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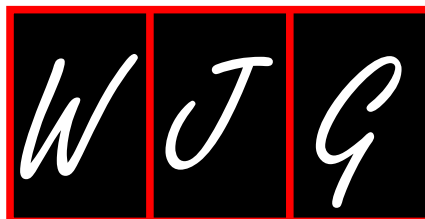
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Non-pharmacological therapies for inflammatory bowel disease: Recommendations for self-care and physician guidance

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Abstract

We performed a scoping review on sought-after complementary therapies for patients with inflammatory bowel disease (IBD), specifically diet, physical activity and exercise (PA/E), and psychotherapy. We aim to update patients with IBD on therapies for self-care and provide physicians with guidance on how to direct their patients for the management of IBD. A search of MEDLINE, EMBASE, and PUBMED was completed in Sept 2016. Studies on diet, PA/E, or psychotherapy in patients with IBD were included. Medical Subject Heading terms and Boolean operators were used. The search was limited to full-text English articles describing an adult population. This review included 67 studies: Diet ($n = 19$); PA/E ($n = 19$); and psychotherapy ($n = 29$). We have made the following recommendations: (1) Diet: Consumption of diets rich in vegetables, fruit and soluble fiber may be beneficial in IBD. A trial of a low FODMAP diet can be considered in those patients with functional gastrointestinal symptoms. Restrictive diets are lacking in evidence and should be avoided; (2) PA/E: Regular low-moderate intensity activity, including cardiovascular and resistance exercise, has been shown to improve quality

of life (QOL) and may improve inflammation; and (3) psychotherapy: Therapies such as cognitive-behavioural interventions, mindfulness, hypnosis, and stress management have been shown to improve QOL, but evidence is limited on their impact on anxiety, depression, and disease activity. Overall, these complementary therapies are promising and should be used to treat patients with IBD from a more holistic perspective.

Key words: Scoping review; Inflammatory bowel disease; Diet; Exercise; Psychotherapy

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Core tip: For diet, consumption of diets rich in vegetables, fruit and soluble fiber may be beneficial in inflammatory bowel disease. A low FODMAP diet can be considered in those patients with functional gastrointestinal symptoms. Restrictive diets are lacking in evidence and should be avoided. Regular low-moderate intensity activity has been shown to improve quality of life (QOL) and may improve inflammation. Therapies such as cognitive-behavioural interventions, mindfulness, hypnosis, and stress management have been shown to improve QOL, but limited evidence shown the impact on anxiety, depression, and disease activity.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract and comprises two main forms: Crohn's disease (CD) and ulcerative colitis (UC). The symptoms of IBD are variable and may include diarrhea, vomiting, rectal bleeding, abdominal pain, weight loss, and malnutrition. Both CD and UC are characterized by periods of inflammation and remission, and the quality of life (QOL) of individuals with IBD may be severely impaired^[1]. Medications treat flares in disease activity, and are usually required to help maintain remission. However, many IBD patients prefer a non-pharmacologic complementary or alternative approach to disease management^[2].

Complementary alternative medicine (CAM) is identified as therapies that are either beyond Western allopathic medicine, not currently a standard therapy, or that are delivered by an alternative practitioner or by self-care^[3]. Internationally, 30%-56% of IBD patients regularly use CAM with reasons for use including a yearning for a sense of control over the disease, ineffectiveness or adverse effects with conventional therapies,

perceived favorable safety profile, and desire for a more holistic approach^[2,4-10]. Such therapies may improve subjective symptoms and QOL^[11,12]. However, lack of communication between patient and doctor regarding CAM use can have serious consequences due to potential interactions and toxicities, unintentional non-adherence, or intentional dosage reduction of the pharmaceutical therapy by the patient^[8-11].

Dietary manipulation, physical activity and exercise (PA/E), and psychological strategies are not mainstream therapies, however such therapies are clinically relevant because they combat high risk environmental factors (*i.e.*, poor nutrition, inactivity, and stress and anxiety) that negatively impact disease activity^[2,13,14]. Unlike other lifestyle therapies such as smoking cessation, there is a lack of clear evidence-based literature that focuses on using diet manipulation, PA/E, and psychological interventions in IBD^[2,7]. The concern is that self-sought CAM may lack an evidence-base or health professionals may fail to make recommendations about CAM leaving patients frustrated^[2,15]. Clear evidence-based guidance to patients and health professionals on CAM would alleviate this problem. The primary purpose of this scoping review is to update patients with IBD on lifestyle therapies for self-care and provide physicians with guidance on how to direct their patients^[15,16]. We include three lifestyle therapies: dietary manipulation, PA/E, and psychological interventions.

A scoping review of Ovid MEDLINE on the effects of diet, PA/E, and psychological interventions on IBD outcomes was performed. The database was searched using the Medical Subject Heading (MSH) terms, Boolean operators, and limitations as shown in Figure 1. Additional limitations applied to the diet section were enteral nutrition and parenteral nutrition, as the focus was on dietary patterns. Similar searches were further run via EMBASE: Excerpta Medica and EMBASE: Classic, PubMed, and PsychINFO.

Figure 2 shows the results of the Ovid MEDLINE search for diet, PA/E, and psychotherapy. After limitations were applied, a single expert reviewer for diet (NH), PA/E (WD), and psychotherapy (GP) screened results. Figure 3 shows the results of the EMBASE: Excerpta Medica and EMBASE: Classic search for additional articles. For diet, an additional 14 articles beyond those already included were identified *via* bibliographies or PubMed. For PA/E, an additional 5 articles beyond those already included were identified *via* bibliographies and no additional articles were identified *via* PubMed. For psychotherapy, an additional 5 articles beyond those already included were identified *via* bibliographies and no additional articles were identified *via* PubMed or PsychINFO.

DIET

Patients with IBD view diet modification as an important treatment modality to holistically manage their disease^[17]. Several small scale diet studies demonstrated improved disease activity and prolonged time to re-

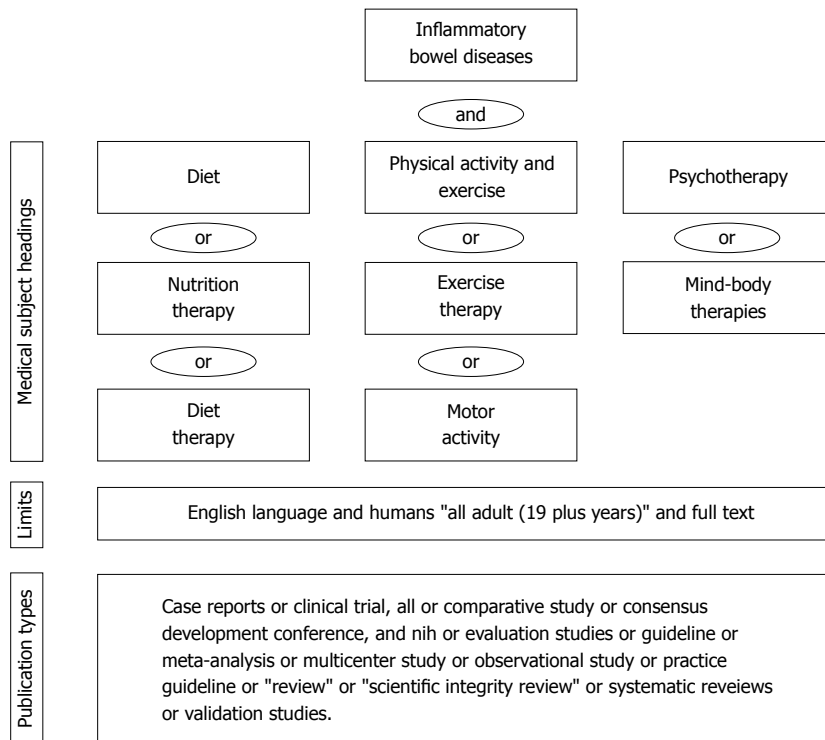


Figure 1 Ovid MEDLINE literature search strategy. Similar searches were run within EMBASE: Excerpta Medica and EMBASE: Classic, PubMed, and PsychINFO databases.

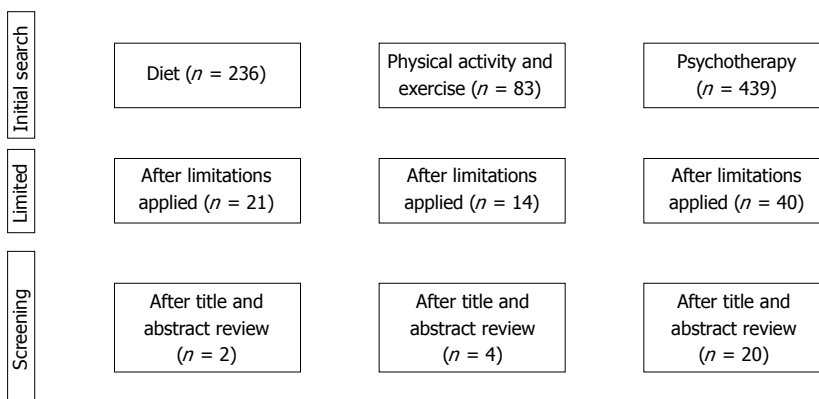


Figure 2 Ovid MEDLINE literature search results. After initial search and limitations, results were further screened by a single expert reviewer.

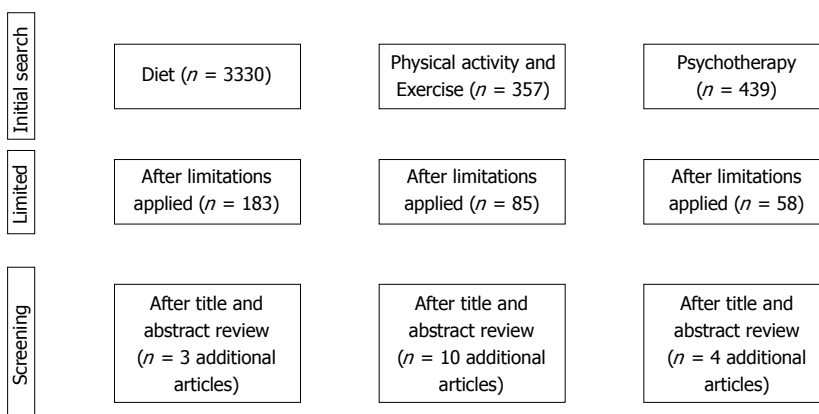


Figure 3 EMBASE: Excerpta Medica and EMBASE: Classic literature search results. After initial search and limitations, results above and beyond those already identified via Ovid MEDLINE search were further screened by a single expert reviewer.

lapse^[18-25]. However, the efficacy of many of these interventions has not been examined rigorously. Regardless, reports indicate up to 68% of patients restrict their diet in an attempt to control symptoms and avoid exacerbation of the disease^[17,26]. Additionally, the lack of clinical nutrition practice guidelines leaves health care practitioners with little direction on how to counsel their patients in this area. Patients then seek diet advice from the internet or patient support groups, rather than from their health care team^[27]. The best available evidence for diet management of IBD is described below.

Fiber

Standard diet therapy as recommended by health professionals includes a low-residue diet (< 10-15 g/d of fiber), especially in patients with risk for gastrointestinal obstruction^[28,29]. Despite this, evidence for the efficacy of low-residue diets in IBD is lacking. Seventy patients with CD were randomized to a low-residue diet (~3 g/d of fiber) or regular diet (13 g/d)^[18]. There was no difference in outcome between the two groups, including symptoms, need for hospitalization, need for surgery, new complications, nutritional status, or postoperative disease recurrence. This study concluded that lifting dietary restrictions, which results in a more appetizing and nutritious diet, neither causes symptomatic deterioration nor precipitates intestinal obstruction in CD.

A randomized controlled trial (RCT) in CD examined the effects of fiber-related dietary instructions specifying daily consumption of whole wheat bran cereal and restriction of refined carbohydrates on QOL and gastrointestinal function ($n = 7$)^[21]. Subjects in the intervention group were instructed to eat whole wheat bran cereal (½ cup) each day, to drink at least 48 ounces of unsweetened fluids each day, and reduce refined sugar. The study concluded that consuming a wheat bran inclusive diet was well-tolerated and there were no negative effects reported. The wheat bran group had increased scores on the Inflammatory Bowel Disease Questionnaires (IBDQ) over time (indicating greater improvement in QOL) than those in the control group ($P = 0.028$). The partial Harvey Bradshaw Index (HBI) scores decreased significantly over time in the active wheat bran intervention group, demonstrating improved GI function compared to participants in the control group ($P = 0.008$). Contrary to these results, a study in UC ($n = 29$) where subjects increased their fiber intake through consumption of whole wheat bread, vegetables, and a supplement of 25 g bran, found no evidence to support the concept that a high-fiber diet is of value in maintaining clinical remission in patients with UC^[30].

A prospective longitudinal cohort study of patients with CD ($n = 1130$) and UC ($n = 489$) examined the association between fiber exposure and the risk of disease flare^[31]. Patients with CD whose median intake of fiber was 23.7 g per day were ~40% less likely to experience a flare at six months as compared with those whose median consumption was 10.4 g of fiber per

day. Fiber intake among patients with UC did not have an impact. Interestingly, patients with CD who reported that they did not avoid high-fiber foods had a 40% lower likelihood of flare than those who avoided high-fiber foods [adjusted OR: 0.59, 95%CI (0.43-0.81)].

A recent meta-analysis examining the role of fiber in the maintenance of remission in IBD, indicates weak evidence for the efficacy of fiber in improving disease outcomes in UC^[32]. The effect of fiber in CD has not been clearly delineated, however studies do not show an increased risk of flaring or complications among patients with IBD consuming higher doses of fiber, suggesting that fiber is safe to consume in IBD^[33].

Fat/animal protein

The search identified no randomized intervention trials that have specifically investigated overall dietary fat intake or animal protein intake in maintenance of remission in IBD. A prospective cohort study of 183 patients with UC found high intake of meat and meat products (processed meats) predicted an increased likelihood of relapse (OR: 5.19, 95%CI: 2.1-12.9)^[34]. An intervention trial in Japan that targeted dietary fat intake by increasing the n-3 fatty acids while concurrently reducing the n-6 fatty acids found that among all IBD patients (CD and UC), participants with a greater n-3/n-6 fatty acid ratio reported higher rates of maintenance of remission ($P < 0.001$)^[35]. In order to achieve this, patients were prohibited from consuming vegetable oil, margarine, salad dressings, mayonnaise and food cooked in vegetable oil, and intake of fish oils (EPA + DHA) was increased to 1700 mg. This study concluded that altering the fatty acid composition of the diet may be useful in maintaining remission in IBD.

Plant-based diets

Vegetarianism is a plant-based dietary pattern that includes different types of diets that vary depending on whether they include animal-derived foods such as milk and eggs^[36]. Consumption of a vegetarian diet is associated with a number of health benefits such as a significantly lower risk for ischemic heart disease mortality (29%), overall cancer incidence (18%)^[37], and lower risk of developing Type 2 Diabetes than non-vegetarians^[38]. A semi-vegetarian diet (SVD) was evaluated prospectively for two years in patients with CD^[19]. Remission rate was 94% ($n = 15/16$) in the subjects consuming a SVD vs 25% the omnivorous diet ($P = 0.0003$). The SVD was a lacto-ovo vegetarian diet that emphasized consumption of grains, daily intake of brown rice, vegetables, and fruits, while limiting intake of animal sources of protein. Fish was allowed once weekly, meat once every 2 wk and eggs/dairy products were allowed without limitation. Foods believed to be risk factors for IBD such as sweets, bread, cheese, margarine, fast foods, carbonated beverages, and juices were discouraged. The concentration of C-reactive protein (CRP) was normal at the final visit in more than half of the patients in remis-

sion on a SVD: The study authors predict that if a SVD is continued long-term and CRP levels are normalized patients are lower risk for relapse.

A Mediterranean diet pattern (MDP) is a widely accepted valid diet intervention able to produce clear benefits for the management of several pathologies and an overall reduction of mortality^[39,40]. The MDP is rich in plant foods (cereals, fruits, vegetables, legumes, tree nuts, seeds and olives), with olive oil as the principal source of added fat, along with high to moderate intakes of fish and seafood, moderate consumption of eggs, poultry and dairy products (cheese and yogurt), low consumption of red meat, and a moderate intake of alcohol (mainly wine during meals)^[41]. A study in CD demonstrated that subjects that followed a Mediterranean inspired diet for 6 wk showed a trend in reduction of inflammatory biomarkers (e.g., CRP) and a trend towards normalization of the gut microbiota^[20].

Comprehensive diet advice

A prospective RCT evaluated the impact of comprehensive dietary guidelines on the clinical course of disease and QOL in patients with UC ($n = 122$) over a 6-mo period^[22]. Participants in the intervention group were provided dietary guidelines in the form of an educational booklet that recommended the following: eat little and often (four to six times a day), drink adequate fluids, decrease excess intake of saturated and trans fatty acids, decrease simple carbohydrates and avoid insoluble fiber, reduce red meat and processed meats and use probiotics. In addition, caffeine, alcohol and processed foods were to be avoided. A total of 69% of the participants in the group that received diet intervention found the advice to be helpful in managing their disease. There was a reduction in the Simple Clinical Colitis Activity Index (SCCAI) in the intervention group with an increase in the control group ($P = 0.0108$) suggesting symptomatic improvement. Although a trend towards clinical improvement was observed, this was not statistically significant.

Exclusion diets

A number of exclusion diets are gaining interest in IBD: the specific carbohydrate diet^[23,42-44], IBD anti-inflammatory diet (IBD-AID)^[24], gluten-free diet^[45], and the low FODMAP diet^[25,46,47]. Functional-like gastrointestinal symptoms (FGS) are common in IBD and are reported in 57% of patients with CD, and 33% of patients with UC despite no evidence of active inflammation^[48]. A low FODMAP diet (LFD) has been proposed for the management of FGS in patients with well-controlled IBD (no active inflammation). This dietary intervention involves the restriction and systematic reintroduction of fermentable oligosaccharides (fructans, galacto-oligosaccharides), disaccharides (lactose), monosaccharides (fructose), and polyols (sorbitol, mannitol), collectively fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs)^[49]. A retrospective follow-up study based on patient-reported questionnaires evaluated the

LFD in patients with IBD ($n = 49$)^[25]. Forty-two percent of subjects with IBD experienced full improvement with the greatest effect on bloating and abdominal pain. Twenty-four percent were completely asymptomatic on the diet, with 66% reporting normalization in stools. The effectiveness of the low FODMAP diet in clinical practice in patients with IBD and coexisting FGS found 78% of patients reported satisfactory relief of symptoms ($P < 0.001$) and significant decreases in severity of all symptoms (e.g., abdominal pain, belching, bloating, flatulence, incomplete evacuation, nausea and heartburn)^[46]. More patients reported normal-frequency stools while following the LFD. A pilot study found similar results, with the symptoms most likely to respond to a LFD being abdominal pain, diarrhea, bloating, and flatulence^[47].

The literature search found no RCTs that have examined the effect of a gluten-free diet on maintenance of remission in IBD. A cross-sectional survey of patients with IBD ($n = 314$) found that 65.5% of patients that followed a gluten-free diet showed improvement in at least one clinical symptom and 38.3% indicated fewer or less severe flares^[45].

The specific carbohydrate diet (SCD) is a novel diet approach that is gaining attention. Although the SCD is praised on multiple IBD patient web sites, it has been poorly studied in objective trials. It restricts complex carbohydrates and eliminates refined sugar from the diet, based on the rationale that the sugars and complex carbohydrates are malabsorbed and could cause alterations in microbiome composition, contributing to the intestinal inflammation of IBD^[50]. In children, a retrospective study ($n = 26$) examined the SCD with concurrent medical therapy ($n = 15$) or diet alone ($n = 11$) for a duration of three to 48 mo (mean of 9.6 ± 0.1 mo)^[43]. Ten additional subjects acted as controls. A comparative analysis of the patients on the SCD vs controls, revealed significant improvement in Pediatric CDAI, CRP, and calprotectin over time for both groups ($P = 0.03$, 0.03 , and 0.03 , respectively). Successful maintenance of remission with the SCD allowed some patients to discontinue medications and maintain disease control on the SCD alone. Although, the strongest efficacy for this diet comes from pediatric studies^[43,44], one recent case series in adults has been completed^[23]. Survey data was collected from 50 individuals that followed the SCD for a mean of 35.4 mo (range 1-216 mo). Thirty-three subjects (66%) noted complete symptom resolution at a mean of 9.9 mo (range 1 to 60 mo) after starting the SCD. Patients' self-report of the effectiveness of the SCD was rated as a mean of 91.3% effective in controlling acute flare symptoms (range = 30% to 100%) and a mean of 92.1% effective at maintaining remission (range = 53% to 100%). Subjects with colonic and ileocolonic CD reported the most benefit from this diet. An additional study conducted an online survey of 417 patients with IBD, and found that SCD had a positive effect, with symptoms progressively decreasing over six months. In addition, over one third of participants felt the SCD helped them achieve remission^[42]. Despite an increasing

number of studies reporting potential benefits of the SCD in IBD, the studies are largely based on patient reported data, are conducted retrospectively, are unblinded, and lack objective markers of inflammation. The effect of the SCD on the clinical course of IBD remains to be validated in large, randomized, intervention trials before it can be recommended in clinical practice.

The IBD-AID is a diet designed to reduce inflammation and provide nutrients to promote a beneficial gut microbiota^[24]. The IBD-AID involves modification of certain carbohydrates (including lactose, wheat, corn and refined sugar), emphasizes the ingestion of pre- and probiotics (e.g., soluble fiber, leeks, onions, and fermented foods), distinguishes between saturated, trans, mono- and polyunsaturated fats, and encourages an overall healthy diet pattern. Textures of the foods (e.g., blenderized, ground, or cooked) are modified as needed^[24]. After following the IBD-AID, 89% of ($n = 24/27$) subjects had a reduction in symptoms. All subjects that followed the diet for > 4 wk ($n = 11$) were able to downscale their medication regimen and all (100%) of the patients had their IBD symptoms reduced, including a reduction in bowel frequency. Of the CD patients ($n = 8$), HBI improved from an average of 11 at baseline (range 1 to 20) to 1.5 (range 0 to 3) after dietary intervention. The UC patients ($n = 3$) had a mean baseline Modified Truelove and Witts Severity Index of 7 at baseline, which improved to 0 after dietary intervention. Although results of this trial appear promising, a large prospective, intervention trial that measures biomarkers of inflammation in blood and stool, along with clinical disease activity, is necessary before the IBD-AID can be recommended to the IBD patient population.

Dairy products, especially milk, are commonly reported to cause symptoms in IBD patients. Patients that declare they are “dairy sensitive” may be sensitive to lactose, not the milk protein. To date, no published intervention trials exist on the response of dairy products in patients with UC. One study reported an increased prevalence of lactose-malabsorption in CD patients with small bowel involvement^[51]. Advice by health professionals varies widely, however IBD patients should be permitted to consume dairy products if they are able to tolerate them and strict lactose exclusion, even though widely practiced, is not usually necessary^[51,52]. Since the lactose content of dairy products varies, a completely lactose-free diet may not be necessary and some patients may tolerate a reduction in lactose intake.

PHYSICAL ACTIVITY AND EXERCISE

Reduced cardiovascular capacity^[53], impaired muscle function^[54,55], and secondary osteoporosis^[56,57] has been reported in patients with IBD. Limited physical activity, particularly with CD^[58], due to fatigue may partially explain these negative outcomes^[54,59-61]. Conversely, regular physical activity seems to improve disease activity and fatigue in patients with IBD^[59,62]. For example,

regimented exercise has been shown to improve disease activity and QOL^[63-65], as well as cardiovascular^[64] and bone health^[65]. The best available evidence for PA/E for IBD is described below.

Physical activity

Patients with CD in remission ($n = 41$, 37.6 ± 10.4 years) were assessed with sex- and age-matched healthy controls ($n = 25$, 37.0 ± 13.0 years) for muscle strength and endurance, as well as other objective measures of physical activity^[54]. Patients with CD had significant impairment in functional capacity (-25.1% , $P < 0.001$) and isometric performance of the lower limbs (-24.8% , $P < 0.001$), assessed by the 12-repetition sit-up test and maximal isometric strength and endurance of leg extensors on leg press. Subjective physical activity questionnaire revealed CD patients scored higher ($P < 0.05$) for work physical activity [2.94 (0.80)] and lower for sport physical activity [2.41 (1.10)] than healthy controls [2.51 (0.44) and 2.66 (0.74)]. However, objective accelerometer measures of overall physical activity were similar. This study is the first known to report independent muscle performance impairment and objective measures of physical activity in CD patients^[54].

Patients with CD ($n = 17$) were surveyed regarding physical activity and stress related to disease activity^[66,67]. Instruments utilized included the International Physical Activity Questionnaire, the Perceived Stress Scale, and the Inflammatory Bowel Disease Questionnaire (IBDQ). There was a direct relationship between physical activity and QOL ($r = -0.551$, $P = 0.022$), with most participants (52.9%) performing “high levels” of physical activity. This study is limited by self-report and exclusion of medication history, as well as inability to determine cause^[67]. In a prospective study, patients with CD ($n = 1308$) and UC ($n = 549$) in remission were assessed for activity levels at baseline via Godin leisure time activity index (LTAI) and disease activity six months from baseline^[62]. Higher activity levels were associated with decreased risk of active disease in both CD ($P = 0.01$) or UC ($P = 0.04$). While large sample size and inclusion of both CD and UC patients is a major strength, the use of Godin LTAI may be a limit because the score produced does not allow determination of intensity or type of physical activity the patients were performing^[62]. Finally, Crohn's and Colitis UK members were surveyed ($n = 918$), with 66% reporting current participation in exercise^[68]. Although 72% reported that exercise “made them feel better”, noting improvement in general well-being and confidence, 23% reported that exercise “made them feel worse” (6% did not answer)^[68]. Of the observational studies, only one surveyed regarding exercise, defined as planned, structured, repetitive and purposive physical activity^[68]. Patients with IBD may prefer “unstructured” physical activity over exercise, although limitations still exist to both^[58]. Limitations to PA/E specific to IBD include pain (joint and abdominal), muscle weakness, health concerns, embarrassment, and toilet access; however, fatigue is by far the most prevalent limitation reported^[68,69].

Fatigue

Some studies have explored whether PA/E influences the experience of fatigue in IBD. The van Langenberg group first assessed fatigue, anxiety, depression, and sleep quality in patients with CD [$n = 181$, 41 (18-68) years] and UC [$n = 113$, 50 (18-72) years] compared to healthy controls [$n = 85$, 38 (17-63) years] in a cross-sectional, longitudinal study^[59]. Patients with CD and UC had significantly worse scores ($P < 0.05$) on all variables compared to healthy controls; however, there was a statistically non-significant trend toward worse Fatigue Impact Scale scores for the CD group in comparison to the UC group. The commencement of a regular exercise program generally led to greater improvements in overall fatigue ($0.05 < P < 0.10$) and was independently associated with concurrently active disease (OR: 3.36, 95%CI: 1.27-8.88) in the CD group. Thus, regular exercise may improve disease activity and ultimately improve fatigue experienced by patients with CD^[59].

Second, muscle fatigue was measured and compared with self-reported fatigue in patients with CD [$n = 27$, 43 (38, 48) years] and sex- and age-matched healthy controls [$n = 22$, 43 (36-49) years]^[70]. The FIS physical component was significantly higher ($P < 0.001$) in CD patients [12 (9, 16)] vs healthy controls [3 (1, 4)], as was muscular fatigue of the knee extensors ($P = 0.047$) determined via the decrement in force production from maximal voluntary contraction on an isokinetic dynamometer [-5.2 (-8.2, -2.2) vs -1.3 (-3.9, 1.4) Nm/min, respectively]. Further, objective muscular fatigue was negatively correlated ($P < 0.05$) with subjective physical fatigue for both CD ($r = -0.52$) and healthy controls ($r = -0.41$). Finally, a physiological basis to fatigue in CD is suggested by significantly ($P = 0.009$) lower levels of serum anabolic hormone insulin-like growth factor-1 (IGF-1), and independent associations of low levels ($P < 0.05$) of IGF-1, vitamin D₃, and magnesium with muscular fatigue. This cross-sectional, observational study is the first known to demonstrate that subjective fatigue correlates with objective fatigue. Despite the ability to suggest a physiological basis of fatigue, the study design could not establish if fatigue is "an end-product of muscle dysfunction or a root cause in CD"^[70].

Third, sleep and physical activity was assessed in CD [$n = 49$, 44 (21, 65 years)] compared to healthy controls [$n = 30$, 46 (21, 63 years)] via accelerometer^[60]. There was a significant ($P < 0.01$) impairment of all physical activity in CD patients vs controls, including more time spent doing sedentary, light, or "lifestyle" (98% vs 96%) rather than moderate-vigorous (2% vs 4%) activities and reduced overall activity (1.32×10^6 vs 1.95×10^6 as per accelerometer counts). Further, lower physical activity was associated ($P < 0.05$) with self-reported global (OR: 5.7, 95%CI: 1.1-29.1) and physical fatigue (OR: 3.9, 95%CI: 1.1-14.5) in a bivariate analysis, as was longer duration since diagnosis (OR: 1.2, 95%CI: 1.03-1.5), systemic inflammation via C-reactive protein (OR: 22.6, 95%CI: 1.1-479.3), and low vitamin D₃ defined as < 50 nmol/L (OR: 13.1, 95%CI: 2.5-68.7)

in a multivariate analysis. In this study, participants that did not achieve any bouts of moderate-vigorous activity were described as having "lower physical activity". This approach to classification may account for discrepancy with a previous study that found no difference between CD patients and healthy controls^[70].

Recently, men and women with IBD in remission were recruited in a matched cross-sectional study^[61]. Fatigued IBD patients ($n = 10$, 36.4 ± 12.3 years), defined as a Checklist Individual Strength-fatigue (CIS-fatigue) score of ≥ 35 , were matched to non-fatigued IBD patients ($n = 10$, 38.2 ± 11.0 years; CIS-fatigue score of < 35). The fatigued group had a lower intensity of daily physical activity (Cohen's d effect size = 1.02; $P = 0.037$), and reduced cardiovascular fitness demonstrated via 6-min walk test (Cohen's d effect size = 0.80; $P = 0.030$)^[61].

Patients with IBD can overcome fatigue to participate in PA/E. While unstructured physical activity may be preferred, those who participate in structured exercise do so 1-2 d per week at a moderate intensity^[58,68]. Structured exercise, such as cardiovascular vs resistance training, may provide additional benefits as described below.

Exercise

Cardiovascular training: In a controlled trial men and women ($n = 12$, 38.3 ± 7.5 years) with CD performed low-intensity walking for 30 min, 3 d per week for 12 wk^[64]. Low-intensity walking was defined as 60% of heart rate maximum (HR_{max}) determined using the Karvonen formula^[71]. Predicted maximal oxygen uptake improved ($P = 0.001$), implying improved cardiovascular fitness. Further, general well-being, QOL, and perceived stress significantly improved [IBDQ ($P < 0.01$)] and IBD (Stress index $P < 0.001$)^[64].

In a follow-up study men and women ($n = 32$) with CD were randomized to low-intensity walking (60% HR_{max}) for 30 min, 3 d per week for 3 mo ($n = 16$, 40.6 ± 11.7 years) or to non-exercise control group ($n = 16$, 37.0 ± 12.7 years)^[65]. Exercise improved QOL and perceived stress [IBDQ ($P < 0.05$)] and IBD Stress Index ($P < 0.05$). Importantly, exercise participants had improved disease activity based on HBI post-intervention compared to baseline ($P < 0.01$) while the non-exercise group worsened ($P = 0.04$).

Recently, men and women ($n = 30$) with IBD were randomized (stratified by disease) to supervised moderate intensity "running" 3 d per week for 10 wk ($n = 15$, 39.7 ± 14.7 years) or control group ($n = 15$, 42.5 ± 13.9 years)^[63]. Moderate intensity "running" was defined as a pace great enough to work up a sweat while maintaining ability to talk. Exercise participants improved on the social well-being sub-scale of the IBDQ ($P = 0.026$) compared to controls. This is the only clinical trial to assess objective markers of inflammation (*i.e.*, leukocytes, C-reactive protein, and fecal calprotectin), however no statistically significant changes were seen in these parameters^[63].

Resistance training: In a RCT men and women ($n =$

117) with CD were randomized to low-impact home-based exercise program performed 2 d per week for 1 year ($n = 53$, 40.1 ± 12.6 years) or control group ($n = 54$, 41.2 ± 14.1 years)^[66]. The exercise program was low-impact and progressive and targeted sites susceptible to secondary osteoporosis (hip and lumbar spine) and major muscle groups (core and lower body). Participants who were $\geq 80\%$ compliant to the exercise improved ($P = 0.02$) percent change of areal bone mineral density (aBMD) at the greater trochanter, derived *via* dual energy X-ray absorptiometry, compared to the control group (95%CI: 0.86-8.48). Pearson's correlation (r) showed total number of exercise sessions completed in the 12 mo was significantly associated with percent change of aBMD at the femoral neck ($r = 0.28$, $P = 0.04$). Disease activity assessed by Simple Disease Activity Score did not improve. This study has numerous strengths, including a RCT design, and is the first and only to determine effects of resistance training on IBD *via* RCT. However, this study was limited by poor compliance^[66], with division of participants into sub-groups based on compliance (low, medium, and high exercise) for further analysis. An exploratory follow-up determined that Acceptance of Illness at baseline was significantly different between sub-groups ($F = 3.57$, $df = 55$, $P < 0.04$) and was the best predictor of exercise uptake ($r = 0.376$, $R^2 = 0.141$)^[72].

Female IBD patients ($n = 148$) were tested for quadriceps strength *via* electromechanical chair dynamometer before assigning a sub-sample ($n = 19$) to progressive resistance training of the quadriceps twice per week for 8 wk^[73]. Intensity was set at 50% of maximum load for the first 4 wk and progressed 10% per week until 80% maximum was achieved. Quadriceps strength improved significantly after the 8 wk of training (pre = 28.5 ± 5.6 kg, post = 39.0 ± 3.2 kg), as did QOL assessed by the IBDQ ($P < 0.001$). This study is limited by the specificity of the training program (*i.e.*, quadriceps only)^[73].

Exercise tolerance: For the most part exercise was well tolerated in the clinical trials^[64-66], although one participant reported mild abdominal symptoms in response to exercise^[63]. Given the current evidence base, these conclusions apply best to those with mildly active disease or disease in remission, and to those with CD rather than UC. While exercise did not exacerbate disease, inflammation^[63] and disease activity^[64,66] was not improved in most clinical trials. Lack of improvements in disease activity may reflect length of the intervention^[63,64] or low compliance to the training programs^[66]. However, QOL was improved.

PSYCHOTHERAPY

IBD has been associated with negative psychosocial outcomes, such as a poor QOL^[74], anxiety and depression^[75], and maladaptive coping^[76,77]. Such outcomes may be a product of the disease^[78] or contributing fac-

tors^[79]. Given that psychological functioning can impact one's sense of well-being^[80] and physical health^[81,82], stress management and mental health treatment may be important for maintaining a good QOL and health in IBD. The evidence for the use of psychotherapeutic approaches used exclusively with people who have IBD is reviewed below.

Cognitive behavioural therapy

Cognitive behavioural therapy (CBT) is a collaborative problem-solving approach between the client and therapist, which aims to collaboratively identify, challenge, and modify maladaptive thoughts and behaviors^[83]. At present, most psychotherapists utilize a cognitive-behavioral approach^[84]. There is some evidence that CBT improves aspects of psychological health in IBD.

Following a CBT group with IBD patients ($n = 28$), IBD-related concerns significantly decreased from pre- to post-treatment and these changes were maintained at 9-mo follow-up^[85]. Using the Rating Form of IBD Patient Concerns (RFIPC), concerns that were reduced included: Impact of disease (pre = 39.4, Post = 28.3, $P = 0.007$), complications (pre = 37.1, post = 23.6, $P = 0.018$), and sexuality (pre = 33.3, post = 22.4, $P = 0.039$). No significant reduction was found for body stigma (pre = 24.6, post = 20.9). IBD-related quality of life (IBDQ) has also shown improvement following CBT interventions; however, these changes appear to be short-lived^[86-88]. Following CBT, patients with IBD report significantly lower substance use for coping^[88], and women report less depressive coping styles at 9-mo follow up^[85]. Results from treatment studies of comorbid IBD and mood or anxiety disorders are mixed; both computerized and face-to-face forms of CBT have been ineffective at reducing anxiety and depression^[88-90], while a face-to-face intervention did lead to less depression symptoms in women^[85].

Some research has explored whether the effects of CBT for patients with IBD depend on the level of psychiatric comorbidity. For instance, in one study, CBT led to short-term improvements in health-related QOL and coping abilities, but only in IBD patients with high mental health needs^[90]. In another study, using a sample with low levels of psychological distress ($n = 28$), a piloted CBT intervention improved IBD-related quality of life (IBDQ) and self-efficacy (IBD self-efficacy scale), and decreased stress [perceived stress questionnaire (PSQ)]^[91]. Within some other studies showing a positive effect following CBT^[85,86], psychiatric illness has been an exclusion criterion.

Physical health outcomes have also been examined in CBT studies for IBD. Piloting a RCT with both CD and UC patients ($n = 174$), the effects of CBT (face-to-face and computerized modalities) were examined^[90]. Neither face-to-face nor computerized CBT had significant effects on disease activity (CDAI and SCCAI) throughout testing. Following treatment, a nearly equal number of patients in the treatment and control groups remained in remission (CBT: 73.2%, controls: 71.7%, $P = 0.868$). An

analysis of a 2-year follow-up on this study showed no impact on disease activity measures^[89]. In another RCT, a computerized form of CBT for IBD patients ($n = 199$) failed to produce any significant effects on clinical index measures (HBI and SCCAI)^[88]. In an uncontrolled trial, a 12-wk CBT group for IBD patients had no significant impact on clinical indexes (CDAI and CAI) or medication use^[85].

Mindfulness-based therapies

Mindfulness originates from Eastern philosophies and was introduced to Western medicine by Jon Kabat-Zinn^[92], who, in 1979, created the Mindfulness-Based Stress Reduction (MBSR) program for patients with chronic illness^[93,94]. Mindfulness can be conceptualized as a non-judgmental, accepting, and intentional quality of attention towards unfolding present-moment experiences^[92,94,95]. Mindfulness has been integrated into a number of psychotherapies supported by the American Psychological Association, including Acceptance and Commitment Therapy and Dialectical Behavioral Therapy.

Mindfulness appears to improve mental health outcomes in IBD. Improved outcomes include health-related QOL (IBDQ)^[96], maintained QOL during flare ups^[97], reduced depression (BDI)^[98], long-lasting reductions in anxiety (STAI)^[98], and use of problem-directed coping strategies [ways of coping checklist (WCC)]^[96]. IBD patients with high levels of stress and more severe abdominal symptoms may benefit more from mindfulness interventions than other IBD patients^[96,97]. In a double-blind RCT with UC patients ($n = 55$), MBSR completers with a high severity of gastrointestinal symptoms at baseline demonstrated a greater reduction in the hindrance of bowel symptoms (IBDQ-bowel subscale) compared to MBSR participants with less severe symptoms - an effect not seen in the control group ($P < 0.001$)^[97]. Berrill and colleagues found similar results in an IBD sample with high levels of stress (PSQ) and/or functional abdominal symptoms (irritable bowel syndrome symptom severity scale)^[96].

Currently, there is limited evidence on the effectiveness of mindfulness-based therapies (MBT) in reducing disease activity in IBD, as measured by clinical indexes and biomarkers of inflammation^[96,98]. However, the aforementioned RCT with UC patients demonstrated that MBSR completers with high stress levels (PSQ) exhibited fewer flare ups post-treatment compared to those in the control group with high stress levels ($P < 0.001$)^[97]. Moreover, meditative techniques, including breathing, body postures, movement, and elements of mindfulness^[99], were associated with reducing an inflammatory biomarker (CRP), in a group of 29 IBD patients. It remains unclear which intervention component(s) were responsible for the effects observed in the latter study.

Psychodynamic psychotherapy

The effect of short-term psychodynamic therapy combined with autogenic training was examined in a pro-

spective, multicenter RCT^[100-102]. Three separate analyses were conducted to examine the influence of the intervention on psychosocial status^[102], disease course^[101], and health care use^[100]. The therapy targeted relaxation, health behaviors, and coping. The sample comprised 108 CD patients across four treatment centers and patients completed an average of 47 wk of therapy.

In terms of psychological outcomes, no significant differences were found between the treatment group and controls with depression (BDI), anxiety (STAI), or QOL (German quality of life scale)^[102]. On measures of disease course (CDAI and physical assessments), the therapy failed to show any promising results^[101]. However, in analyzing the effect on health care use, the treatment group displayed significantly less hospital days and sick leave days^[100].

Hypnosis

Hypnosis is described as "an ability to sustain a state of attentive, receptive, intense focal concentration with diminished peripheral awareness in response to a signal"^[103]. There is evidence of its lasting effects on health and well-being in a variety of populations, with proposed mechanisms including immune and cognitive changes^[104,105]. As a psychological intervention for IBD, the clinician delivers hypnotic suggestions to improve psychological and gastrointestinal health^[104]. There is a lack of evidence for hypnosis as an effective intervention for anxiety and depression in IBD; however, there is some evidence of its effect on other psychological outcomes^[104,106].

In a RCT with UC patients ($n = 37$), a 7-session hypnosis intervention produced the following effect sizes on QOL and self-efficacy measures: IBDQ-bowel subscale ($d = 0.50$), IBDQ-systemic health subscale ($d = 0.48$), IBDQ-total scale ($d = 0.41$), and the IBD self-efficacy scale ($d = 0.34$)^[104]. However, there were no significant effects on perceived health competence (perceived health competence scale), stress (PSQ), IBD-related concerns (RFIPC), or medication adherence (medication adherence scale).

There have been observations of long-term reductions in disease severity (clinical assessments) and medication use following hypnosis, although this was found in an uncontrolled study with a small sample size ($n = 13$)^[106]. In the aforementioned RCT of seven hypnosis sessions, those in the treatment condition had a significantly higher number of days until relapse compared to controls, $F = 4.8$ (1, 48), $P = 0.03$, and 68% of patients in the treatment condition maintained remission (subjective markers of flare) for one year, whereas this was the case with only 40% of the controls, χ^2 (1) = 3.9, $P = 0.04$ ^[104]. Indeed, in an RCT in which hypnosis was used to treat UC ($n = 25$), biomarkers of autonomic activity and inflammation were significantly reduced within 30 min following a single 50-min session of hypnosis^[107]. Specifically, hypnosis had significant effects on heartrate, reduced serum interleukin-6 levels by 53% (a measure of systemic inflammation), and

reduced three of six measures of rectal inflammation.

Stress management

Studies were classified as stress management interventions if they either provided education on stress and/or coping, or utilized relaxation techniques. Such interventions appear to positively impact psychological functioning in IBD. In most studies that assessed disease-related stress, ratings on the IBD-related QOL (IBDQ) and IBD-related stress (IBD stress index) were significantly reduced post-treatment^[108-110]. Anxiety [hospital anxiety and depression scale (HADS) and STAI] is also effectively targeted by these interventions^[111,112]. However, there is limited support for the use of stress management for IBD patients with comorbid depression^[111-113].

Studies that assessed disease activity following stress management interventions show mixed results. Following a stress management program for IBD patients, significant reductions in CDAI scores were observed^[109]. However, two recent studies showed no effect on disease activity (HBI, CAI, and CDAI)^[108,112]. Stress management interventions might improve self-reported pain and other symptoms. For example, in three RCTs using relaxation training for IBD patients, significant reductions were found on the visual analogue scale (VAS)^[110], McGill pain questionnaire and pain and distress scale^[114], and symptom-monitoring diaries^[115]. In contrast, in a study of IBD patients with low levels of disease activity, researchers failed to find any significant reductions on the VAS^[113].

Supportive-expressive group therapy

In a prospective, uncontrolled pilot study, supportive-expressive group therapy was examined with IBD patients ($n = 30$)^[116]. This therapy aimed to encourage self-expression and reduce feelings of isolation. On psychological measures, there were no significant changes in IBD-related concerns (RFIPC), IBD-related quality of life (IBDQ), or anxiety or depression (HADS) post-treatment, however, there were changes in coping (ways of coping inventory). That is, patients reported less use of maladaptive coping styles, including denial, suppression, and self-blame. On measures of IBD symptoms, no significant changes occurred post-treatment, despite a reduction in symptoms^[116].

Solution-focused therapy

Vogelaar and colleagues assessed the value of solution-focused therapy (SFT) in improving fatigue in IBD in two separate studies^[117,118]. SFT is a brief form of psychotherapy that focuses on the individual's adequate coping abilities^[118]. In the first study, SFT was compared against problem-solving therapy and a control condition in CD patients with high levels of fatigue ($n = 40$). No significant differences were found on any of the psychological outcomes, which included measures of QOL (IBDQ and EuroQol-5D), and anxiety and depression (HADS). In

the most recent study of highly fatigued patients ($n = 98$), the authors found short-term therapeutic effects on QOL (IBDQ) ($P = 0.02$) and depression (HADS) ($P = 0.03$) following SFT; however, no significant differences in anxiety were found between the treatment group and controls. When assessing fatigue, the initial study failed to find significant differences in fatigue scores on the checklist of individual strength (CIS) between treatment groups and controls, however, a greater number of patients in the SFT condition showed improvements. In the latter study, patients were assessed on measures of physical health outcomes from post-treatment to 9-mo follow-up. A significantly greater number of individuals in the treatment group exhibited low fatigue scores (CIS) compared to controls post-treatment ($P = 0.03$); however, this effect was only sustained until 6-mo follow-up ($P = 0.19$). In this study, SFT did not have any significant effects on clinical indexes, sleep quality, medication use, or blood parameters.

Multi-component behavioral treatment

Multi-component behavioral treatment (MCBT) is a psychological intervention that combines muscle relaxation techniques, thermal biofeedback, training in coping, and education in IBD^[119]. In an RCT using MCBT with 21 IBD patients, researchers examined outcomes on the BDI, STAI, IBD stress index, hassles scale, and psychosomatic symptom checklist^[119]. The IBD Stress Index was the only psychological measure to significantly decrease from pre- to post-treatment in the MCBT condition ($P < 0.05$). On a self-report of IBD symptoms, a significantly greater number of controls reported symptom reductions than the treatment group following the study (82% vs 65%, $\chi^2 = 14.58$, $P < 0.01$).

CONCLUSION

The non-pharmacological therapies reviewed are intended to be used as an adjunct to conventional therapies. Evidence-based recommendations for diet, PA/E, and psychotherapy are provided. However, recommendations may be limited to a particular subset of IBD patients (e.g., those in remission).

The existing body of science on the impact of diet on IBD has its limitations. High quality, well-designed RCTs are lacking, as the majority of intervention trials are of short duration and lack objective measurements of disease activity. Researchers rely on patient self-reporting, which introduces bias. At this time, no single diet should be recommended for all patients with IBD; however, a diet rich in vegetables, fruit and fiber appears to be of benefit (Table 1). Of note, this is for patients with IBD who are in remission. There is an even greater paucity of evidence based information for dietary recommendations for patients with active disease. Unique dietary recommendations should be developed for each patient, depending on the course of the disease. Patients should be counseled regarding the lack of objective evidence for

Table 1 Summary of best available evidence for diet management of inflammatory bowel disease (remission)

Diet	Recommendation	Ref.
Fiber	There is a lack of evidence that fiber intake should be restricted in patients with IBD. Soluble fiber sources are encouraged ^[32] . A high fiber diet is likely safe in patients with IBD and may impart a weak benefit ^[33] . Cruciferous vegetables, fruit peels, nuts, seeds should be avoided in patients with known fibrostenotic stricture with obstructive symptoms ^[29,33]	Hwang <i>et al</i> ^[29] , 2014 Wedlake <i>et al</i> ^[32] , 2014 Kaplan <i>et al</i> ^[33] , 2016
Dairy products	Strict avoidance of dairy products is not justified unless it clearly worsens diarrhea ^[52] . For patients who are lactose intolerant, it may still be possible to consume small amounts of dairy products with lower amounts of lactose such as fermented dairy products (yogurt and kefir), cottage cheese, butter and aged cheeses ^[29]	Richman/Rhodes ^[52] , 2013
Low-FODMAP	A low-FODMAP diet may be worth trying in patients with IBD who have FGS such as bloating, abdominal pain or watery diarrhea that have persisted despite appropriate treatments ^[25,52]	Maagaard <i>et al</i> ^[25] , 2016
Plant-based	Plant-based diets such as a lacto-ovo vegetarian diet or Mediterranean diet pattern may reduce gut inflammation in IBD ^[19,20]	Chiba <i>et al</i> ^[19] , 2010 Marlow <i>et al</i> ^[20] , 2013
Fat/animal protein	Avoidance of trans fatty acids from processed foods, margarine and fast foods may be warranted ^[34,52] . A diet low in animal fat, particularly from processed meat and red meat (< 2/wk) is encouraged ^[34,122]	Jowett <i>et al</i> ^[34] , 2004 Owczarek <i>et al</i> ^[122] , 2016
Specific carbohydrate/ IBD-AID/ gluten-free	The effect of the SCD, IBD-AID and the gluten-free diet on clinical course in IBD remains to be elucidated in future trials	

IBD: Inflammatory bowel disease; FODMAP: Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; SCD: Specific carbohydrate diet; AID: Anti-inflammatory diet.

Table 2 Summary of best available evidence for physical activity and exercise in inflammatory bowel disease

Type	Recommendation	Ref.
Physical activity	Lower levels of physical activity are associated with fatigue ^[60,61] , systemic inflammation ^[60] , and reduced cardiovascular fitness ^[61] , whereas higher levels of physical activity may improve quality of life ^[67] and decrease risk of active disease ^[62] . Unstructured "lifestyle" and work-related physical activity may be preferential over exercise ^[58,60,67] , although both are encouraged	van Langenberg <i>et al</i> ^[60] , 2015 Vogelaar <i>et al</i> ^[61] , 2015 Jones <i>et al</i> ^[62] , 2015 Crumbock <i>et al</i> ^[67] , 2009 Mack <i>et al</i> ^[58] , 2011
Exercise	Structured exercise may improve overall fatigue ^[70] , general well-being ^[68] , and disease activity ^[70] . Thus, exercise, including cardiovascular and resistance training, should supplement "lifestyle" physical activity	Van Langenberg <i>et al</i> ^[70] , 2014 Chan <i>et al</i> ^[68] , 2013
Cardiovascular training	Low-moderate intensity cardiovascular training may improve cardiovascular fitness ^[64] , disease activity ^[65] , perceived stress ^[64,65] , and quality of life ^[64,65] , including social and general well-being ^[63,64] . Cardiovascular training should be incorporated into exercise regimen a minimum of 30 mins, 3 d per week	Klare <i>et al</i> ^[63] , 2015 Loudon <i>et al</i> ^[64] , 1999 Ng <i>et al</i> ^[65] , 2007
Resistance training	Low-moderate intensity progressive resistance training may improve bone health ^[66] , strength ^[73] , and quality of life ^[73] . More evidence is needed for a specific prescription	Robinson <i>et al</i> ^[66] , 1998 de Souza <i>et al</i> ^[73] , 2014

the use of restrictive diets, as well as the potential risks these diets can have in patients who are predisposed to nutritional deficiencies. Patients should consult with a registered dietitian for individualized diet counseling to assess current intake, evaluate nutritional status, and assist in manipulating diet to prevent nutritional deficiencies and improve QOL.

Current exercise guidelines suggest cardiovascular training 20-60 min at 60%-90% maximum heart rate 3-5 d per week and resistance training a minimum of 2 d per week are outdated and not based on actual evidence in an IBD population^[120,121]. Further research is needed to improve our understanding and to create development of specific exercise guidelines for patients with IBD. Evidence thus far emphasizes that patients should perform regular low-moderate intensity physical activity, including cardiovascular and resistance exercise, as it may positively impact QOL and inflammation (Table 2). Exercise also has the potential to prevent impaired cardiovascular and muscular function and secondary osteoporosis associated with IBD and is generally well

tolerated^[59,62,69]. Patients should, however, consult a physician prior to commencing a regular exercise regime^[120-122], as exercise tolerance may be lessened with active disease. Physicians should also discuss with patients the potential for PA/E related fatigue.

With respect to psychotherapy interventions in IBD, there has been more examination of CBT, MBT, hypnosis, and stress management than other interventions (Table 3). There is evidence that CBT and MBT improve coping and QOL, yet evidence for improvement of comorbid anxiety and depression in this population is limited. Many of the latter interventions were tailored to the needs of individuals with IBD, however, they were not designed to exclusively treat anxiety and depression. Thus, along with IBD-related adaptations, more symptom-specific interventions may be necessary to effectively target anxiety and depression in this population. CBT and MBT are also seemingly limited in their impact on disease activity; longer follow up assessments may be necessary, as health benefits from stress reduction may take time. Hypnosis in IBD has demonstrated

Table 3 Summary of best available evidence for psychological interventions in inflammatory bowel disease

Intervention	Recommendation	Ref.
Cognitive behavioural therapy	May be useful for developing adaptive coping skills ^[85,88,90] , reducing IBD-related stress ^[85] , and improving quality of life ^[86-88,90] . Therapeutic gains are observed in individuals with varying degrees of distress. ^[85,86,90,91] Outcomes on anxiety and depression are inconsistent ^[85,86,88-90]	Mussell <i>et al</i> ^[85] , 2003 Díaz-Sibaja <i>et al</i> ^[86] , 2009 Keefer <i>et al</i> ^[87] , 2012a McCombie <i>et al</i> ^[88] , 2016 Mikocka-Walus <i>et al</i> ^[89] , 2016 Mikocka-Walus <i>et al</i> ^[90] , 2015 Keefer <i>et al</i> ^[91] , 2012
Mindfulness-based therapies	Could foster adaptive coping ^[96] and maintain quality of life during flare ups, particularly among individuals with moderate-severe distress or abdominal symptoms ^[96,97] . The evidence for managing anxiety and depression ^[98] , as well as disease activity ^[97,99] , is limited.	Berrill <i>et al</i> ^[96] , 2014 Jedel <i>et al</i> ^[97] , 2014 Schoultz <i>et al</i> ^[98] , 2015 Gerbarg <i>et al</i> ^[99] , 2015
Hypnosis	Demonstrates the most promise for managing disease activity ^[104,106,107]	Keefer <i>et al</i> ^[104] , 2013 Miller/Whorwell ^[106] , 2008 Mawdsley <i>et al</i> ^[107] , 2008
Stress management	These interventions appear to target anxiety ^[110-112] , reduce IBD-related stress ^[109,110] , and improve quality of life ^[108,110] . There is some support for managing pain ^[110,114,115]	Boye <i>et al</i> ^[108] , 2011 Milne <i>et al</i> ^[109] , 1986 Mizrahi <i>et al</i> ^[110] , 2012 Larsson <i>et al</i> ^[111] , 2003 Smith <i>et al</i> ^[112] , 2012 Shaw/Ehrlich ^[114] , 1987 Garcia-Vega/Fernandez-Rodriguez ^[115] , 2004
Psychodynamic psychotherapy, supportive expressive group therapy, solution-focused therapy, multi-component behavioural treatment	Insufficient evidence to make recommendations at this time	

IBD: Inflammatory bowel disease.

some evidence for reducing disease activity; however, there is no evidence of its ability to decrease anxiety and depression. As with the CBT and MBT studies, the hypnosis interventions were not specific to anxiety and depression, which could explain such findings. Stress management interventions have led to lower disease-related stress, anxiety, and reports of pain, yet their influence on disease-activity remains mixed. Future research could explore modifications of evidence-based psychotherapies that specifically target anxiety and depression, and examine the application of these in IBD. Research into interventions showing promise for physical health improvements in IBD, such as hypnosis, could also continue being explored.

The non-pharmacological therapies reviewed are promising, but should be viewed as adjunct therapies to treat IBD patients holistically. Longer-term, carefully designed, non-pharmacological intervention trials are urgently needed to determine the optimal treatment modality for patients. Such trials should assess both subjective measures such as QOL, as well as objective measures of inflammation. While the recommendations provided are based on existing evidence, additional research on non-pharmacological approaches for the management of IBD is needed.

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