nm; CG 180°/s, 60.1 (34.9) Nm; KE peak torque CD < KE peak torque CG (<i>P</i> = 0.001, <i>P</i> = 0.011); EF peak torque¹ : CD 60°/s, 25.4 (11.2) Nm; CD 120°/s, 22.3 (9.1) Nm; CG 60°/s, 26.0 (12.4) Nm; CG 120°/s, 22.2 (11.2) Nm; EF peak torque CD = EF peak torque CG (<i>P</i> = 0.664, <i>P</i> = 0.747)
--------------------------------------	--	--	---

¹Baseline values are shown.

95%CI: 95% confidence interval; AD: Ankle dorsiflexor; AF: Arm flexor; BMI: Body mass index; BW: Body weight; CD: Crohn's disease; CG: Control group; EF: Elbow flexor; EMG: Electromyography; IBD: Inflammatory bowel disease; IFX: Infliximab; IQR: Interquartile range; KE: Knee extensor; KF: Knee flexor; N/A: Not available; PA: Physical activity; RCT: Randomized controlled trial; RF: Rectus femoris; ref: Reference; SD: Standard deviation; UC: Ulcerative colitis; VL: Vastus lateralis.

[59-61].

A 12-wk walking program in physically inactive patients with CD resulted in a significant improvement in cardiorespiratory fitness as determined by a practical field test[60]. Improvements in cardiorespiratory fitness, as measured by VO₂ peak during CPET, were also observed in patients with CD who completed a 3-mo program of high-intensity interval training (HIIT) or moderate-intensity continuous training[59]. A greater increase in VO₂ peak was found in CD patients who followed the HIIT program than in CD patients who followed the moderate-intensity continuous training program compared with CD patients who received usual care. A secondary analysis of this study showed that the work rate at peak exercise increased only in those patients who underwent the HIIT program[61].

The effect of resistance training on HRPF components was studied by two randomized controlled trials[51,55]. Jones *et al*[51] found that a 6-mo impact (*e.g.* rope skipping, jumps) and resistance training program in patients with CD significantly improved upper and lower limb muscular strength as measured with gold standard tests (*i.e.* knee extensor and elbow flexor muscular strength testing with isokinetic dynamometry) as well as upper and lower limb muscular endurance measured with practical field tests (*i.e.* handgrip strength, chair-stand test, and arm-curl test). In contrast, Zhao *et al*[55] did not observe significant changes in various practical field tests for muscular strength and muscular endurance after an 8-wk resistance training program with either protein supplementation or placebo in patients with IBD diagnosed with sarcopenia.

Two studies investigated interventions that included both aerobic and resistance training for the duration of 8 wk and 12 wk[56,57]. Cronin *et al*[56] demonstrated favorable changes in body fat and lean tissue mass as well as in cardiorespiratory fitness measured by the Rockport 1-mile test in physically inactive patients with IBD after an 8-wk intervention as compared to physically inactive patients with IBD receiving usual care. However, the intervention study by van Erp *et al*[57], conducted in severely fatigued patients with IBD, failed to demonstrate improvements in the gold standard outcome for cardiorespiratory fitness (*i.e.* VO₂max achieved during CPET) after 12 wk. Yet, they did report an improvement in work rate at peak exercise. The effects of aerobic exercise and resistance exercise were compared in a randomized pilot study by Seeger *et al*[58]. After 12 wk, both patients with CD who performed aerobic exercise and patients with CD who performed resistance exercise showed a gain in muscular strength as determined by practical field tests.

DISCUSSION

This scoping review aimed to provide an overview of studies on the assessment of HRPF components in patients with IBD and to review the effects of physical activity and physical exercise training interventions on HRPF components in patients with IBD. Accurate measurement of the HRPF concept is the first step towards the investigation and implementation of targeted physical activity or physical exercise training interventions to improve clinical outcomes and patient-reported outcomes in IBD. The findings of this scoping review indicated a shortcoming in the present literature regarding the accurate assessment of the HRPF concept, as most studies considered only one or two HRPF components, and no single study assessed flexibility. In addition, large heterogeneity existed in assessment methods, with frequent use of non-validated tests. According to limited studies that used gold standard tests, cardiorespiratory fitness seemed to be reduced in patients with IBD, but findings on muscular strength and endurance were inconsistent. An overall positive effect on HRPF components was present for physical activity or physical exercise training interventions. Important insights and research gaps that resulted from the thematic mapping of the evidence are outlined below, along with

Table 4 Description and main findings of studies examining the effect of physical activity and physical exercise training interventions on health-related physical fitness components in patients with inflammatory bowel disease

Ref.	Study design, country	Sample size, <i>n</i>	Sample features	CD, UC, IBD-U (<i>n</i>)	Female sex, (%)	Age in yr, mean (SD)	Disease activity	Healthy control group	Intervention, IG	Comparator, CG	HRPF components assessed	Effect on HRPF components
Mählmann <i>et al</i> [53], 2017	Pilot study, Switzerland	21	Pediatric patients	12, 7, 3	48%	13.88	Remission (<i>n</i> = 14) or active disease (<i>n</i> = 7)	Age-matched and sex-matched HC (<i>n</i> = 23)	Moderate-intensity aerobic exercise training with active video gameplay (<i>n</i> = 21), 5 sessions/wk (30 min) for 8 wk	N/A	Cardiorespiratory fitness with 6-min walk test (practical field test) at wk 8	Distance reached in 6 min increased in patients with active disease from 655 (95%CI: 542-769) m to 758 (95%CI: 610-906) m, and in patients in remission from 655 (95%CI: 542-769) m to 758 (95%CI: 610-906) m, and in CG from 678 (95%CI: 640-715) m to 727 (95%CI: 74-93) m, without between-group differences (<i>P</i> = N/A)
Trivić <i>et al</i> [54], 2022	Intervention study, Croatia	42	Pediatric patients	22, 18, 2	40%	N/A for total sample	Remission (<i>n</i> = 42)	N/A	Personalized home-based structured resistance training (<i>n</i> = 42), 3 sessions/wk for 6 mo	N/A	Body composition (LBM) with DEXA; muscular endurance 30 s sit-ups, push-ups, back extensions, squats, and holding a plank position for as long as possible (practical field tests), all at 6 mo	Improvement in LBM from 37.12 (SD: 1.43) kg to 38.75 (SD: 1.61) kg, (<i>P</i> = 0.012) but not in LBM z-score. Improvement in muscular endurance tasks: Number of sit-up repetitions from 19.32 (SD: 5.82) to 21.00 (SD: 6.53) (<i>P</i> = 0.024), back extension repetitions from 27.39 (SD: 12.09) to 38.27 (SD: 16.10) (<i>P</i> < 0.001), push-up repetitions from 17.37 (SD: 6.67) to 24.59 (SD: 7.58) (<i>P</i> < 0.001), squat repetitions from 22.10 (SD: 4.87) to 24.88 (SD: 6.23) (<i>P</i> < 0.001), and time holding the plank position from 81.0 (SD: 46.26) s to 114.34 (SD: 74.06) s (<i>P</i> < 0.001)
Loudon <i>et al</i> [60], 1999	Pilot study, Canada	16	Sedentary adult patients	16, 0, 0	83%	38.3 (7.5)	Remission or mild active disease (<i>n</i> = N/A)	N/A	Supervised indoor (group) walking program, 3 sessions/wk (of 20-35 min) for 12 wk	N/A	Cardiorespiratory fitness with CAFT step test (practical field test) at wk 12	Improvement in estimated VO ₂ max from 30.6 (SD: 4.7) mL/kg/min to 32.4 (SD: 4.8) mL/kg/min (<i>P</i> = 0.0013)
Bottoms <i>et al</i> [61], 2019	Secondary analysis of Tew <i>et al</i> [59], United Kingdom	25	Adult patients	25, 0, 0	60%	N/A for total sample	Remission or mild active disease (<i>n</i> = N/A)	N/A	HIIT (<i>n</i> = 13) or MICT (<i>n</i> = 12), 3 sessions/wk for 3 mo	N/A	Cardiorespiratory fitness with CPET (gold standard test) at week 4, 8, and 12	Increase in WRpeak after HIIT from baseline to week 4 with mean difference of 20.5 (SD: 10.8) W (<i>P</i> = 0.03), and from week 4 to week 12 with 12.30 (SD: 6.32) W, (<i>P</i> = 0.02); No change in WRpeak after MICT
Cronin <i>et al</i> [56], 2019	Cross-over RCT, Ireland	17	Physically inactive adult patients	N/A for total sample	N/A for total sample	25 (6.5)	Remission (<i>n</i> = 17)	N/A	Combined aerobic and resistance exercise program (<i>n</i> = 13, of which 7 crossed-over), 3 sessions/wk (of 60	Usual care (<i>n</i> = 7)	Body composition (body fat and lean tissue mass) with DEXA, cardiorespiratory fitness with Rockport 1-mile walk test (practical field test), all at	Total body fat decreased in the IG with 2.1% (IQR: -2.15 to -0.45) but increased in the CG with 0.1% (IQR: -0.4-1), (<i>P</i> = 0.022); total lean tissue mass increased in the IG with 1.59 (IQR: 0.68-2.69) kg but decreased in the CG with 1.38 (IQR: -2.45-

								min) for 8 wk		week 8		0.26) kg, ($P = 0.003$); improvement of estimated VO_2max in the IG from 43.41 mL/kg/min to 46.01 mL/kg/min, ($P = 0.03$)
Tew <i>et al</i> [59], 2019	Pilot RCT, United Kingdom	36	Adult patients	36, 0, 0	53%	36.9 (11.2)	Remission ($n = 32$) or mildly active disease ($n = 4$)	N/A	HIIT ($n = 13$) or MICT ($n = 12$), 3 sessions/wk for 3 mo	Usual care ($n = 11$)	Cardiorespiratory fitness with CPET (gold standard test) at 3 mo	Change in VO_2peak from 27.3 (SD: 7.7) mL/kg/min to 29.7 (SD: 8.2) mL/kg/min after HIIT. Change in VO_2peak from 28.7 (SD: 8.6) mL/kg/min to 29.3 (SD: 6.6) mL/kg/min after MICT. Change in VO_2peak from 28.6 (SD: 10.0) mL/kg/min to 28.5 (SD: 9.2) mL/kg/min after usual care. Mean change in VO_2peak from baseline to 3 mo relative to the usual care was greater following HIIT than MICT (+2.4 vs +0.7 mL/kg/min) ($P = \text{N/A}$)
Jones <i>et al</i> [51], 2020	RCT, United Kingdom	47	Adult patients	47, 0, 0	68%	49.3 (13.0)	Remission ($n = 31$) or mild active disease ($n = 16$)	Age-matched, sex-matched, PA-matched, BMI-matched, and ethnicity-matched HC ($n = 33$)	Combined impact and resistance exercise training ($n = 23$), 3 sessions/wk (of 60 min) for 6 mo	Usual care ($n = 24$)	Muscular strength and endurance with isokinetic dynamometry (gold standard test) as well as with HGS, chair-stand test, and arm-curl test (practical field tests), all at 6 mo	Improvement of all muscular strength and endurance tests in the IG compared to the CG: mean difference KE peak torque 60°/s, 22.4 (95%CI: 12.1-32.8) Nm; KE peak torque 180°/s, 16.8 (95%CI: 9.0-24.5) Nm; EF peak torque 60°/s, 6.8 (95%CI: 3.9-9.6) Nm; EF peak torque 180°/s, 6.3 (95%CI: 3.3-9.3) Nm; HGS, 8.3 (95%CI: 6.2-10.5) kg; Chair-stand test, 4 (95%CI: 3-6) repetitions; arm-curl test, 7 (95%CI: 5-8) repetitions; All $P < 0.001$
Seeger <i>et al</i> [58], 2020	Pilot RCT, Germany	45	Adult patients	45, 0, 0	63%	N/A for total sample	Remission or mild active disease ($n = \text{N/A}$)	N/A	Moderate endurance training ($n = 17$, only $n = 9$ were analyzed), or moderate muscle training ($n = 15$, only $n = 13$ analyzed), 3 sessions/wk (of 30-40 min) for 12 wk	Usual care ($n = 13$)	Muscular strength with HGS and isometric HHD (practical field tests) at week 12	Improvement of HGS and QS in both endurance training IG ($P = 0.01$, $P = 0.035$) and muscle training IG ($P = 0.01$, $P = 0.002$), while HGS decreased and QS did not change in CG ($P = 0.01$, $P = 0.23$)
Van Erp <i>et al</i> [57], 2021	Pilot study, The Netherlands	25	Adult patients with severe fatigue	21, 3, 1	40%	45 (2.6)	Remission ($n = 25$)	N/A	Aerobic and progressive resistance training, 3 sessions/wk (of 60 min) for 12 wk	N/A	Cardiorespiratory fitness with a CPET (gold standard test) at week 12	No significant change in VO_2max . A significant change in WRpeak from 2.4 (SD: 0.5) W/kg to 2.7 (SD: 0.5) W/kg ($P = 0.002$)
Zhao <i>et al</i> [55], 2022	RCT, China	28	Adult patients with low nutritional risk state [RT + WP intervention ($n = 15$), RT + placebo intervention ($n = 13$)]	N/A	31%	44.1	Remission ($n = 3$), or mild ($n = 12$), moderate ($n = 9$), or severe ($n = 4$) active disease	N/A	Unsupervised resistance training ($n = 28$), 3 sessions/wk for 8 wk		Muscular strength with HGS and muscular endurance with 3-m walk speed and 5-time chair-stand-test (all practical field tests), all at week 8	HGS changed from 36.7 (SD: 10.8) kg to 42.6 (SD: 8.4) kg in the RT + WP group and from 31.7 (SD: 12.6) kg to 32.9 (SD: 12.5) kg in the RT + placebo group. 3-m walk speed changed from 1.0 (SD: 0.3) m/s to 0.9 (SD: 0.1) m/s in the RT + WP group and from 1.1 (SD: 0.2) m/s to 1.0 (SD: 0.2) m/s in the RT + placebo group. Time to perform the 5-time chair-stand test changed from 7.0 (SD: 1.5) s to 6.2

(SD: 1.4) s in the RT + WP group and from 6.6 (SD: 1.6) s to 6.2 (SD: 1.3) s in the RT + placebo group. All are not statistically significant ($P = N/A$)

95%CI: 95% confidence interval; BMI: Body mass index; CAFT: Canadian aerobic fitness test; CD: Crohn's disease; CG: Control group; CPET: Cardiopulmonary exercise test; DEXA: Dual-energy X-ray absorptiometry; EF: Elbow flexor; HC: Healthy controls; HGS: Handgrip strength; HHD: Hand-held dynamometry; HIIT: High-intensity interval training; HRPF: Health-related physical fitness; IBD-U: Inflammatory bowel disease unclassified; IG: Intervention group; IQR: Interquartile range; KE: Knee extensor; LBM: Lean body mass; MICT: Moderate-intensity continuous training; N/A: Not available; PA: Physical activity; QS: Quadriceps strength; RCT: Randomized controlled trial; RT: Resistance training; SD: Standard deviation; UC: Ulcerative colitis; VO₂max: Maximal oxygen uptake; VO₂peak: Oxygen uptake at peak exercise; WP: Whey protein; WRpeak: Work rate at peak exercise.

recommendations for future research.

Current evidence for an impaired HRPF in patients with IBD is limited, which is partially attributable to a lack of accurate assessment methodology in a significant proportion of the studies as well as the inclusion of small sample sizes and different populations. Cardiorespiratory fitness, as determined by direct measurement of VO₂max/VO₂peak, seems to be reduced in pediatric and adult patients with IBD. However, this is based on only four studies that made comparisons with healthy control subjects or reference values. Controversial findings emerged from studies that assessed muscular strength and endurance by gold standard assessment methods. This might indicate that it depends on, for example, the specific muscle group examined, test protocol, patient- or disease-specific factors, and/or the control group or reference values used for comparison, as to whether muscular strength and endurance are affected. Better-designed studies are warranted to objectively assess the components of HRPF in patients with IBD and to subsequently investigate their associations with patient-specific and disease-specific factors as well as with clinical and patient-reported outcomes to ascertain whether any particular components are insufficient or below normal values (*e.g.* in certain patient subgroups) and could be improved with appropriate interventions. Due to the heterogeneity of the disease, large patient populations are required for these studies to ensure that relevant patient subgroups are adequately represented.

This review showed substantial heterogeneity in assessment methods used for the different components of HRPF in the included studies. As gold standard assessment methods are often too complex to implement on a large scale, there is a need for less demanding alternative assessment methods. To enable the assessment of HRPF in routine clinical practice and to perform studies in large populations with long-term follow-up, future research should focus on determining the validity and reliability of screening instruments and easily applicable practical field tests for HRPF within the IBD population. It is crucial to investigate these aspects, as patients with IBD frequently experience fatigue or joint arthralgia, which may limit the capacity to undertake exercise tests, or patients may avoid or give up exercise for fear of exacerbating bowel symptoms[62]. For instance, clinical implementation of a validated practical patient-reported screening tool (*e.g.* the Duke activity status index for cardiorespiratory fitness) may serve in identifying patients at risk for impaired HRPF [63]. These patients could then be offered a comprehensive objective assessment using validated practical field tests by dedicated physical therapists or exercise physiologists to evaluate the specific intolerance with regard to the different components of HRPF. Subsequently, a personalized physical exercise training program may then be proposed to those patients with an impaired HRPF.

Overall, a positive effect of physical activity or physical exercise training interventions on HRPF components was present in patients with IBD in remission or with mild active disease. However, these findings should be interpreted with caution given the important methodological limitations of the studies. Studies were often underpowered to detect true statistically significant effects. Even though pilot research is necessary to explore the feasibility, acceptability, and safety of an intervention preliminary to the subsequent implementation of a full-scale trial, large high-quality methodology randomized controlled trials or quasi-experiments are warranted to establish the benefits of physical activity or physical

exercise training in patients with IBD. In addition to high methodological quality, future trials should also consider the quality of the exercise therapy program to ensure therapeutic potential. Quality of the exercise therapy program involves patient selection, type and timing of the outcome assessment, the dosage and type of the exercise program, trained supervision, safety, and adherence[64].

Patients in remission or with mild disease activity have been the main focus of the current intervention studies, often excluding patients with moderate to severe disease. In addition, research on the effectiveness of physical activity or physical exercise training in the context of preoperative optimization in patients with IBD is virtually absent[65]. Since preoperative optimization of cardiorespiratory fitness and muscular strength has been shown to reduce postoperative complications and enhance recovery in unfit patients undergoing abdominal surgery, it seems likely that patients with IBD would benefit from these interventions as well[66,67]. Future trials involving participants with moderate to severely active disease or those awaiting surgery are warranted. Furthermore, current studies were limited by a lack of proper preselection based on the pre-existing fitness level of participants receiving an intervention. Patient selection based on HRPF components that align with the purpose of the study is required to evaluate the true effectiveness of the intervention. For instance, if the intervention purpose is to improve cardiorespiratory fitness, then those patients with reduced cardiorespiratory fitness should be included to ensure optimal effects of the intervention[64]. Current studies are frequently limited by the inclusion of patients who have adequate cardiorespiratory fitness or muscular strength, leaving little opportunity for improvement.

The type and timing of the primary outcome assessment is another major limitation among current intervention studies. The majority of studies lack accurate assessment of HRPF components over time with validated assessment methods as a primary endpoint, making it difficult to assess the true effects of the intervention. Only 10 of 22 studies reported the effects of the intervention on HRPF components, with frequent use of non-validated practical field tests. Physical exercise training is, by definition, intended to improve components of HRPF, in contrast to physical activity. Hence, an accurate assessment of HRPF is imperative to ascertain the true effects of physical exercise training in patients with IBD. Since not all studies reported a clear rationale towards the (direct or indirect) improvement of HRPF components within the purpose of the study, which is an important part of the definition of physical exercise training in contrast to physical activity, it was not possible to differentiate between physical activity interventions and physical exercise training interventions in this review. To study the effects of both types of interventions separately from one another, future studies should provide a more detailed description of the chosen interventions, along with the congruent outcome measure. Furthermore, future trials should also include longer follow-ups to determine whether these potential beneficial effects persist after the intervention.

Other frequently reported endpoints were quality of life, fatigue, depression, anxiety, and stress, which are multifactorial by origin and often influenced by other factors such as social support, medication use, and bowel symptoms. Especially for subjective outcomes, the Hawthorn effect (*i.e.* change due to received attention or assessment) instead of the intervention under examination can explain the observed effects of these trials[68]. A better understanding of the exact mechanism by which physical activity or physical exercise training may help to improve such parameters of subjective well-being (*e.g.* as an indirect effect of the improvement of HRPF components) is warranted.

Large variability was observed in the dosage and type of physical activity and physical exercise training programs in the included studies. To ensure high therapeutic potential of an intervention in patients with IBD, the underlying framework of the intervention (*i.e.* the 'Frequency, Intensity, Time, Type' principle) should be based on a potential or proven rationale (based on anatomical, physiological, or behavioral relevance) towards the purpose of the intervention, and should preferably be individually tailored to a patient's needs[64]. Most studies implemented interventions of low-to-moderate intensities and showed that these were feasible and well tolerated in patients with IBD in remission or with mild disease activity. In general, high-intensity training is usually not recommended in patients with IBD as this may lead to an increase in inflammation and an exacerbation of symptoms[69]. However, existing evidence does not provide much support for these recommendations.

Only one study examined the effect of a high-intensity training intervention in patients with IBD as compared to moderate-continuous training[59]. The findings of this study showed that neither mode of training intensity increased bowel symptoms and that high-intensity training caused a greater change in cardiorespiratory fitness than moderate-continuous training. Furthermore, Ploeger *et al*[70] showed that a single bout of HIIT did not cause an acute exacerbation of inflammation parameters in youth with CD. More research on the safety and efficacy of different training dosages and types for patients with IBD is needed to elucidate the optimal training paradigm.

Many studies conducted physical activity or physical exercise training interventions that were (partly) home-based and unsupervised. Although interventions under the supervision of trained professionals can positively influence the impact of the intervention by encouraging adherence, unsupervised interventions might better reflect non-research contexts where supervised programs will not always be feasible due to expense or a lack of trained personnel.

To our knowledge, this is the first review dedicated to HRPF in pediatric and adult patients with IBD, with an emphasis on the assessment of the various HRPF components and the effect of physical activity and physical exercise training interventions on HRPF components. The major strengths of this review were its broad scope and the extensive systematic search across multiple databases. This review revealed a large volume of research and identified several research gaps that give rise to new research opportunities. This review also had some limitations. First, the classification of studies to the different components of HRPF that were assessed was based on the researchers' judgment and thus may have been influenced by their interpretation. Second, as a traditional scoping review approach was used, all published literature was considered, regardless of study quality. This precluded the weighting of higher-quality studies *vs* lower-quality studies in formulating conclusions.

CONCLUSION

This review revealed a gap in the present literature concerning the assessment of the complete HRPF concept as well as significant heterogeneity in assessment methods used to assess the components of HRPF. Cardiorespiratory fitness seems to be diminished in patients with IBD, yet conflicting evidence exists with regard to muscular strength and endurance. More well-designed large-scale studies are warranted to assess the status of the various components of HRPF in patients with IBD using validated assessment methods and to subsequently investigate their association with patient-specific and disease-specific factors as well as clinical and patient-reported outcomes. Furthermore, an overall favorable impact of physical activity and physical exercise training interventions on HRPF components was present. However, important methodological limitations were identified. Future well-designed studies on the effect of such interventions on disease outcomes are required to determine the optimal training paradigm before (inter)national guidelines regarding physical activity and physical exercise training can be integrated into the holistic therapeutic care for patients with IBD.

ARTICLE HIGHLIGHTS

Research background

Reaching the Selecting Therapeutic Targets in Inflammatory Bowel Disease-II (STRIDE-II) therapeutic targets for inflammatory bowel disease (IBD) requires an interdisciplinary approach. Lifestyle interventions to enhance and maintain health-related physical fitness (HRPF) could potentially aid in improving subjective health, decreasing disability, or even controlling inflammation. However, ambiguity remains about the status and impact of HRPF (encompassing body composition, cardiorespiratory fitness, muscular strength, muscular endurance, and flexibility) in IBD patients, hindering the development of physical activity and physical exercise training guidelines.

Research motivation

Accurate evaluation of HRPF components is imperative for a deeper understanding of the state of HRPF in IBD patients as well as to clearly define endpoints in intervention studies to determine whether physical activity or physical exercise training can improve HRPF components in patients with IBD. Hence, accurate assessment of the HRPF concept is the initial step toward investigating and implementing targeted physical activity or physical exercise training interventions, aiming to improve clinical outcomes and patient-reported outcomes in IBD.

Research objectives

The primary objective of this scoping review was to provide an overview of studies on the assessment of HRPF components in patients with IBD. The second objective was to review the effects of physical activity and physical exercise training interventions on HRPF in patients with IBD.

Research methods

A systematic search was conducted in multiple databases for original studies that included patients with IBD, assessed one or more HRPF components, and/or evaluated physical activity or physical exercise training interventions.

Research results

Sixty-eight articles were included. No study examined the complete concept of HRPF, and considerable heterogeneity existed in assessment methods, with frequent use of non-validated tests. According to studies that used gold standard tests, cardiorespiratory fitness seemed to be reduced, but findings on muscular strength and endurance were inconsistent. A limited number of studies that evaluated physical activity or physical exercise training interventions reported effects on HRPF, overall showing a positive impact.

Research conclusions

The findings of this scoping review indicated a shortcoming in the present literature regarding the accurate assessment of the HRPF concept, as most studies considered only one or two HRPF components, and no single study assessed flexibility. Important methodological limitations of studies that evaluated physical activity or physical exercise training interventions were identified.

Research perspectives

More well-designed large-scale studies are warranted to assess the status of the various components of HRPF in patients with IBD using validated assessment methods and to subsequently investigate their association with patient-specific and disease-specific factors as well as clinical and patient-reported outcomes. Furthermore, more research on the effect of physical activity or physical exercise training interventions on disease outcomes is required to determine the optimal training paradigm before (inter)national guidelines regarding physical activity and physical exercise training can be integrated in the holistic therapeutic care for patients with IBD.

FOOTNOTES

Author contributions: Demers K, Bak MTJ, Bongers BC, Jonkers DMAE, de Vries AC, Pierik MJ, and Stassen LPS contributed to the conception and design of this review; Demers K performed the literature search; Demers K and Bak MTJ performed study selection and data acquisition; Demers K drafted the manuscript; Bak MTJ, Bongers BC, Jonkers DMAE, de Vries AC, Pierik MJ, and Stassen LPS critically revised the manuscript for important intellectual content; All authors revised the manuscript and approved the final version.

Conflict-of-interest statement: Karlijn Demers, Michiel TJ Bak, and Bart C Bongers declare no conflicts of interest. Daisy MAE Jonkers reports grant from the public-private partnership grants of Dutch Top Institute of Food and Nutrition (TIFN), Top Knowledge Institute (TKI) Agri&Food and Health Holland, by the Carbokinetics program as part of the NWO-CCC Partnership Program, by Organic A2BV/Mothersfinest BV and, EU/FP7 SysmedIBD/305564, BIOM/305479 and Character/305676, H2020 DISCOVERIE/848228, all outside the submitted work. Annemarie C de Vries has served on advisory boards for Takeda, Janssen, Bristol Myers Squibb, Abbvie, Pfizer, and Galapagos and has received unrestricted research grants from Takeda, Janssen, and Pfizer outside the submitted work. Marieke J Pierik reports grants and non-financial support from Falk Pharma, grants from European commission, grants from ZONMW (Dutch national research fund), grants and non-financial support from Takeda, grants and non-financial support from Johnson and Johnson, grants and non-financial support from Abbvie, non-financial support from Ferring, non-financial support from Immunodiagnostics, non-financial support from MSD, all outside the submitted work. Laurents PS Stassen has served as a speaker and received research support from Takeda, outside the submitted work.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: Netherlands

ORCID number: Karlijn Demers 0000-0003-3709-9959; Michiel TJ Bak 0000-0001-8515-425X; Bart C Bongers 0000-0002-1948-9788; Annemarie C de Vries 0000-0002-3988-9201; Daisy MAE Jonkers 0000-0001-8981-8965; Marieke J Pierik 0000-0001-6981-6516; Laurents PS Stassen 0000-0002-3383-9035.

S-Editor: Lin C

L-Editor: Webster JR

P-Editor: Yu HG

REFERENCES

- Baumgart DC, Sandborn WJ. Crohn's disease. *Lancet* 2012; **380**: 1590-1605 [PMID: 22914295 DOI: 10.1016/S0140-6736(12)60026-9]
- Ordás I, Eckmann L, Talamini M, Baumgart DC, Sandborn WJ. Ulcerative colitis. *Lancet* 2012; **380**: 1606-1619 [PMID: 22914296 DOI: 10.1016/S0140-6736(12)60150-0]
- Tsai L, Ma C, Dulai PS, Prokop LJ, Eisenstein S, Ramamoorthy SL, Feagan BG, Jairath V, Sandborn WJ, Singh S. Contemporary Risk of Surgery in Patients With Ulcerative Colitis and Crohn's Disease: A Meta-Analysis of Population-Based Cohorts. *Clin Gastroenterol Hepatol* 2021; **19**: 2031-2045.e11 [PMID: 33127595 DOI: 10.1016/j.cgh.2020.10.039]
- Raine T, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, Bachmann O, Bettenworth D, Chaparro M, Czuber-Dochan W, Eder P, Ellul P, Fidalgo C, Fiorino G, Gionchetti P, Gisbert JP, Gordon H, Hedin C, Holubar S, Iacucci M, Karmiris K, Katsanos K, Kopylov U, Lakatos PL, Lytras T, Lyutakov I, Noor N, Pellino G, Piovani D, Savarino E, Selvaggi F, Verstockt B, Spinelli A, Panis Y, Doherty G. ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment. *J Crohns Colitis* 2022; **16**: 2-17 [PMID: 34635919 DOI: 10.1093/ecco-jcc/jjab178]
- Torres J, Bonovas S, Doherty G, Kucharzik T, Gisbert JP, Raine T, Adamina M, Armuzzi A, Bachmann O, Bager P, Biancone L, Bokemeyer B, Bossuyt P, Burisch J, Collins P, El-Hussuna A, Ellul P, Frei-Lanter C, Furfaro F, Gingert C, Gionchetti P, Gomollon F, González-Lorenzo M, Gordon H, Hlavaty T, Juillerat P, Katsanos K, Kopylov U, Krustins E, Lytras T, Maaser C, Magro F, Marshall JK, Myreliid P, Pellino G, Rosa I, Sabino J, Savarino E, Spinelli A, Stassen L, Uzzan M, Vavricka S, Verstockt B, Warusavitarne J, Zmora O, Fiorino G. ECCO Guidelines on Therapeutics in Crohn's Disease: Medical Treatment. *J Crohns Colitis* 2020; **14**: 4-22 [PMID: 31711158 DOI: 10.1093/ecco-jcc/jjz180]
- Burisch J, Jess T, Martinato M, Lakatos PL; ECCO -EpiCom. The burden of inflammatory bowel disease in Europe. *J Crohns Colitis* 2013; **7**: 322-337 [PMID: 23395397 DOI: 10.1016/j.crohns.2013.01.010]
- Romberg-Camps MJ, Bol Y, Dagnelie PC, Hesselink-van de Kruijs MA, Kester AD, Engels LG, van Deursen C, Hameeteman WH, Pierik M, Wolters F, Russel MG, Stockbrügger RW. Fatigue and health-related quality of life in inflammatory bowel disease: results from a population-based study in the Netherlands: the IBD-South Limburg cohort. *Inflamm Bowel Dis* 2010; **16**: 2137-2147 [PMID: 20848468 DOI: 10.1002/ibd.21285]
- Lönnfors S, Vermeire S, Greco M, Hommes D, Bell C, Avedano L. IBD and health-related quality of life -- discovering the true impact. *J Crohns Colitis* 2014; **8**: 1281-1286 [PMID: 24662394 DOI: 10.1016/j.crohns.2014.03.005]
- Turner D, Ricciuto A, Lewis A, D'Amico F, Dhaliwal J, Griffiths AM, Bettenworth D, Sandborn WJ, Sands BE, Reinisch W, Schölmerich J, Bemelman W, Danese S, Mary JY, Rubin D, Colombel JF, Peyrin-Biroulet L, Dotan I, Abreu MT, Dignass A; International Organization for

- the Study of IBD. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology* 2021; **160**: 1570-1583 [PMID: 33359090 DOI: 10.1053/j.gastro.2020.12.031]
- 10 **Bouchard C SR.** Physical activity, fitness and health: the model and key concepts. In: Bouchard C, Shepard RJ, Stephens T, editors: Physical activity, fitness and health, International Proceedings and Consensus Statement. Illinois: Human Kinetics, 1994
- 11 **Ross R,** Blair SN, Arena R, Church TS, Després JP, Franklin BA, Haskell WL, Kaminsky LA, Levine BD, Lavie CJ, Myers J, Niebauer J, Sallis R, Sawada SS, Sui X, Wisløff U; American Heart Association Physical Activity Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Cardiovascular and Stroke Nursing; Council on Functional Genomics and Translational Biology; Stroke Council. Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement From the American Heart Association. *Circulation* 2016; **134**: e653-e699 [PMID: 27881567 DOI: 10.1161/CIR.0000000000000461]
- 12 **Lee IM,** Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT; Lancet Physical Activity Series Working Group. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012; **380**: 219-229 [PMID: 22818936 DOI: 10.1016/S0140-6736(12)61031-9]
- 13 **Han M,** Qie R, Shi X, Yang Y, Lu J, Hu F, Zhang M, Zhang Z, Hu D, Zhao Y. Cardiorespiratory fitness and mortality from all causes, cardiovascular disease and cancer: dose-response meta-analysis of cohort studies. *Br J Sports Med* 2022; **56**: 733-739 [PMID: 35022163 DOI: 10.1136/bjsports-2021-104876]
- 14 **Chekroud SR,** Gueorguieva R, Zheutlin AB, Paulus M, Krumholz HM, Krystal JH, Chekroud AM. Association between physical exercise and mental health in 1·2 million individuals in the USA between 2011 and 2015: a cross-sectional study. *Lancet Psychiatry* 2018; **5**: 739-746 [PMID: 30099000 DOI: 10.1016/S2215-0366(18)30227-X]
- 15 **Berkel AEM,** van Wijk L, van Dijk DPJ, Prins SN, van der Palen J, van Meeteren NLU, Olde Damink SWM, Klaase JM, Bongers BC. The association between preoperative body composition and aerobic fitness in patients scheduled for colorectal surgery. *Colorectal Dis* 2022; **24**: 93-101 [PMID: 34612581 DOI: 10.1111/codi.15941]
- 16 **Cuijpers ACM,** Heldens AFJM, Bours MJL, van Meeteren NLU, Stassen LPS, Lubbers T, Bongers BC. Relation between preoperative aerobic fitness estimated by steep ramp test performance and postoperative morbidity in colorectal cancer surgery: prospective observational study. *Br J Surg* 2022; **109**: 155-159 [PMID: 34536001 DOI: 10.1093/bjs/znac292]
- 17 **Beavers KM,** Brinkley TE, Nicklas BJ. Effect of exercise training on chronic inflammation. *Clin Chim Acta* 2010; **411**: 785-793 [PMID: 20188719 DOI: 10.1016/j.cca.2010.02.069]
- 18 **Gleeson M,** Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. *Nat Rev Immunol* 2011; **11**: 607-615 [PMID: 21818123 DOI: 10.1038/nri3041]
- 19 **Caspersen CJ,** Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985; **100**: 126-131 [PMID: 3920711]
- 20 **American College of Sports Medicine.** ACSM's health-related physical fitness assessment manual. 5th ed. Philadelphia: Wolters Kluwer, 2014
- 21 **Gibson AL,** Wagner DR, Heyward VH. Advanced Fitness Assessment and Exercise Prescription. 8th ed. Illinois: Human Kinetics, 2018
- 22 **Dasso NA.** How is exercise different from physical activity? A concept analysis. *Nurs Forum* 2019; **54**: 45-52 [PMID: 30332516 DOI: 10.1111/nuf.12296]
- 23 WHO Guidelines on Physical Activity and Sedentary Behaviour. Geneva: World Health Organization; 2020– [PMID: 33369898]
- 24 **Elia J,** Kane S. Adult Inflammatory Bowel Disease, Physical Rehabilitation, and Structured Exercise. *Inflamm Bowel Dis* 2018; **24**: 2543-2549 [PMID: 29850914 DOI: 10.1093/ibd/izy199]
- 25 **van Langenberg DR,** Papanondy MC, Gibson PR. Sleep and physical activity measured by accelerometry in Crohn's disease. *Aliment Pharmacol Ther* 2015; **41**: 991-1004 [PMID: 25783784 DOI: 10.1111/apt.13160]
- 26 **Mack DE,** Wilson PM, Gilmore JC, Gunnell KE. Leisure-time physical activity in Canadians living with Crohn disease and ulcerative colitis: population-based estimates. *Gastroenterol Nurs* 2011; **34**: 288-294 [PMID: 21814062 DOI: 10.1097/SGA.0b013e3182248732]
- 27 **Schakman O,** Gilson H, Thissen JP. Mechanisms of glucocorticoid-induced myopathy. *J Endocrinol* 2008; **197**: 1-10 [PMID: 18372227 DOI: 10.1677/JOE-07-0606]
- 28 **Vogelaar L,** van den Berg-Emons R, Bussmann H, Rozenberg R, Timman R, van der Woude CJ. Physical fitness and physical activity in fatigued and non-fatigued inflammatory bowel disease patients. *Scand J Gastroenterol* 2015; **50**: 1357-1367 [PMID: 25966749 DOI: 10.3109/00365521.2015.1046135]
- 29 **Dhaliwal A,** Quinlan JI, Overthrow K, Greig C, Lord JM, Armstrong MJ, Cooper SC. Sarcopenia in Inflammatory Bowel Disease: A Narrative Overview. *Nutrients* 2021; **13** [PMID: 33671473 DOI: 10.3390/nu13020656]
- 30 **van Langenberg DR,** Della Gatta P, Warmington SA, Kidgell DJ, Gibson PR, Russell AP. Objectively measured muscle fatigue in Crohn's disease: correlation with self-reported fatigue and associated factors for clinical application. *J Crohns Colitis* 2014; **8**: 137-146 [PMID: 23938210 DOI: 10.1016/j.crohns.2013.07.006]
- 31 **Cioffi I,** Imperatore N, Di Vincenzo O, Santarpia L, Rispo A, Marra M, Testa A, Contaldo F, Castiglione F, Pasanisi F. Association between Health-Related Quality of Life and Nutritional Status in Adult Patients with Crohn's Disease. *Nutrients* 2020; **12** [PMID: 32168964 DOI: 10.3390/nu12030746]
- 32 **Bryant RV,** Trott MJ, Bartholomeusz FD, Andrews JM. Systematic review: body composition in adults with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013; **38**: 213-225 [PMID: 23763279 DOI: 10.1111/apt.12372]
- 33 **Thangarajah D,** Hyde MJ, Konteti VK, Santhakumaran S, Frost G, Fell JM. Systematic review: Body composition in children with inflammatory bowel disease. *Aliment Pharmacol Ther* 2015; **42**: 142-157 [PMID: 26043941 DOI: 10.1111/apt.13218]
- 34 **Ding NS,** Tassone D, Al Bakir I, Wu K, Thompson AJ, Connell WR, Malietzis G, Lung P, Singh S, Choi CR, Gabe S, Jenkins JT, Hart A. Systematic Review: The Impact and Importance of Body Composition in Inflammatory Bowel Disease. *J Crohns Colitis* 2022; **16**: 1475-1492 [PMID: 35325076 DOI: 10.1093/ecco-jcc/jjac041]
- 35 **Tricco AC,** Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, Moher D, Peters MDJ, Horsley T, Weeks L, Hempel S, Akl EA, Chang C, McGowan J, Stewart L, Hartling L, Aldcroft A, Wilson MG, Garrity C, Lewin S, Godfrey CM, Macdonald MT, Langlois EV, Soares-Weiser K, Moriarty J, Clifford T, Tunçalp Ö, Straus SE. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med* 2018; **169**: 467-473 [PMID: 30178033 DOI: 10.7326/M18-0850]

- 36 **American Thoracic Society**; American College of Chest Physicians. ATS/ACCP Statement on cardiopulmonary exercise testing. *Am J Respir Crit Care Med* 2003; **167**: 211-277 [PMID: [12524257](#) DOI: [10.1164/rccm.167.2.211](#)]
- 37 **Drouin JM**, Valovich-mcLeod TC, Shultz SJ, Gansneder BM, Perrin DH. Reliability and validity of the Biodex system 3 pro isokinetic dynamometer velocity, torque and position measurements. *Eur J Appl Physiol* 2004; **91**: 22-29 [PMID: [14508689](#) DOI: [10.1007/s00421-003-0933-0](#)]
- 38 **Abernethy P**, Wilson G, Logan P. Strength and power assessment. Issues, controversies and challenges. *Sports Med* 1995; **19**: 401-417 [PMID: [7676101](#) DOI: [10.2165/00007256-199519060-00004](#)]
- 39 **Ly LP**, Handelsman DJ. Muscle strength and ageing: methodological aspects of isokinetic dynamometry and androgen administration. *Clin Exp Pharmacol Physiol* 2002; **29**: 37-47 [PMID: [11917904](#) DOI: [10.1046/j.1440-1681.2002.03606.x](#)]
- 40 **Corbin CB**, Noble L. Flexibility. *Journal of Physical Education and Recreation* 1980; **51**: 23-60 [DOI: [10.1080/00971170.1980.10622349](#)]
- 41 **American College of Sports Medicine**. ACSM's Resource Manual for Guidelines for Exercise Testing and prescription. 7th ed. Philadelphia: Wolters Kluwer, 2013
- 42 **Kissmeyer-Nielsen P**, Jensen MB, Laurberg S. Perioperative growth hormone treatment and functional outcome after major abdominal surgery: a randomized, double-blind, controlled study. *Ann Surg* 1999; **229**: 298-302 [PMID: [10024114](#) DOI: [10.1097/0000658-199902000-00020](#)]
- 43 **Ploeger HE**, Takken T, Wilk B, Issenman RM, Sears R, Suri S, Timmons BW. Exercise capacity in pediatric patients with inflammatory bowel disease. *J Pediatr* 2011; **158**: 814-819 [PMID: [21146188](#) DOI: [10.1016/j.jpeds.2010.10.020](#)]
- 44 **Nguyen T**, Ploeger HE, Obeid J, Issenman RM, Baker JM, Takken T, Parise G, Timmons BW. Reduced fat oxidation rates during submaximal exercise in adolescents with Crohn's disease. *Inflamm Bowel Dis* 2013; **19**: 2659-2665 [PMID: [24105390](#) DOI: [10.1097/01.MIB.0000436958.54663.4f](#)]
- 45 **Otto JM**, O'Doherty AF, Hennis PJ, Mitchell K, Pate JS, Cooper JA, Grocott MP, Montgomery HE. Preoperative exercise capacity in adult inflammatory bowel disease sufferers, determined by cardiopulmonary exercise testing. *Int J Colorectal Dis* 2012; **27**: 1485-1491 [PMID: [22842663](#) DOI: [10.1007/s00384-012-1533-4](#)]
- 46 **Lee D**, Lewis JD, Shults J, Baldassano RN, Long J, Herskovitz R, Zemel B, Leonard MB. The Association of Diet and Exercise With Body Composition in Pediatric Crohn's Disease. *Inflamm Bowel Dis* 2018; **24**: 1368-1375 [PMID: [29718224](#) DOI: [10.1093/ibd/izy024](#)]
- 47 **Lee DY**, Wetzsteon RJ, Zemel BS, Shults J, Organ JM, Foster BJ, Herskovitz RM, Foerster DL, Leonard MB. Muscle torque relative to cross-sectional area and the functional muscle-bone unit in children and adolescents with chronic disease. *J Bone Miner Res* 2015; **30**: 575-583 [PMID: [25264231](#) DOI: [10.1002/jbmr.2375](#)]
- 48 **Salacinski AJ**, Regueiro MD, Broeder CE, McCrory JL. Decreased neuromuscular function in Crohn's disease patients is not associated with low serum vitamin D levels. *Dig Dis Sci* 2013; **58**: 526-533 [PMID: [22949179](#) DOI: [10.1007/s10620-012-2372-4](#)]
- 49 **Zaltman C**, Braulio VB, Outeiral R, Nunes T, de Castro CL. Lower extremity mobility limitation and impaired muscle function in women with ulcerative colitis. *J Crohns Colitis* 2014; **8**: 529-535 [PMID: [24315794](#) DOI: [10.1016/j.crohns.2013.11.006](#)]
- 50 **Geerling BJ**, Badart-Smook A, Stockbrügger RW, Brummer RJ. Comprehensive nutritional status in patients with long-standing Crohn disease currently in remission. *Am J Clin Nutr* 1998; **67**: 919-926 [PMID: [9583850](#) DOI: [10.1093/ajcn/67.5.919](#)]
- 51 **Jones K**, Baker K, Speight RA, Thompson NP, Tew GA. Randomised clinical trial: combined impact and resistance training in adults with stable Crohn's disease. *Aliment Pharmacol Ther* 2020; **52**: 964-975 [PMID: [33119156](#) DOI: [10.1111/apt.16002](#)]
- 52 **Geerling BJ**, Badart-Smook A, Stockbrügger RW, Brummer RJ. Comprehensive nutritional status in recently diagnosed patients with inflammatory bowel disease compared with population controls. *Eur J Clin Nutr* 2000; **54**: 514-521 [PMID: [10878655](#) DOI: [10.1038/sj.ejcn.1601049](#)]
- 53 **Mählmann L**, Gerber M, Furlano RI, Legeret C, Kalak N, Holsboer-Trachsler E, Brand S. Aerobic exercise training in children and adolescents with inflammatory bowel disease: Influence on psychological functioning, sleep and physical performance – An exploratory trial. *Ment Health Phys Act* 2017; **13**: 30-39 [DOI: [10.1016/j.mhpa.2017.09.002](#)]
- 54 **Trivić I**, Sila S, Mišak Z, Niseteo T, Batoš AT, Hojsak I, Kolaček S. Impact of an exercise program in children with inflammatory bowel disease in remission. *Pediatr Res* 2023; **93**: 1999-2004 [PMID: [36319697](#) DOI: [10.1038/s41390-022-02362-8](#)]
- 55 **Zhao J**, Huang Y, Yu X. Effects of nutritional supplement and resistance training for sarcopenia in patients with inflammatory bowel disease: A randomized controlled trial. *Medicine (Baltimore)* 2022; **101**: e330386 [PMID: [36042627](#) DOI: [10.1097/MD.00000000000030386](#)]
- 56 **Cronin O**, Barton W, Moran C, Sheehan D, Whiston R, Nugent H, McCarthy Y, Molloy CB, O'Sullivan O, Cotter PD, Molloy MG, Shanahan F. Moderate-intensity aerobic and resistance exercise is safe and favorably influences body composition in patients with quiescent Inflammatory Bowel Disease: a randomized controlled cross-over trial. *BMC Gastroenterol* 2019; **19**: 29 [PMID: [30755154](#) DOI: [10.1186/s12876-019-0952-x](#)]
- 57 **van Erp LW**, Roosenboom B, Komdeur P, Dijkstra-Heida W, Wisse J, Horjus Talabur Horje CS, Liem CS, van Cingel REH, Wahab PJ, Groenen MJM. Improvement of Fatigue and Quality of Life in Patients with Quiescent Inflammatory Bowel Disease Following a Personalized Exercise Program. *Dig Dis Sci* 2021; **66**: 597-604 [PMID: [32239380](#) DOI: [10.1007/s10620-020-06222-5](#)]
- 58 **Seeger WA**, Thieringer J, Esters P, Allmendinger B, Stein J, Schulze H, Dignass A. Moderate endurance and muscle training is beneficial and safe in patients with quiescent or mildly active Crohn's disease. *United European Gastroenterol J* 2020; **8**: 804-813 [PMID: [32580666](#) DOI: [10.1177/2050640620936383](#)]
- 59 **Tew GA**, Leighton D, Carpenter R, Anderson S, Langmead L, Ramage J, Faulkner J, Coleman E, Fairhurst C, Seed M, Bottoms L. High-intensity interval training and moderate-intensity continuous training in adults with Crohn's disease: a pilot randomised controlled trial. *BMC Gastroenterol* 2019; **19**: 19 [PMID: [30696423](#) DOI: [10.1186/s12876-019-0936-x](#)]
- 60 **Loudon CP**, Corroll V, Butcher J, Rawsthorne P, Bernstein CN. The effects of physical exercise on patients with Crohn's disease. *Am J Gastroenterol* 1999; **94**: 697-703 [PMID: [10086654](#) DOI: [10.1111/j.1572-0241.1999.00939.x](#)]
- 61 **Bottoms L**, Leighton D, Carpenter R, Anderson S, Langmead L, Ramage J, Faulkner J, Coleman E, Fairhurst C, Seed M, Tew G. Affective and enjoyment responses to 12 wk of high intensity interval training and moderate continuous training in adults with Crohn's disease. *PLoS One* 2019; **14**: e0222060 [PMID: [31539378](#) DOI: [10.1371/journal.pone.0222060](#)]
- 62 **Fagan G**, Osborne H, Schultz M. Physical Activity in Patients with Inflammatory Bowel Disease: A Cross-Sectional Study. *Inflamm Intest Dis* 2021; **6**: 61-69 [PMID: [34124177](#) DOI: [10.1159/000511212](#)]
- 63 **Hlatky MA**, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, Cobb FR, Pryor DB. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 1989; **64**: 651-654 [PMID: [2782256](#) DOI: [10.1016/0002-9149\(89\)90496-7](#)]

- 64 **Hoogeboom TJ**, Kousemaker MC, van Meeteren NL, Howe T, Bo K, Tugwell P, Ferreira M, de Bie RA, van den Ende CH, Stevens-Lapsley JE. i-CONTENT tool for assessing therapeutic quality of exercise programs employed in randomised clinical trials. *Br J Sports Med* 2021; **55**: 1153-1160 [PMID: 33144350 DOI: 10.1136/bjsports-2019-101630]
- 65 **Bak MTJ**, Ruitkamp MFE, van Ruler O, Campmans-Kuijpers MJE, Bongers BC, van Meeteren NLU, van der Woude CJ, Stassen LPS, de Vries AC. Prehabilitation prior to intestinal resection in Crohn's disease patients: An opinion review. *World J Gastroenterol* 2022; **28**: 2403-2416 [PMID: 35979261 DOI: 10.3748/wjg.v28.i22.2403]
- 66 **Berkel AEM**, Bongers BC, Kotte H, Weltevreden P, de Jongh FHC, Eijsvogel MMM, Wymenga M, Bigirwamungu-Bargeman M, van der Palen J, van Det MJ, van Meeteren NLU, Klaase JM. Effects of Community-based Exercise Prehabilitation for Patients Scheduled for Colorectal Surgery With High Risk for Postoperative Complications: Results of a Randomized Clinical Trial. *Ann Surg* 2022; **275**: e299-e306 [PMID: 33443905 DOI: 10.1097/SLA.0000000000004702]
- 67 **Barberan-García A**, Ubré M, Roca J, Lacy AM, Burgos F, Risco R, Momblán D, Balust J, Blanco I, Martínez-Pallí G. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. *Ann Surg* 2018; **267**: 50-56 [PMID: 28489682 DOI: 10.1097/SLA.0000000000002293]
- 68 **Sedgwick P**, Greenwood N. Understanding the Hawthorne effect. *BMJ* 2015; **351**: h4672 [PMID: 26341898 DOI: 10.1136/bmj.h4672]
- 69 **Bilski J**, Brzozowski B, Mazur-Bialy A, Sliwowski Z, Brzozowski T. The role of physical exercise in inflammatory bowel disease. *Biomed Res Int* 2014; **2014**: 429031 [PMID: 24877092 DOI: 10.1155/2014/429031]
- 70 **Ploeger H**, Obeid J, Nguyen T, Takken T, Issenman R, de Greef M, Timmons B. Exercise and inflammation in pediatric Crohn's disease. *Int J Sports Med* 2012; **33**: 671-679 [PMID: 22562735 DOI: 10.1055/s-0032-1304323]
- 71 **Ohrström M**, Jansson O, Wohlfart B, Ekelund M. Working capacity and resting energy expenditure after ileal pouch-anal anastomosis. *Br J Surg* 2004; **91**: 618-624 [PMID: 15122615 DOI: 10.1002/bjs.4519]
- 72 **Jensen MB**, Houborg KB, Vestergaard P, Kissmeyer-Nielsen P, Mosekilde L, Laurberg S. Improved physical performance and increased lean tissue and fat mass in patients with ulcerative colitis four to six years after ileoanal anastomosis with a J-pouch. *Dis Colon Rectum* 2002; **45**: 1601-1607 [PMID: 12473882 DOI: 10.1007/s10350-004-7246-1]
- 73 **Brevinge H**, Berglund B, Bosaeus I, Tölli J, Nordgren S, Lundholm K. Exercise capacity in patients undergoing proctocolectomy and small bowel resection for Crohn's disease. *Br J Surg* 1995; **82**: 1040-1045 [PMID: 7648147 DOI: 10.1002/bjs.1800820813]
- 74 **Zhang Y**, Zhang L, Gao X, Dai C, Huang Y, Wu Y, Zhou W, Cao Q, Jing X, Jiang H, Zhu W, Wang X. Validation of the GLIM criteria for diagnosis of malnutrition and quality of life in patients with inflammatory bowel disease: A multicenter, prospective, observational study. *Clin Nutr* 2022; **41**: 1297-1306 [PMID: 35537380 DOI: 10.1016/j.clnu.2022.04.016]
- 75 **Cabalzar AL**, Azevedo FM, Lucca FA, Reboredo MM, Malaguti C, Chebli JMF. Physical activity in daily life, exercise capacity and quality of life in patients with crohn's disease on infliximab-induced remission: a preliminary study. *Arq Gastroenterol* 2019; **56**: 351-356 [PMID: 31618395 DOI: 10.1590/S0004-2803.201900000-65]
- 76 **Cabalzar AL**, Oliveira DJF, de Moura Reboredo M, Lucca FA, Chebli JMF, Malaguti C. Muscle function and quality of life in the Crohn's disease. *Fisioterapia em Movimento* 2017; **30**: 337-345
- 77 **Sarli B**, Dogan Y, Poyrazoglu O, Baktir AO, Eyvaz A, Altinkaya E, Tok A, Donudurmaci E, Ugurlu M, Ortakoyluoglu A, Saglam H, Arinc H. Heart Rate Recovery Is Impaired in Patients with Inflammatory Bowel Diseases. *Med Princ Pract* 2016; **25**: 363-367 [PMID: 27164968 DOI: 10.1159/000446318]
- 78 **Fiorindi C**, Cuffaro F, Piemonte G, Cricchio M, Addasi R, Dragoni G, Scaringi S, Nannoni A, Ficari F, Giudici F. Effect of long-lasting nutritional prehabilitation on postoperative outcome in elective surgery for IBD. *Clin Nutr* 2021; **40**: 928-935 [PMID: 32684485 DOI: 10.1016/j.clnu.2020.06.020]
- 79 **Subramaniam K**, Fallon K, Ruut T, Lane D, McKay R, Shadbolt B, Ang S, Cook M, Platten J, Pavli P, Taupin D. Infliximab reverses inflammatory muscle wasting (sarcopenia) in Crohn's disease. *Aliment Pharmacol Ther* 2015; **41**: 419-428 [PMID: 25580985 DOI: 10.1111/apt.13058]
- 80 **Altowati MMA**, Shepherd S, McMillan M, McGrogan P, Russell R, Ahmed SF, Wong SC. Persistence of Muscle-bone Deficits Following Anti-tumour Necrosis Factor Therapy in Adolescents With Crohn Disease. *J Pediatr Gastroenterol Nutr* 2018; **67**: 738-744 [PMID: 30052566 DOI: 10.1097/MPG.0000000000002099]
- 81 **Asscher VER**, Waars SN, van der Meulen-de Jong AE, Stuyt RJJ, Baven-Pronk AMC, van der Marel S, Jacobs RJ, Haans JJJ, Meijer LJ, Klijnsma-Slagboom JD, Duin MH, Peters MER, Lee-Kong FVYL, Provoost NE, Tijdean F, van Dijk KT, Wieland MWM, Versteegen MGM, van der Meijis ME, Maan ADI, van Deudekom FJ, Mooijaart SP, Maljaars PWJ. Deficits in Geriatric Assessment Associate With Disease Activity and Burden in Older Patients With Inflammatory Bowel Disease. *Clin Gastroenterol Hepatol* 2022; **20**: e1006-e1021 [PMID: 34153476 DOI: 10.1016/j.cgh.2021.06.015]
- 82 **Bin CM**, Flores C, Alvares-da-Silva MR, Francesconi CF. Comparison between handgrip strength, subjective global assessment, anthropometry, and biochemical markers in assessing nutritional status of patients with Crohn's disease in clinical remission. *Dig Dis Sci* 2010; **55**: 137-144 [PMID: 19229617 DOI: 10.1007/s10620-008-0692-1]
- 83 **Bryant RV**, Ooi S, Schultz CG, Goess C, Grafton R, Hughes J, Lim A, Bartholomeusz FD, Andrews JM. Low muscle mass and sarcopenia: common and predictive of osteopenia in inflammatory bowel disease. *Aliment Pharmacol Ther* 2015; **41**: 895-906 [PMID: 25753216 DOI: 10.1111/apt.13156]
- 84 **Casanova MJ**, Chaparro M, Molina B, Merino O, Batanero R, Dueñas-Sadornil C, Robledo P, García-Albert AM, Gómez-Sánchez MB, Calvet X, Trallero MDR, Montoro M, Vázquez I, Charro M, Barragán A, Martínez-Cerezo F, Megias-Rangil I, Huguet JM, Martí-Bonmati E, Calvo M, Campderá M, Muñoz-Vicente M, Merchante A, Ávila AD, Serrano-Aguayo P, De Francisco R, Hervías D, Bujanda L, Rodriguez GE, Castro-Laria L, Barreiro-de Acosta M, Van Domselaar M, Ramirez de la Piscina P, Santos-Fernández J, Algaba A, Torra S, Pozzati L, López-Serrano P, Arribas MDR, Rincón ML, Peláez AC, Castro E, García-Herola A, Santander C, Hernández-Alonso M, Martín-Noguerol E, Gómez-Lozano M, Monedero T, Villoria A, Figuerola A, Castaño-García A, Banales JM, Díaz-Hernández L, Argüelles-Arias F, López-Díaz J, Pérez-Martínez I, García-Talavera N, Nuevo-Siguairo OK, Riestra S, Gisbert JP. Prevalence of Malnutrition and Nutritional Characteristics of Patients With Inflammatory Bowel Disease. *J Crohns Colitis* 2017; **11**: 1430-1439 [PMID: 28981652 DOI: 10.1093/ecco-jcc/jjx102]
- 85 **Cioffi I**, Marra M, Imperatore N, Pagano MC, Santarpia L, Alfonsi L, Testa A, Sammarco R, Contaldo F, Castiglione F, Pasanisi F. Assessment of bioelectrical phase angle as a predictor of nutritional status in patients with Crohn's disease: A cross sectional study. *Clin Nutr* 2020; **39**: 1564-1571 [PMID: 31303525 DOI: 10.1016/j.clnu.2019.06.023]
- 86 **Davies A**, Nixon A, Tshintzas K, Stephens FB, Moran GW. Skeletal muscle anabolic and insulin sensitivity responses to a mixed meal in adult patients with active Crohn's disease. *Clin Nutr ESPEN* 2021; **41**: 305-313 [PMID: 33487282 DOI: 10.1016/j.clnesp.2020.11.014]

- 87 **Davies A**, Nixon A, Muhammed R, Tsintzas K, Kirkham S, Stephens FB, Moran GW. Reduced skeletal muscle protein balance in paediatric Crohn's disease. *Clin Nutr* 2020; **39**: 1250-1257 [PMID: 31178247 DOI: 10.1016/j.clnu.2019.05.017]
- 88 **Jansen I**, Prager M, Valentini L, Büning C. Inflammation-driven malnutrition: a new screening tool predicts outcome in Crohn's disease. *Br J Nutr* 2016; **116**: 1061-1067 [PMID: 27546478 DOI: 10.1017/S0007114516003044]
- 89 **Knudsen AW**, Naver A, Bisgaard K, Nordgaard-Lassen I, Becker U, Krag A, Slinde F. Nutrition impact symptoms, handgrip strength and nutritional risk in hospitalized patients with gastroenterological and liver diseases. *Scand J Gastroenterol* 2015; **50**: 1191-1198 [PMID: 25876708 DOI: 10.3109/00365521.2015.1028994]
- 90 **Lee N**, Radford-Smith GL, Forwood M, Wong J, Taaffe DR. Body composition and muscle strength as predictors of bone mineral density in Crohn's disease. *J Bone Miner Metab* 2009; **27**: 456-463 [PMID: 19333683 DOI: 10.1007/s00774-009-0059-5]
- 91 **Lu ZL**, Wang TR, Qiao YQ, Zheng Q, Sun Y, Lu JT, Han XX, Fan ZP, Ran ZH. Handgrip Strength Index Predicts Nutritional Status as a Complement to Body Mass Index in Crohn's Disease. *J Crohns Colitis* 2016; **10**: 1395-1400 [PMID: 27402912 DOI: 10.1093/ecco-jcc/jjw121]
- 92 **Marra M**, Di Vincenzo O, Cioffi I, Sammarco R, Scafì L, Pasanisi F. The Relationship between Body Composition and Physical Activity in Patients with Crohn's Disease. In: 7th International Conference on Sport Sciences Research and Technology Support; 2019 Sep 20-21; Austria
- 93 **Norman K**, Kirchner H, Lochs H, Pirlich M. Malnutrition affects quality of life in gastroenterology patients. *World J Gastroenterol* 2006; **12**: 3380-3385 [PMID: 16733855 DOI: 10.3748/wjg.v12.i21.3385]
- 94 **Tsiountsioura M**, Wong JE, Upton J, McIntyre K, Dimakou D, Buchanan E, Cardigan T, Flynn D, Bishop J, Russell RK, Barclay A, McGrogan P, Edwards C, Gerasimidis K. Detailed assessment of nutritional status and eating patterns in children with gastrointestinal diseases attending an outpatients clinic and contemporary healthy controls. *Eur J Clin Nutr* 2014; **68**: 700-706 [PMID: 24424079 DOI: 10.1038/ejcn.2013.286]
- 95 **Ünal NG**, Oruç N, Tomey O, Ömer Özütemiz A. Malnutrition and sarcopenia are prevalent among inflammatory bowel disease patients with clinical remission. *Eur J Gastroenterol Hepatol* 2021; **33**: 1367-1375 [PMID: 33470696 DOI: 10.1097/MEG.0000000000002044]
- 96 **Valentini L**, Schaper L, Buning C, Hengstermann S, Koernicke T, Tillinger W, Guglielmi FW, Norman K, Buhner S, Ockenga J, Pirlich M, Lochs H. Malnutrition and impaired muscle strength in patients with Crohn's disease and ulcerative colitis in remission. *Nutrition* 2008; **24**: 694-702 [PMID: 18499398 DOI: 10.1016/j.nut.2008.03.018]
- 97 **Werkstetter KJ**, Ullrich J, Schatz SB, Prell C, Koletzko B, Koletzko S. Lean body mass, physical activity and quality of life in paediatric patients with inflammatory bowel disease and in healthy controls. *J Crohns Colitis* 2012; **6**: 665-673 [PMID: 22398103 DOI: 10.1016/j.crohns.2011.11.017]
- 98 **Wiroth JB**, Filippi J, Schneider SM, Al-Jaouani R, Horvais N, Gavarry O, Bermon S, Hébuterne X. Muscle performance in patients with Crohn's disease in clinical remission. *Inflamm Bowel Dis* 2005; **11**: 296-303 [PMID: 15735436 DOI: 10.1097/01.mib.0000160810.76729.9c]
- 99 **Steell L**, Johnston BA, Dewantoro D, Foster JE, Gaya DR, Macdonald J, McMillan M, Russell RK, Seenan JP, Ahmed SF, Gray SR, Wong SC. Muscle deficits with normal bone microarchitecture and geometry in young adults with well-controlled childhood-onset Crohn's disease. *Eur J Gastroenterol Hepatol* 2020; **32**: 1497-1506 [PMID: 32675776 DOI: 10.1097/MEG.0000000000001838]
- 100 **Yamamoto H**, Takeshima F, Haraguchi M, Akazawa Y, Matsushima K, Kitayama M, Ogihara K, Tabuchi M, Hashiguchi K, Yamaguchi N, Miyaaki H, Kondo H, Nakao K. High serum concentrations of growth differentiation factor-15 and their association with Crohn's disease and a low skeletal muscle index. *Sci Rep* 2022; **12**: 6591 [PMID: 35449185 DOI: 10.1038/s41598-022-10587-0]
- 101 **Bian D**, Liu X, Wang C, Jiang Y, Gu Y, Zhong J, Shi Y. Association between Dietary Inflammatory Index and Sarcopenia in Crohn's Disease Patients. *Nutrients* 2022; **14** [PMID: 35215553 DOI: 10.3390/nu14040901]
- 102 **Hradsky O**, Soucek O, Maratova K, Matyskova J, Copova I, Zarubova K, Bronsky J, Sumnik Z. Supplementation with 2000 IU of Cholecalciferol Is Associated with Improvement of Trabecular Bone Mineral Density and Muscle Power in Pediatric Patients with IBD. *Inflamm Bowel Dis* 2017; **23**: 514-523 [PMID: 28267045 DOI: 10.1097/MIB.0000000000001047]
- 103 **Maratova K**, Hradsky O, Matyskova J, Copova I, Soucek O, Sumnik Z, Bronsky J. Musculoskeletal system in children and adolescents with inflammatory bowel disease: normal muscle force, decreased trabecular bone mineral density and low prevalence of vertebral fractures. *Eur J Pediatr* 2017; **176**: 1355-1363 [PMID: 28840427 DOI: 10.1007/s00431-017-2988-7]
- 104 **Ward LM**, Ma J, Rauch F, Benchimol EI, Hay J, Leonard MB, Matzinger MA, Shenouda N, Lentle B, Cosgrove H, Scharke M, Konji VN, Mack DR. Musculoskeletal health in newly diagnosed children with Crohn's disease. *Osteoporos Int* 2017; **28**: 3169-3177 [PMID: 28791436 DOI: 10.1007/s00198-017-4159-0]
- 105 **Koch B**, Schäper C, Ittermann T, Spielhagen T, Dörr M, Völzke H, Opitz CF, Ewert R, Gläser S. Reference values for cardiopulmonary exercise testing in healthy volunteers: the SHIP study. *Eur Respir J* 2009; **33**: 389-397 [PMID: 18768575 DOI: 10.1183/09031936.00074208]
- 106 **Fairbairn MS**, Blackie SP, McElvaney NG, Wiggs BR, Paré PD, Pardy RL. Prediction of heart rate and oxygen uptake during incremental and maximal exercise in healthy adults. *Chest* 1994; **105**: 1365-1369 [PMID: 8181321 DOI: 10.1378/chest.105.5.1365]
- 107 **Tew GA**, Carpenter R, Seed M, Anderson S, Langmead L, Fairhurst C, Bottoms L. Feasibility of high-intensity interval training and moderate-intensity continuous training in adults with inactive or mildly active Crohn's disease: study protocol for a randomised controlled trial. *Pilot Feasibility Stud* 2017; **3**: 17 [PMID: 28373911 DOI: 10.1186/s40814-017-0133-z]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

