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Authors' Affiliation:
[1]Copernicus Memorial Hospital, Pabianicka 62, 93-513, Łódź, Poland; Orcid: 0009-0003-5289-0842; Email: wojdal5@gmail.com
[2]Rydygier Specialist Hospital in Krakow, Osiedle Złotej Jesieni 1, 31-820 Kraków, Poland; Orcid: 0009-0007-2530-689X; Email: katarzynacieplucha@outlook.com
[3]University Clinical Hospital No. 1 of the Medical University of Lodz, Kopcińskiego 22, 90-153 Łódź, Poland; Orcid: 0009-0005-6855-0660; Email: ola.wadolowska98@gmail.com
[4]University Clinical Hospital No. 2 of the Medical University of Lodz; Stefana Żeromskiego 113, 90-549 Łódź, Poland; Orcid: 0009-0005-4342-5468; Email: bp.przybyl@gmail.com
[5]Hospital of the Ministry of Interior and Administration in Lodz, Północna 42, 91–425 Łódź: Lodz, Poland; Orcid: 0009-0001-3159-1371; Email: zuzanna.mogilany@outlook.com
[6]University Clinical Hospital No. 2 of the Medical University of Lodz: Łódź, ul. Stefana Żeromskiego 113, 90-549 Łódź, Poland; Orcid: 0009-0000-5989-4385; Email: b.serafin.juszczak@gmail.com
[7]Central Clinical Hospital of Medical University of Lodz; Pomorska 251, 92-213 Łódź, Poland; Orcid: 0009 0005-2422-429X; Email: karolina.m.kusek@gmail.com
[8]Rydygier Specialist Hospital in Krakow; Osiedle Złotej Jesieni 1, 31-820 Kraków, Poland; Orcid: 0009-0002-1216-9973; Email: mariamirandawydra@gmail.com
[9]Central Clinical Hospital, of Medical University of Lodz; Pomorska 251, Łódź, Poland; Orcid: 0009-0005-1924-6208; Email: michaljanwilk@gmail.com
[10]St. Raphael's Voivodeship Specialist Hospital in Czerwona Góra, Czerwona Góra 10, 26-060 Chęciny, Poland; Orcid: 0009-0005-4331-1807; Email: daniel.narozniak@gmail.com

*Corresponding author:
Jan Wojdal, Copernicus Memorial Hospital, Pabianicka 62, 93-513, Łódź, Poland; Email: wojdal5@gmail.com

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DISCOVERY SCIENTIFIC SOCIETY

Crohn's Disease - Role of Diet and Physical Activity in Inducing and Maintaining Remission

Jan Wojdal[1]*, Katarzyna Ciepłucha[2], Aleksandra Wądołowska[3], Barbara Przybył[4], Zuzanna Mogilany[5], Blanka Serafin-Juszczak[6], Karolina Kusek[7], Maria Wydra[8], Michał Wilk[9], Daniel Narożniak[10]

ABSTRACT

Background: Diet and physical activity are modifiable factors recommended to assist pharmacotherapy in Crohn's Disease (CD); however, their relative effectiveness and underlying mechanisms remain insufficiently understood. Methods: We systematically searched PubMed, Scopus, and Google Scholar (Jan 2005 – Mar 2025) for randomised controlled trials, cohort studies, and systematic reviews comparing exclusive enteral nutrition (EEN), partial enteral nutrition (PEN), the Crohn's Disease Exclusion Diet (CDED ± PEN), or goal-directed exercise interventions. Results: EEN induced remission in 60-85% of paediatric and 50-65% of adult patients and achieved the highest early mucosal healing rates. CDED + 50% PEN achieved comparable week-6 remission and superior 12-week steroid-free durability (76 % vs 45 % with EEN). PEN alone maintained remission but was inferior for primary induction (~40%). The RTC showed that walking, moderate continuous training, high-intensity interval training, and impact-resistance programs were safe in quiescent CD, improved VO_2peak, muscle strength, and bone mineral density, and did not precipitate relapse. Higher habitual activity levels lowered the risk of six-month flare-ups. Conclusion: EEN and CDED+PEN are the most effective non-pharmacological induction regimens, while CDED offers better long-term adherence. Structured aerobic and resistance exercises are safe and offer functional advantages, but their effect on mucosal remission requires confirmation. To improve personalised maintenance algorithms, we need large randomised controlled trials (RCTs) that combine exercise with a standardised diet.

Keywords: Crohn's Disease; Exclusive Enteral Nutrition; Partial Enteral Nutrition; Crohn's Disease Exclusion Diet; Exercise Therapy.

1. INTRODUCTION

One of the most well-known chronic inflammatory bowel diseases is Crohn's Disease (CD), which affects the gastrointestinal tract, as well as the joints, skin, eyes, and hepatobiliary system. The inflammatory process of the mucosa leads to

malnutrition as well as fibrostenotic blockage and penetrating fistulae, which create obstacles for children's growth and reduce their quality of life across all age groups (Gajendran et al., 2018). Most patients experience persistent treatment failure or develop drug intolerance or fatigue after therapeutic advancement. It is evident that optimising non-pharmacological approaches for attaining and sustaining remission is essential (Mills et al., 2011; Ashton et al., 2019). Patients' disease behaviour is chiefly influenced by diet and physical activity, which are two modifiable factors (Goens et al., 2020). Western diets can lead to dysbiosis, damage to epithelial barriers, and increased innate immune responses. But omega-3 fatty acids, as well as fiber, fruits, and vegetables, are protective factors (Hashash et al., 2024). Over the last decade, doctors have formulated three diets: Exclusive Enteral Nutrition (EEN), partial enteral nutrition (PEN), and the Crohn's Disease Exclusion Diet (CDED)- to induce and maintain remission. The implementation of these diets produces diverse outcomes among child and adult populations, which continue to be studied by many scientific researchers (Verburgt et al., 2021).

The dietary impact on gut microbiota and immunomodulation effects of these diets continues to be investigated (Hashash et al., 2024). The medical community remains active in debating the use of physical exercise in Crohn's Disease, despite its growing relevance to discussions on remission (Pedersen and Febbraio, 2012). Crohn's Disease also poses significant physical and psychological challenges to its patients, but the sports aspects of the disease are accorded minimal priority (Tew et al., 2019). Studies on walking, resistance training, and interval training demonstrate the safety of these interventions and their favorable impacts on fitness level, bone mineral density, and reduction in fatigue, with no disease relapses (Jones et al., 2020; Pedersen and Febbraio, 2012). The studies have not demonstrated the impact on mucosal function. The contraction of skeletal muscle releases myokines, including interleukin-6, which have anti-inflammatory effects. The targeted exercise approach has been shown to be beneficial for patients with CD in achieving remission status, according to Clarke et al., (2014). Further research is essential to determine the effects of physical activity on disease progression, as initial trials have demonstrated promising outcomes.

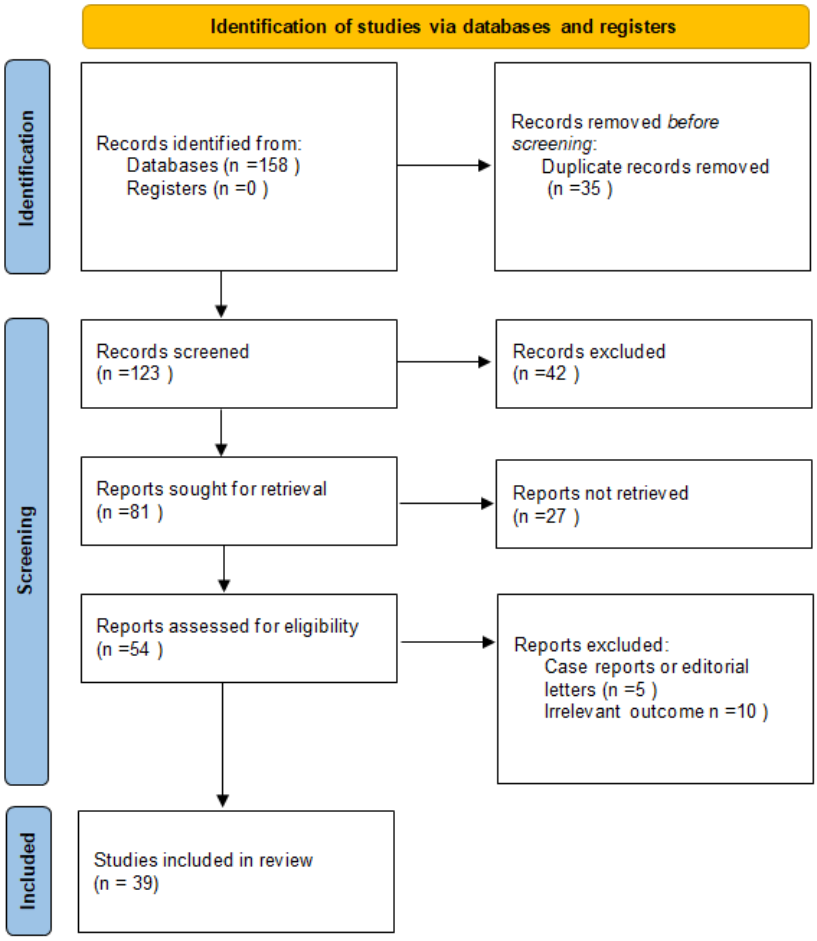

Figure 1. Prisma flow chart of selected studies

This review aims to compile recent evidence on exercise and dietary therapies used to induce and maintain remission in patients with CD. It clarifies the scientific basis of particular nutritional exclusions and supplements and compares the effectiveness and practicality profiles of formula-based versus whole-food interventions in both pediatric and adult populations.

2. REVIEW METHODS

The researchers conducted a systematic review by analyzing publications from the past 20 years using the PubMed, Scopus, and Google Scholar databases. The analysis focused on three types of research studies, including original randomized trials, prospective and retrospective cohort studies, and case-control investigations. The research included studies which: (a) Used a predetermined dietary approach to induce or sustain remission in Crohn's Disease and documented clinical or biochemical or endoscopic remission results; or (b) Used a standardised exercise protocol with defined parameters of intensity, frequency and duration to measure valid disease activity indices, inflammatory markers or functional outcomes (bone mineral density, cardiorespiratory fitness, muscle strength, fatigue or health-related quality of life). The review excluded all articles that presented as reviews, comments, editorials, letters, or case reports. The researchers extracted data on Crohn's specific subgroup from inflammatory bowel disease studies that examined collective results. Article screening was conducted in accordance with the PRISMA guidelines, resulting in the selection of 39 studies (Figure 1).

3. RESULTS & DISCUSSION

3.1. Biological Basis for Lifestyle Intervention

Gut–immune–microbiota axis

The genetically predisposed immune system of some individuals evolves to respond excessively to imbalances in intestinal microbiota, leading to the development of Crohn's Disease. It has two main features: depletion of Faecalibacterium prausnitzii and other SCFA-producing species, and expansion of Proteobacteria, resulting in the disruption of tight junctions, increased microbial translocation, and Th1/Th17-biased inflammation (Svolos et al., 2019).

SCFAs, barrier integrity, and immune regulation

SCFAs, particularly butyrate, are being fed to colonocyte communities, solidifying epithelial junctional complexes and promoting mucus secretion, while also provoking regulatory T-cell differentiation and inhibiting NFκB signaling. Reduced SCFA availability in Inflammatory Bowel Disease (IBD) comes with an impaired barrier state and enhanced inflammatory response (Levine et al., 2020).

Modulation through diet of these pathways

Diet is the strongest day-to-day controller of microbiota structure and metabolite production. The Crohn's Disease Exclusion Diet (CDED) and Exclusion Enteral Nutrition (EEN) eliminate emulsifiers and other inflammatory additives while restoring normal macronutrient intake (Ng et al., 2007). The diets have been proven not only to shift microbiota towards butyrate producers but also to decrease inflammatory biomarkers (faecal calprotectin and C-reactive protein) and, in some studies, mucosal cytokine expression (Nasser et al., 2024).

Systemic inflammation, body composition, and exercise

Without a doubt, transmural inflammation causes systemic high levels of CRP, TNF-α, and IL-6, which are responsible for disrupting erythropoiesis, mitochondrial metabolism, and muscle protein synthesis. CD patients exhibit reduced aerobic capacity, weaker muscles, and increased fatigue compared to healthy controls (Verburgt et al., 2021). The results of randomized trials involving CD patients show that structured exercise programs help reduce specific impairments without triggering flare-ups: Low-intensity walking improved quality of life (Ng et al., 2007), and HIIT and moderate continuous exercise were well tolerated while increasing VO_2peak (Levine et al., 2019), and a six-month impact/resistance program enhanced lumbar spine bone mineral density and muscle strength and fatigue scores (Szczubełek et al., 2021).

Exercise as an anti-inflammatory and microbiota-modulating factor

Exercise at moderate intensity produces both fitness advantages and systemic anti-inflammatory effects. Skeletal muscle contraction triggers the release of myokines, including IL-6, which mediates endocrine anti-inflammatory action, and IL-10 and irisin, which

suppress NF-κB signaling and promote epithelial repair (Sasson et al., 2021). The literature shows limited evidence about exercise-induced increases in microbial diversity and SCFA production (Schreiner et al., 2020).

Clinical implications

The interaction between exercise and diet interventions has a stronger positive impact on the gut microbiota than the aggregate effect of the two interventions. Exercise has been shown to yield better outcomes, including symptom improvement, improved body composition, and reduced fatigue, compared to the results obtained with standard care (Szczubełek et al., 2021).

3.2. Dietary Strategies

Exclusive Enteral Nutrition (EEN)

Exclusive Enteral Nutrition is a therapeutic regimen in which 100 % of caloric requirements are provided for 6–8 weeks by a nutritionally complete liquid formula (elemental, semi-elemental, or polymeric), administered orally or through a nasogastric tube; all other foods are strictly excluded (Hashash et al., 2024). Energy targets are calculated from age- and weight-based predictive equations, and gradual food reintroduction follows the induction phase (Ashton et al., 2019).

The intervention triggers steroid use and is recommended as the first-line induction treatment in the pediatric CD (Ruemmele et al., 2014). It was first proposed in the early 1970s, when Voitk et al., (1973) reported an improvement of symptoms in adults with elemental formulas. Malchow et al., (1990) affirmed that a defined formula diet, when used, could cause a remission equivalent to that of steroids. Meta-analyses through the 1990s and 2000s established comparable efficacy to steroids in children, shifting practice patterns toward nutrition-based induction (Swaminath et al., 2017). With accumulating evidence for mucosal healing and growth benefits, EEN was incorporated into ECCO/ESPGHAN pediatric guidelines in 2014 (Voitk et al., 1973) and has since been refined into practical protocols widely adopted in Europe, Australia, and Canada (Ashton et al., 2019).

Efficacy of EEN in paediatric Crohn's Disease

Meta-analysis of four randomized trials (n = 144) reported remission of 78% (95% CI 60–90%) at 6–8 weeks (Dziechciarz et al., 2007), while the other combined eight studies (n = 451) showed no difference versus corticosteroids and three-fold higher odds of mucosal healing (Swaminath et al., 2017). Grover et al., (2014) achieved 84% clinical and 67% transmural remission within eight weeks in their cohort study.

Efficacy of EEN in adult Crohn's Disease

A systematic review of 24 studies found remission rates of 50%-65% in the most common presentation of CD (Wall et al., 2013). In more complex disease types, Yang et al., (2017) reported an 80% remission rate at week 12. Other findings include a significant reduction in fistula formation. A prospective study using EEN achieved biochemical and clinical remission in 65% of adults within 6 weeks. For adults, adherence rather than intrinsic efficacy is the primary barrier, with social factors limiting the uptake of a diet (Wall et al., 2013).

Partial Enteral Nutrition (PEN)

PEN is a diet in which a formula supplies approximately 25%-75% of the total energy needs, with the remaining energy provided through a monitored whole-food menu. Unlike EEN, PEN permits limited food consumption, thus keeping the anti-inflammatory benefits of formula feeding while increasing social acceptability and adherence (Sasson et al., 2021). Modern recommendations favor polymeric formulas of about 30-50 kcal/kg/day adjusted to age, nutritional condition, and disease activity (Levine et al., 2020). The concept emerged in the 1990s when researchers showed that formula supplementation prolonged remission in children populations that were previously treated with EEN (Wilschanski et al., 1996). PEN is not as effective as EEN when used as an induction method in children (Swaminath et al., 2017), which led to the introduction of diet-formula hybrid methods.

Efficacy of PEN in paediatric Crohn's Disease

In the Johnson trial, clinical remission (defined by a Pediatric Crohn's Disease Activity Index score of <10) was achieved at week 6 in 42% of patients with PEN versus 79% with EEN. However, both groups showed comparable improvements in weight gain and serum albumin levels (Wall et al., 2018). A later cohort confirmed that supplementary PEN after EEN lengthened relapse-free survival to 12 months and supported linear growth (Wilschanski et al., 1996).

Efficacy of PEN in adult Crohn's Disease

Studies on the adult population highlight a role for PEN in maintenance. Wall et al. reported a 67 % steroid-free remission at week 8 in a mixed EEN/PEN diet (Johnson et al., 2006). Observational studies suggest that adding PEN may enhance the durability of biologic therapy and reduce the risk of recurrence after surgery, although the evidence remains limited (Wall et al., 2018).

Crohn's Disease Exclusion Diet (CDED)

The CDED is a dietary regimen that restricts many of its constituents deemed toxic to the mucous membrane, which can foster dysbiosis or cause innate immune stimulation (Correia et al., 2024). The dietary plan suggests eating fruits, vegetables, rice, potatoes, poultry, and fish, while discouraging the consumption of meats, gluten, lactose, and emulsifiers. During the induction (weeks 0-6), 50% of energy intake comes from a polymeric formula such as Modulen. During the consolidation phase (weeks 7-12), the dose is reduced to 25%, followed by a transition to an unrestricted maintenance phase (Svolos et al., 2019). CDED was conceived by Sigall-Boneh et al., (2014), who combined a targeted food-exclusion list with PEN and achieved high remission in a mixed pediatric-adult cohort. Clinical trials have verified efficacy in patients with refractory conditions who are not responding to biologic therapy (Sigall Boneh et al., 2017). Adults' evidence demonstrates corticosteroid-free remission at week 6 in 63% and sustained efficacy to week 24 (Yanai et al., 2022). A systematic review of 15 trials (n = 475) from 2024 places CDED as the most researched whole-food diet for Crohn's Disease (Zhu et al., 2023).

Efficacy of CDED in paediatric Crohn's Disease

The original 12-week pilot reported remission (PCDAI < 10) in 79% of participants at week 6 and in 84% at week 12. In real-world cohort studies, clinical and biochemical responses within three weeks, as well as mucosal improvement in up to two-thirds of children, have been described (Sigall Boneh et al., 2021).

Efficacy of CDED in adult Crohn's Disease

Sigall Boneh et al., (2017) reported that 62% of patients who did not respond to anti-TNF therapy after six weeks achieved remission on CDED. As Yanai et al., (2022) report, the CDED-AD trial has revealed a 63% clinical remission rate at the end of week 6 and a 54% rate at the end of week 24, along with a parallel reduction in C-reactive protein and faecal calprotectin. Israeli, Spanish, and Polish studies indicate a 58-72% rate of induction remission and good tolerance with single therapy using CDED.

3.3. Comparison results

EEN and PEN

EEN has a better remission rate in the short term as opposed to PEN. In the third stage of clinical trials (phase III), 79.5% of the pediatric population achieved clinical remission following 6 weeks on EEN, and only 41.8% on the PEN regimen. Johnson et al., (2006) highlight that the PEN diet only improves symptoms, whereas EEN is also responsible for suppressing inflammation. A multi-centre North American cohort confirmed these findings: EEN induced remission in 76% of children, PEN in 50%, and normalized faecal calprotectin (FCP) levels more frequently (45% vs. 14%) (Lee et al., 2015).

For adults, PEN is especially explored as a maintenance option. The Japanese randomized control trial showed that providing 50% of energy as elemental formula halved 2-year relapse compared with an unrestricted diet (35% vs. 64%; HR 0.40; 95%CI 0.16-0.98), supporting PEN as a feasible steroid-sparing maintenance strategy when EEN is impractical (Takagi et al., 2006) (Table 1).

Table 1. Comparative effectiveness EEN VS PEN

Article	Main result (EEN vs. PEN)	95 % CI
Johnson et al., 2006	Clinical remission at 6 week: 79.5 % vs. 41.8 %	NR
Lee et al., 2015	Clinical remission at 8 week: 76% vs. 50%; FCP < 250 μg/g: 45 % vs 14 %	NR
Takagi et al., 2006	Two-year relapse: 35 % vs. 64 %; HR 0.40	0.16-0.98

*FCP= Fecal Calprotectin; CI = confidence interval; HR = hazard ratio; NR = not reported.

CDED coupled with PEN VS EEN

The pivotal multicenter trial by Levine et al. randomized 74 children with mild to moderate disease to six weeks of EEN or CDED + 50% PEN, followed by a free diet (EEN arm) or CDED + 25% PEN (CDED arm) through week 12 (Levine et al., 2019). Both diets yielded comparable week-6 remission rates (75% vs. 59%), but CDED maintained corticosteroid-free remission significantly better at week 12 (75.6% vs. 45%). CDED was tolerated by 97.5% of participants compared to 73.7%. Intestinal permeability was normalized in 69% of CDED subjects vs. 56% of EEN subjects. A smaller Slovenian prospective trial comparing an anti-inflammatory diet derived from CDED+PEN with standard EEN reported identical week-6 clinical and endoscopic remission rates (81.8% each) (Urlep et al., 2023). Real-world Croatian data using a modified CDED protocol found no difference in week-6 remission (70 %) and confirmed non-inferiority to EEN in biomarker normalization levels (Niseteo et al., 2022).

Both diets improve weight z-scores and serum albumin. CDED's inclusion of solid food mitigates social isolation and tube-feeding requirements, which explains the higher adherence observed across trials (Correia et al., 2024). Head-to-head trials of CDED + PEN versus EEN are summarized in Table 2.

Table 2. Comparative effectiveness of CDED coupled with PEN VS EEN

Article	**Main result** (CDED coupled with PEN vs. EEN)	95 % CI
Levine et al., 2019	Remission rates at 6 weeks: 75% vs. 59%;	NR
	Sustained corticosteroid-free remission at week 12: 75.6% vs 45.1%	1.34-10.59
	Tolerance: 97.5% vs 73.7%	1.68-115.14
Urlep et al., 2019	Clinical and endoscopic remission at week 6: 81.8% vs. 81.8%	NR
Niseteo et al., 2022	Clinical remission at week 6: 75% vs. 65.9%	NR

NR = not reported;

3.4. Physical Activity in Crohn's Disease

Safety considerations

People in remission or low disease activity can safely exercise with proper, individually adjusted exercise programs (Szczubełek et al., 2021). During active flare phases, it is recommended that patients refrain from intense or impact exercises; however, they can still do low-load mobilizing and respiratory exercises. The pre-exercise assessment should check for corticosteroid exposure that may lead to osteopenia or osteoporosis, evaluate previous fractures and strictures, and assess postoperative status (Verburgt et al., 2021).

Structured exercise interventions in Crohn's Disease

A study of 207 patients found that those who walked at low intensity for 30 minutes, three times a week, for 12 weeks experienced better health-related quality of life and did not experience disease recurrence (Ng, 2007). The combination of impact and resistance training, performed three times a week for six months, resulted in increased bone mineral density (BMD) and muscle strength, while reducing fatigue without increasing disease activity indices (Szczubełek et al., 2021). Details of these exercise trials are presented in Table 3.

Table 3. Practical prescription- FITT summary

Study (year)	**n (CD) / disease status**	**Intervention (FITT)**	**Outcomes assessed**	**Main findings**	**Safety**
Ng et al., 2007	32 (remission/ mild)	Walking, 3 sessions per week, 30 min, 12 weeks (low intensity)	QoL (IBDQ, SF-36); CDAI	↑ QoL on all scales; CDAI unchanged	No flares/ withdrawals

Tew et al., 2019	36 (stable CD)	HIIT: 8 × 1 min at 90 % HRmax + 1 min recovery MICT: 30 min at ~ 65 % HRmax Both 3 sessions per week, 12 weeks	VO_2 peak; feasibility; QoL	Both programmes feasible; VO_2peak ↑ (HIIT > MICT); QoL improved	No serious AEs; no disease exacerbation
Jones et al., 2020	47 (stable CD)	Impact drills + progressive resistance training, 3 sessions per week, 6 months	Lumbar-spine BMD (DXA); muscle strength; fatigue; QoL	↑ BMD (L1–L4); ↑ strength; ↓ fatigue; ↑ QoL	No increase in CDAI or biomarkers

Abbreviations: QoL – quality of life; IBDQ – Inflammatory Bowel Disease Questionnaire; CDAI – Crohn's Disease Activity Index; HIIT – high-intensity interval training; MICT – moderate-intensity continuous training; HRmax – maximal heart rate; VO_2peak – peak oxygen uptake; BMD – bone mineral density; DXA – dual-energy X-ray absorptiometry; AE – adverse event.

Disease activity, biomarkers, and relapse risk

Because sample sizes were small and biomarkers (CRP and faecal calprotectin) were secondary endpoints, the effects on mucosal inflammation remain inconclusive (Ng et al., 2007). In a large prospective cohort of patients in remission, however, higher habitual exercise was associated with a lower 6-month risk of active disease in the Crohn's subgroup (adjusted RR 0.72) (Jones et al., 2020).

Mechanistically, contracting skeletal muscle releases myokines (e.g., interleukin-6 in its endocrine, antiinflammatory role, IL10, irisin) that inhibit NFκB signalling and may support epithelial repair (Sasson et al., 2021). Exercise is also linked to greater gut microbial diversity and the production of SCFAs in humans, although diet is a significant confounder, and data specific to CD are lacking (Schreiner et al., 2020).

Aerobic training (FITT framework)

Aerobic training typically consists of 3 sessions per week for at least 12 weeks, each lasting 30–45 minutes. Intensities ranging from low (comfortable walking) to high (90% HR max) have been tested safely in remission. The study showed increased VO_2 peak, decreased fatigue, and improved QoL, while disease rates remain unchanged (Levine et al., 2019).

Resistance and impact training

Impact-loading exercises and progressive resistance training, three times per week over six months, have shown clinically significant improvements in patients with stable Crohn's Disease. Among these are improvements in lumbar spine bone mineral density (BMD), gains in muscular strength, and reductions in fatigue without triggering disease flares (Jones et al., 2020). These outcomes are consistent with the larger body of exercise literature in IBD that has demonstrated that structured aerobic programmes (both high-intensity interval and moderate-intensity continuous training) are viable, well-tolerated, and help improve cardiorespiratory fitness without exacerbating symptoms (Tew et al., 2019), and that even light-intensity regimens can produce beneficial increases in quality of life (Ng et al., 2007). Mechanistically, skeletal muscle is considered an endocrine organ, and resistance and impact exercise acutely stimulate a myokine milieu (e.g., exercise-induced IL-6, with downstream anti-inflammatory signaling) that can counter systemic inflammation and promote metabolic health (Pedersen et al., 2012). The interaction between exercise and the gut ecosystem has also been studied. Training and diet extremes have been shown to mediate changes in gut microbial diversity and composition, which may be a plausible route through which training contributes to mucosal immunity and host-microbe crosstalk associated with Crohn's Disease (Clarke et al., 2014). A periodized program with the emphasis on multi-joint resistance exercises and the slow introduction of low-to-moderate impact exercises may be prescribed to patients considered at risk of sarcopenia or bone loss induced by glucocorticoids, as long as the disease activity remains stable (Jones et al., 2020). Impact may only be added when the risk of fracture is low and only gradually. In patients with impaired BMD or other predisposing risk factors, treatment commences with low-impact loading and resistance, gradually increasing over time. Programmes must be personalised based on up-to-date fitness, symptom burden, and comorbidities with a close follow-up on tolerance and disease activity (Tew et al., 2019).

Currently, CD-specific data are scarce. Yoga, breathing exercises, and mindfulness have been shown to reduce perceived stress and fatigue in other chronic inflammatory conditions, and may be considered adjuncts, acknowledging the lack of robust CD endpoints.

Gaps and future directions

Primary endpoints seldom include endoscopy or faecal calprotectin, underscoring the need for larger RCTs; the optimal "dose" and modality by phenotype (penetrating vs stricturing CD) remain unknown; no adult RCTs combine structured exercise with standardised diet (EEN/CDED/PEN); and multi-omic studies tracking exercise-induced microbiota/metabolite shifts in CD are lacking.

4. CONCLUSION

EEN and CDED + 50% PEN represent the most effective dietary protocols for treatment, while CDED should be selected when liquid-only adherence is uncertain. PEN (<75% formula with unrestricted food) should not be used for initial induction treatment. The combination of supervised aerobic and resistance training sessions (3–5 times per week at moderate intensity) is safe during remission and enhances fitness levels, bone mineral density, and reduces fatigue; however, the effects on mucosal health require further verification. Research needs to include longer RCTs that link diet with exercise, while separating participants by CD phenotype (structuring vs. penetrating CD), and incorporating endoscopic, microbiome, and metabolomic assessments to develop improved, personalized lifestyle-based maintenance algorithms.

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Author's Contribution

Conceptualization: Barbara Przybył, Karolina Kusek
Methodology: Aleksandra Wądołowska, Jan Wojdal
Formal Analysis: Maria Wydra, Michał Wilk
Sources: Katarzyna Ciepłucha, Blanka Serafin-Juszczak
Visualization: Maria Wydra, Zuzanna Mogilany
Investigation: Karolina Kusek, Aleksandra Wądołowska
Supervision: Blanka Serafin-Juszczak, Daniel Narożniak
Validation: Zuzanna Mogilany, Barbara Przybył
Writing – Original Draft: Jan Wojdal, Michał Wilk
Writing – Review & Editing: Katarzyna Ciepłucha
Project administration: Daniel Narożniak
All authors have read and agreed with the published version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data associated with this work are present in the paper.

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