

# Lower Impact of Disease on Daily Life and Less Fatigue in Patients With Inflammatory Bowel Disease Following a Lifestyle Intervention

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**Background:** Despite the potential benefits of diet and physical activity, evidence for beneficial effects of a combined lifestyle intervention is lacking in patients with inflammatory bowel disease (IBD). Therefore, we assessed its effects on impact of disease on daily life, clinical disease activity, fatigue, and health-related quality of life (HRQoL) in patients with IBD.

**Methods:** A 6-month single-arm intervention study was performed in adult IBD patients in remission or with mildly active disease. Participants received personal dietary and physical activity advice from a dietician and a physiotherapist in 6 consults. At baseline and over time, questionnaires on diet quality, physical activity, and disease-related outcomes were completed and fecal calprotectin was determined. Data were analyzed by linear mixed models.

**Results:** During the intervention, diet quality significantly increased ( $P < .001$ ), but the level of physical activity remained the same. Over time, impact of the disease on daily life reduced ( $P = .009$ ) and fatigue decreased ( $P = .001$ ), while clinical disease activity, HRQoL, and fecal calprotectin did not change. Improvement in diet quality was significantly associated with a lower impact of disease on daily life ( $\beta = 0.09$ ; 95% confidence interval [CI], 0.03 to 0.15;  $P = .003$ ) and less fatigue ( $\beta = -0.13$ ; 95% CI, -0.20 to -0.07;  $P < .001$ ) but not with clinical disease activity, HRQoL, and fecal calprotectin. No associations were found with physical activity.

**Conclusions:** This combined lifestyle intervention significantly improved diet quality, and this improvement was associated with a reduction in the impact of disease on daily life and fatigue in patients with IBD in remission or with mildly active disease.

## Lay Summary

Diet quality significantly improved following a lifestyle intervention based on general dietary and physical activity guidelines. This improvement in diet quality was associated with a reduction in the impact of disease on daily life and fatigue in patients with IBD.

**Key Words:** Crohn's disease, Ulcerative colitis, lifestyle intervention, diet, physical activity

## INTRODUCTION

Westernization of lifestyle, characterized by unhealthy dietary habits and decreased physical activity, not only has been linked to the increased incidence and prevalence of inflammatory bowel disease (IBD), but also may affect the disease course in patients with established IBD.<sup>1–3</sup> IBD is mainly treated with medication. In addition to medication, many IBD patients look for supportive and adjunctive therapies.<sup>4–6</sup> They frequently ask their physicians for advice on diet and lifestyle to improve or even cure their disease.<sup>7</sup> Several studies suggest influence of various lifestyle factors, including diet and physical activity, on the course of disease. A healthy lifestyle may support maintenance of remission and improve health-related quality of life (HRQoL),<sup>2,3</sup> which is important because IBD is characterized by a clinical course with periods of active disease alternating with periods of remission and has

a significant impact on daily life.<sup>8</sup> One study even found a healthy lifestyle, in terms of a healthy diet and weight and a sufficient level of physical activity, to be associated with reduced mortality in IBD patients.<sup>9</sup>

Many different types of exclusion diets have been proposed in the treatment of IBD, such as the specific carbohydrate diet (SCD) and CD-TREAT.<sup>7</sup> However, adherence can be a challenge, and large controlled trials are lacking to conclude if these restrictive exclusion diets benefit IBD patients.<sup>7</sup> Furthermore, restrictive diets can also have potential adverse effects. For example, reducing fiber intake might have detrimental effects on the microbiota by less prebiotic actions, and there is a risk of undernutrition when insufficient attention is paid to nutritional adequacy.<sup>7</sup> However, some studies have shown that the exclusion of certain food components seems to benefit IBD patients, such as industrialized, processed foods,

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animal fat, and red and processed meat.<sup>10,11</sup> Excluding these foods not only may reduce proinflammatory processes, but also is in line with the general dietary guidelines on healthy eating. These guidelines recommend a diet rich in vegetables, fruit, and fiber, which also appears to benefit IBD patients.<sup>4</sup>

In addition to dietary interventions, several studies have evaluated different physical activity interventions, and limited but promising evidence suggests that physical activity can benefit overall health, physical well-being, and HRQoL.<sup>5</sup> Regular physical activity is associated with an increased biodiversity of the gut microbiome and release of protective myokines like interleukin-6 from working skeletal muscles, both promoting an anti-inflammatory state.<sup>12,13</sup> In a prospective cohort study, a higher level of physical activity was associated with a lower risk of relapse among IBD patients in remission.<sup>14</sup> In a review, it was recommended to maintain an active lifestyle consisting of endurance and resistance exercise.<sup>6</sup> Combining all evidence, regular physical activity of low-moderate intensity, including cardio and resistance exercise, may positively affect HRQoL and inflammation in IBD patients.<sup>4</sup>

Although studies have been performed assessing the effects of diet or physical activity interventions, little information is available on combined lifestyle interventions in IBD patients. In other chronic conditions such as type 2 diabetes and obesity, interventions in which diet and physical activity are combined seem to be more effective than diet-only or physical activity-only interventions.<sup>15</sup> So far, 2 combined lifestyle intervention studies have been performed in IBD patients by a research group from Germany. Their intervention focused on psychological aspects such as stress reduction and management, while diet and physical activity were secondary aspects of which changes were not reported, and their intervention lasted only 10 weeks.<sup>16,17</sup> No studies to date have examined effects of a lifestyle intervention focusing on diet and physical activity in IBD patients. Therefore, we performed a 6-month combined lifestyle intervention study in which we provided personal dietary and physical activity advice to improve the lifestyle of IBD patients. The aim of this study was to investigate the effect of this 6-month lifestyle intervention primarily on the impact of disease on daily life and secondarily on clinical disease activity, HRQoL, and fatigue. In addition to these subjective measures, changes in fecal calprotectin were investigated. Patient experiences with the combined lifestyle intervention were also evaluated in this study.

## METHODS

### Study Population

Participants were recruited between February 2020 and February 2021 via the outpatient clinic of Hospital Gelderse

Vallei in Ede, the Netherlands. Inclusion criteria were a histologically proven diagnosis of Crohn's disease (CD) or ulcerative colitis (UC, total, or left-sided) at least 2 years before recruitment, 18 to 70 years of age, remission or mildly active disease that did not require immediate medication change, and at least 1 flare-up in the past 2 years. Participants were excluded when they already adhered well to the Dutch dietary guidelines (*Eetscore* Food Frequency Questionnaire [*Eetscore*-FFQ] > 120 points), used prednisone, had a stoma or pouch, and when they already participated in another intervention study. This study was approved by the Medical Ethical Committee of Wageningen University (METC nr. 19/18) and conducted in accordance with the Declaration of Helsinki and is registered on the Netherlands Trial Register (NL8267). All participants provided written informed consent.

### Study Design

A 6-month single-arm intervention study was performed. Participants were intensively supervised by a dietician and a physiotherapist for 3 months. During these first 3 months, the focus was to change lifestyle. Five consults were scheduled for each participant, of which 3 were planned to be performed at the hospital and 2 by telephone. Owing to coronavirus disease 2019 (COVID-19) restrictions, 2 hospital consults were replaced by video consults for the majority of participants (Figure 1). After 3 months, participants were followed up for another 3 months. During these second 3 months, the focus was to maintain lifestyle change; participants had 1 follow-up telephone consult to support them in maintaining their lifestyle change and to answer questions. Between consults, participants had the opportunity to email their dietician or physiotherapist with questions. Several measurements were performed at 4 time points (baseline and 1 month, 3 months, and 6 months after baseline) to assess the effects of the intervention.

### Lifestyle Intervention

During the 6-month combined lifestyle intervention, participants adhered as well as possible to a healthy diet and physical activity level through intensive advice from a dietician and a physiotherapist. Dietary recommendations were based on the Dutch dietary guidelines with a few adjustments.<sup>18</sup> In short, the recommended diet was mainly plant based and rich in vegetables, fruits, whole grains, and nuts. Tea, coffee, and water were the preferred drinks. Furthermore, participants were advised to limit their intake of red and processed meat, soft drinks, and other processed foods. The recommended intake of vegetables (>300 g/d) was higher than the

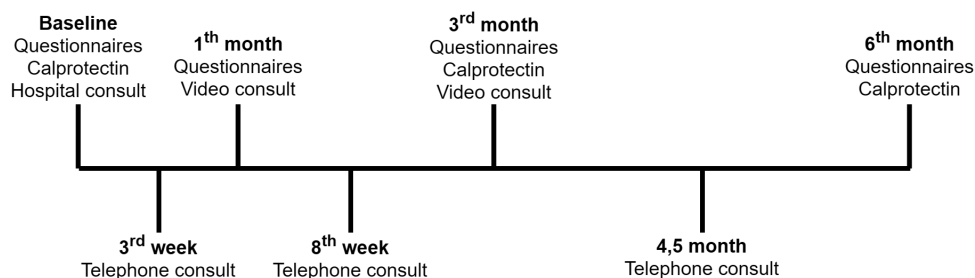


Figure 1. Overview of study design.

Dutch dietary guidelines to achieve a higher fiber intake that is known for its beneficial effects on IBD symptoms and the gut microbiota.<sup>19</sup> Besides, there was a stricter limit on red meat intake (maximum 100 g/wk) because red meat seems to be associated with disease relapse and detrimental effects on the gut microbiota.<sup>20</sup> Physical activity recommendations were based on the Dutch physical activity guidelines: exercise at moderate intensity for 30 minutes per day at least 5 days per week.<sup>21</sup> A combination of cardio (eg, walking, running, cycling, and swimming) and resistance exercise was advised and the statement “more exercise is better” applied. The exact dietary and physical activity adjustments were expected to vary per person because baseline diet quality and level of physical activity would differ per person, but the targets were the same. Therefore, a personalized approach was applied and discussed between the participant, dietician, and physiotherapist. By setting goals, giving feedback, shaping knowledge, and repeating advice, the goal was to achieve a long-term behavior change.<sup>22</sup> Throughout the study, participants were supported by a booklet with dietary and physical activity guidelines, an app with recipes, and a booklet with examples of physical activity exercises.

## Study Assessments

### *Assessment of diet quality and level of physical activity*

Diet quality was assessed using the *Eetscore*-FFQ. This is a short FFQ that is scored with the Dutch Healthy Diet 2015-index that is based on the Dutch dietary guidelines.<sup>23</sup> Dietary assessment by the *Eetscore*-FFQ is based on 16 food components (vegetables, fruit, whole-grain products, legumes, nuts, dairy, fish, tea, fats and oils, coffee, red meat, processed meat, sweetened beverages and fruit juices, alcohol, salt, and unhealthy choices) with a score from 0 to 10 per component, resulting in a total score between 0 and 160. Higher scores indicate better adherence to the dietary guidelines.

Physical activity was assessed using the Short Questionnaire to Assess Health-Enhancing Physical Activity.<sup>24</sup> The Short Questionnaire to Assess Health-Enhancing Physical Activity contains questions regarding multiple activities during an average week in the past month, namely commuting activities, leisure-time activities, household activities, and activities at work or school. Number of days per week, average time per day, and intensity of every activity were reported. The total level of physical activity was calculated by summing up different activity scores that were calculated by the duration of an activity in minutes per week times the corresponding metabolic equivalent of the task. Higher scores indicate a higher level of physical activity.

### *Assessment of clinical effects of lifestyle intervention*

Several questionnaires were used to assess clinical effects of the lifestyle intervention. The primary outcome, impact of disease on daily life, was assessed using the Inflammatory Bowel Disease Disability Index (IBD-DI), a 28-item questionnaire covering limitations across 5 domains: overall health, body functions (sleep, mood, abdominal pain, defecation, weight), body structures (blood in stool, arthralgia), activity participation (work/education, interpersonal activities), and environmental factors (effects of medication, food, family and health care).<sup>25,26</sup> The total score ranges from -80 (maximum

degree of disability) to 22 (no disability); thus, higher scores represent less impact of disease on daily life.

Clinical disease activity was assessed using the patient Harvey-Bradshaw index (P-HBI) for participants with CD and the patient Simple Clinical Colitis Activity Index (P-SCCAI) for participants with UC.<sup>27,28</sup> Higher scores represent more active disease.

HRQoL was assessed using the Inflammatory Bowel Disease Questionnaire (IBDQ), a 32-item questionnaire to assess disease specific HRQoL with a score range from 32 to 224.<sup>29</sup> Higher scores represent better HRQoL.

Fatigue was assessed using the Inflammatory Bowel Disease Fatigue Scale (IBD-F), patient self-assessment scale that consists of 2 parts: 5 questions about the frequency, duration, and severity of fatigue, followed by 30 questions about the impact of fatigue on daily life.<sup>30</sup> Scores on the first part range from 0 to 20 and on the second part from 0 to 120. Higher scores represent more (impact of) fatigue.

### *Assessment of biochemical effects of lifestyle intervention*

Inflammation was assessed by fecal calprotectin. Participants were provided with materials and instructions to collect fecal samples at home at baseline and at 3 and 6 months. Samples were stored in participants' refrigerators before transfer to the study laboratory for analysis. Fecal calprotectin was determined using a sandwich enzyme-linked immunosorbent assay. Fecal calprotectin concentrations for this assay ranged from 0 to 2500 µg/g.

### *Assessment of participant characteristics*

All participants completed a general questionnaire on demographics, level of education, smoking, medication use, and previous IBD-related surgeries. Disease phenotype according to the Montreal classification was derived from their medical records.

### *Evaluation of lifestyle intervention*

After 6 months, participants completed a questionnaire consisting of questions about meeting expectations, number and timing of consults, and feasibility of dietary and physical activity advice to gain insight into their experiences with the intervention.

### *Sample Size Calculation and Statistical Analysis*

Sample size calculation revealed that a sample of 24 participants was needed to detect a change in IBD-DI of 10 points with an SD of 17 points, a 5% significance level, and a power of 80%. Accounting for a 20% dropout, a total of 30 participants needed to be enrolled.

Normally distributed data are presented as mean ± SD, skewed data as median with interquartile range (IQR), and categorical data as counts and percentages. Linear mixed models were used to analyze changes in diet quality, physical activity, and disease-related outcomes within subjects over time (fixed main factor) to account for repeated measures. Baseline values were used as reference. If effect of time was significant, pairwise comparisons between baseline and each subsequent time point were performed with Bonferroni correction to adjust for multiple comparisons. Further linear mixed models were performed to assess whether changes in diet quality and physical activity (fixed main covariates) were associated with changes in the disease-related outcomes

(dependent variables). Again, baseline values were used as reference with time as repeated measure. A random intercept was used with an identity covariance structure. Linear mixed model data are reported as the fixed effect estimates with 95% confidence intervals (CIs) or SE. A *P* value of <.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics version 24 (IBM Corp, Armonk, NY, USA).

## RESULTS

### Participant Characteristics

In total, 29 participants were included. Within 2 weeks after the start, 1 participant required extra medication for active disease and was therefore excluded from the study. It was unlikely that her flare-up was due to the lifestyle intervention, as we learned afterward that she withheld information about increasing complaints before the start of the study. During the study, 3 female participants withdrew after 2, 3, and 8 weeks, respectively, because of time constraints. One other female participant dropped out after 8 weeks because she was diagnosed with breast cancer. In total, 24 (83%) participants completed the study. For the analysis, all participants with at least 2 measurements were included, resulting in 26 participants for the analysis. Baseline characteristics of these participants are shown in Table 1. Most participants were female (58%), had UC (54%), and were highly educated (61%). Their median age was 36 (IQR, 30-52) years, mean body mass index was  $26.4 \pm 3.8$  kg/m<sup>2</sup>, and median disease duration was 11 (IQR, 5-14) years.

### Assessment of Diet Quality and Level of Physical Activity

At baseline, mean diet quality was  $94.4 \pm 3.1$  and mean total physical activity score was  $8006 \pm 936$  (Figure 2, Supplementary Table 1). During the intervention, diet quality improved in all participants. Mean diet quality significantly improved with 39 points to  $133.5 \pm 3.1$  after 1 month (*P* < .001) and was still  $128.5 \pm 3.2$  after 6 months (*P* < .001). When looking at the different components of diet quality, a significant increase was seen in the intake of vegetables, fruit, wholegrain products, legumes, nuts, dairy, and fish (*P* < .01 for all), while a significant decrease was seen in the intake of red meat, processed meat, sweetened beverages, alcohol, and unhealthy choices (*P* < .01 for all) (Figure 3). The intake of fat and oils (*P* = .76) and salt (*P* = .08) did not significantly change. We also observed no significant changes in total physical activity score or in the amounts of low-, moderate-, and high-intensity physical activity. However, mean body mass index significantly decreased from  $26.4 \pm 3.8$  kg/m<sup>2</sup> at baseline to  $25.0 \pm 3.9$  kg/m<sup>2</sup> after 6 months (*P* < .001).

### Assessment of Clinical Effects of Lifestyle Intervention

The estimated marginal means and standard errors of all disease-related outcomes at each time point are shown in Figure 4 (Supplementary Table 1). Impact of disease on daily life (IBD-DI) (*P* = .009) and fatigue (IBD-F) (*P* = .001) significantly reduced over time, while no change was found for clinical disease activity and HRQoL. In pairwise comparisons between baseline and subsequent time points, mean IBD-DI significantly increased between baseline and 3 months (*P* = .037) and baseline and 6 months (*P* = .011), although not

**Table 1.** Baseline characteristics of study population (n = 26)

Female	15 (58)
Age, y	36 (30-52)
BMI, kg/m <sup>2</sup>	26.4 ± 3.8
Level of education <sup>a</sup>	
Low	2 (8)
Intermediate	8 (31)
High	16 (61)
Current smoker	2 (8)
Crohn's disease	12 (46)
A1—Diagnosis <16 y	1 (8)
A2—Diagnosis 17-40 y	9 (75)
A3—Diagnosis >40 y	2 (17)
L1—Ileum	4 (33)
L2—Colon	2 (17)
L3—Ileocolon	6 (50)
L4—Upper GI tract	1 (8)
B1—Nonstricturing, nonpenetrating	9 (75)
B2—Stricturing, nonpenetrating	2 (17)
B3—Stricturing, penetrating	1 (8)
Perianal	1 (8)
Ulcerative colitis	14 (54)
E1—Proctitis	0 (0)
E2—Left-sided colitis	7 (50)
E3—Pancolitis	7 (50)
Disease duration, y	11 (5-14)
Medication use	
5-ASA	10 (38)
Corticosteroids	1 (4)
Immunomodulators	11 (42)
Biologicals	14 (54)
None	0 (0)
Prior IBD-related surgery	3 (12)

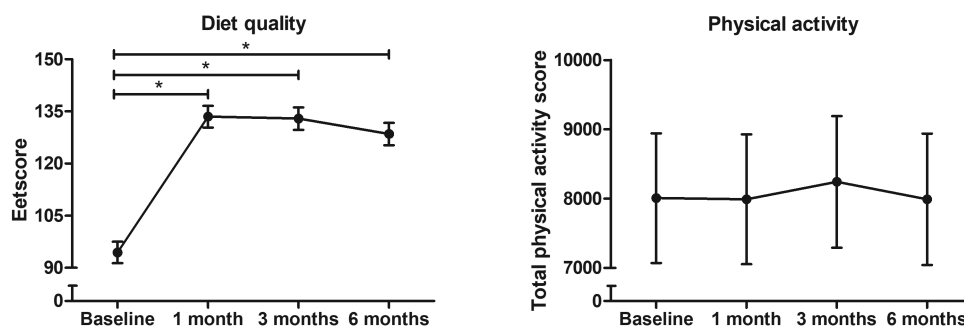
Values are n (%), median (interquartile range), or mean ± SD.

Abbreviations: 5-ASA, 5-aminosalicylic acid; BMI, body mass index; GI, gastrointestinal; IBD, inflammatory bowel disease.

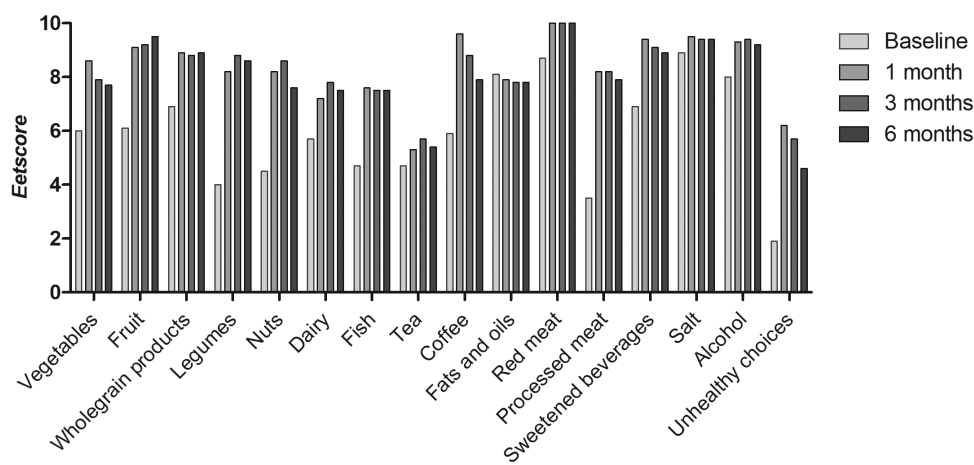
<sup>a</sup>Education level: no education, primary or lower vocational education and lower general secondary education (low); secondary vocational education and higher general secondary education (intermediate); higher vocational education and university (high).

between baseline and 1 month (*P* = .38). Pairwise comparisons for IBD-F showed a significant decrease in mean IBD-F between baseline and 3 months (*P* = .002) and between baseline and 6 months (*P* = .008), although not between baseline and 1 month (*P* = .07).

When looking at associations between lifestyle change and change in disease-related outcomes, linear mixed models showed that improvement in diet quality over time was significantly associated with impact of disease on daily life ( $\beta$  = 0.09; 95% CI, 0.03 to 0.15; *P* = .003) and fatigue ( $\beta$  = -0.13; 95% CI, -0.20 to -0.07; *P* < .001) (Table 2). These associations remained when corrected for physical activity. Physical activity alone was not associated with any of the disease-related outcomes. Overall, the association between diet quality and disease-related outcomes was small, with each 10-point increase in diet quality being associated with a 0.9-point reduction in impact of disease on daily life and a 1.3-point decrease in fatigue.



**Figure 2.** Diet quality and physical activity at baseline, 1 month, 3 months, and 6 months. Data are presented as the estimated marginal mean  $\pm$  SE as derived from the linear mixed model analysis with time as main fixed factor. Diet quality scores can range from 0 to 160. \* $P < .001$ .



**Figure 3.** Scores per food component at baseline, 1 month, 3 months, and 6 months. Data are presented as the estimated marginal mean as derived from the linear mixed model analysis with time as main fixed factor. Higher scores indicate better adherence to dietary guidelines. Except for fat and oils and salt intake, all food components improved, with a significance level of  $P < .01$ .

### Assessment of Biochemical Effects of Lifestyle Intervention

At baseline, median fecal calprotectin was 15 (IQR, 5-42)  $\mu\text{g/g}$ , which reflects that all participants were in remission. No significant change was found over time ( $P = .69$ ) (Figure 4, Supplementary Table 1) and no associations were found with diet quality and physical activity ( $P = .85$  and  $P = .62$ ) (Table 2).

### Evaluation of Lifestyle Intervention

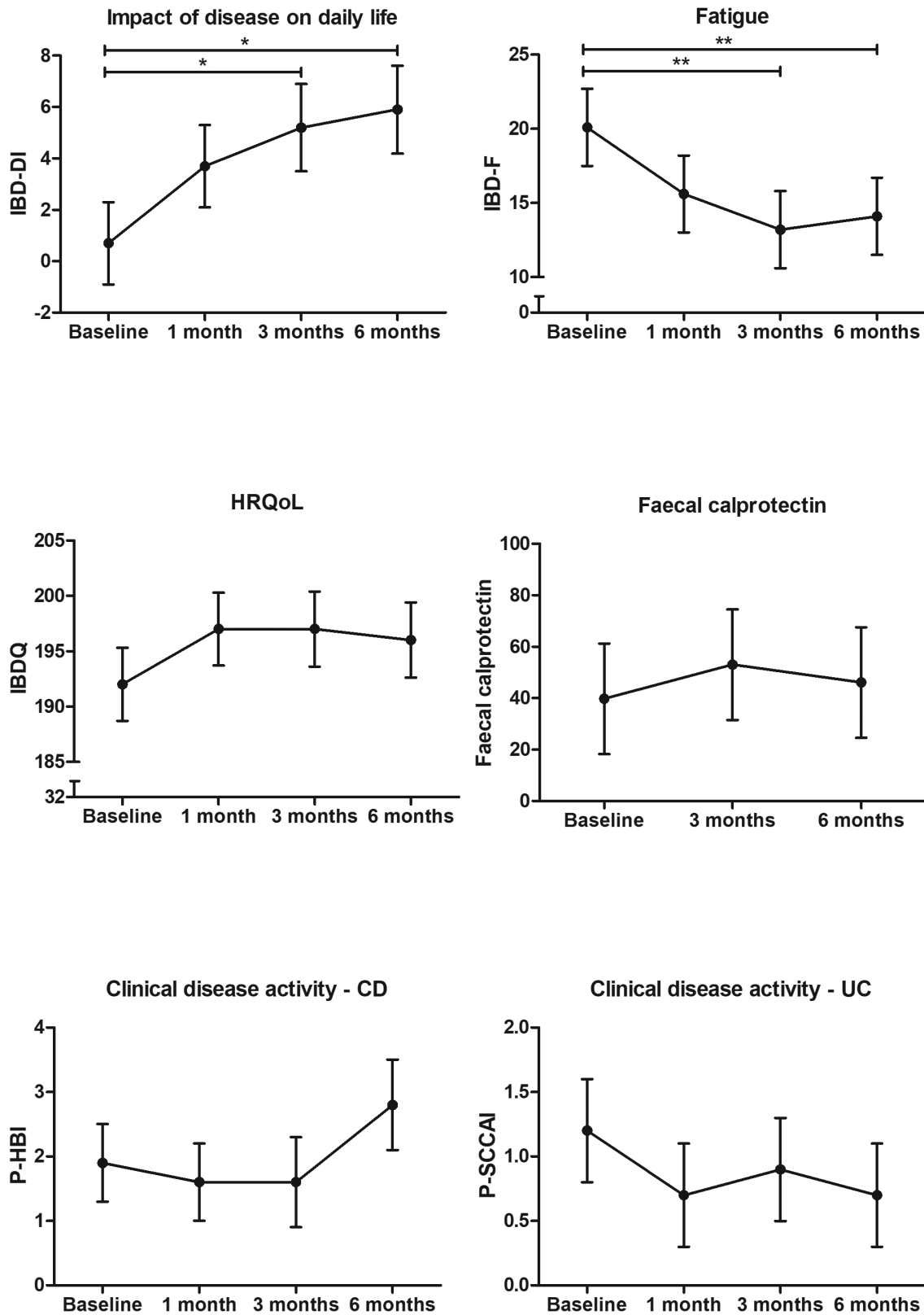
The lifestyle intervention was rated with a 8.4 out of 10, and 79% of participants would recommend the lifestyle intervention to other patients with IBD. Consults with the dietician were rated with a  $4.5 \pm 0.5$  and consults with the physiotherapist were rated with a  $4.4 \pm 0.7$  on a 5-point Likert scale. The time interval between consults was rated a  $4.1 \pm 0.8$  on a 5-point Likert scale. Participants found the physical activity advice more feasible and easy to apply in daily life than the dietary advice (8.1 out of 10 vs 7.4 out of 10). After 6 months, the extent to which participants felt able to continue the recommendations without guidance of a dietician and physiotherapist was rated with a 7.9 out of 10.

## DISCUSSION

In this single-arm intervention study in IBD patients in remission or with mildly active disease, we found that a lifestyle

intervention that combined dietary and physical activity advice significantly improved diet quality, while level of physical activity remained the same. Over time, a significant decrease was found in impact of disease on daily life and fatigue, while no significant change was observed in clinical disease activity, HRQoL, and fecal calprotectin. Improvement in diet quality was associated with a reduction in impact of disease on daily life and fatigue. No association was found with clinical disease activity, HRQoL, and fecal calprotectin, nor was physical activity associated with any of the outcomes. The majority of participants would recommend this lifestyle intervention to other patients with IBD.

To our knowledge, this is the first study in IBD patients to examine the effects of a combined lifestyle intervention focusing on diet and physical activity. Therefore, it is difficult to compare the current study with previous lifestyle studies, as they all differ in treatment approach, patient inclusion, outcomes, and follow-up. Nevertheless, one research group performed 2 other combined lifestyle intervention studies in IBD patients. Those consisted of a 10-week training program, including stress management, moderate exercise, moderate Mediterranean diet, and behavioral techniques.<sup>17,31</sup> In their first study, no effect was found on HRQoL or disease status in 15 UC patients 3 months after completion of the intervention.<sup>31</sup> Their second study only included UC patients with a reduced HRQoL ( $\text{IBDQ} < 170$ ) and showed a significant improvement in HRQoL in 47 UC patients at week 12, while disease status did not change.<sup>17</sup> Whether the



**Figure 4.** Disease-related outcomes at baseline, 1 month, 3 months, and 6 months. Data are presented as the estimated marginal mean  $\pm$  SE as derived from the linear mixed model analysis with time as main fixed factor. \* $P < .05$ , \*\* $P < .01$ . Impact of disease on daily life scores can range from -80 to +22: higher scores represent less disabilities and thus less impact of disease on daily life. Fatigue scores can range from 0 to 120. Health-related quality-of-life (HRQoL) scores can range from 32 to 224. Faecal calprotectin ( $n = 24$ ): statistical tests were performed on the log2 scale. Hereafter, data were back transformed for presentation in this figure. Median faecal calprotectin: baseline 15 (interquartile range [IQR], 5-42)  $\mu\text{g/g}$ , 3 months 18 (IQR, 8-31)  $\mu\text{g/g}$ , 6 months 12 (IQR, 4-54)  $\mu\text{g/g}$ . CD, Crohn's disease; IBD-DI, Inflammatory Bowel Disease Disability Index; IBD-F, Inflammatory Bowel Disease Fatigue Scale; IBDQ, Inflammatory Bowel Disease Questionnaire; P-HBI, patient Harvey Bradshaw index; P-SCCAI, patient Simple Clinical Colitis Activity Index; UC, ulcerative colitis.

**Table 2.** Linear mixed model analysis of associations between lifestyle change and outcomes over time

	Diet Quality		Physical Activity <sup>a</sup>		Diet Quality + Physical Activity <sup>a</sup>	
	$\beta$ (95%CI)	P Value	$\beta$ (95%CI)	P Value	$\beta$ (95%CI)	P Value
Impact of disease on daily life (IBD-DI)	0.09 (0.03 to 0.15)	.003	0.02 (-0.03 to 0.06)	.49	Diet quality: 0.09 (0.04 to 0.15) PA: 0.03 (-0.02 to 0.07)	.001 .21
Clinical disease activity						
CD (P-HBI)	0.004 (-0.02 to 0.03)	.75	-0.01 (-0.03 to 0.005)	.16	Diet quality: -0.005 (-0.03 to 0.02) PA: -0.01 (-0.03 to 0.005)	.74 .16
UC (P-SCCAI)	-0.009 (-0.02 to 0.005)	.20	-0.008 (-0.02 to 0.001)	.10	Diet quality: -0.008 (-0.02 to 0.005) PA: -0.007 (-0.02 to 0.002)	.21 .10
Fatigue (IBD-F)	-0.13 (-0.20 to -0.07)	<.001	-0.03 (-0.09 to 0.03)	.35	Diet quality: -0.14 (-0.20 to -0.07) PA: -0.03 (-0.09 to 0.02)	<.001 .21
Health-related quality of life (IBDQ)	0.12 (-0.01 to 0.24)	.07	0.05 (-0.04 to 0.14)	.29	Diet quality: 0.13 (-0.001 to 0.25) PA: 0.06 (-0.03 to 0.15)	.05 .20
Fecal calprotectin (n = 24)	-0.002 (-0.02 to 0.02)	.85	-0.003 (-0.01 to 0.01)	.62	Diet quality: -0.002 (-0.02 to 0.02) PA: -0.003 (-0.01 to 0.01)	.81 .61

Data are tested by using linear mixed models with an identity covariance structure and indicating time as repeated measure. Impact of disease on daily life, disease activity, fatigue, health-related quality of life, and fecal calprotectin are dependent variables and diet quality and PA are added as fixed main covariates to the model.

Bold values are significant.

Abbreviations: CD, Crohn's disease; CI, confidence interval; IBD-DI, Inflammatory Bowel Disease Disability Index; IBD-F, Inflammatory Bowel Disease Fatigue Scale; IBDQ, Inflammatory Bowel Disease Questionnaire; P-HBI, patient Harvey Bradshaw index; P-SCCAI, patient Simple Clinical Colitis Activity Index; PA, physical activity; UC, ulcerative colitis.

<sup>a</sup>Per 100 points change in total physical activity score.

intervention actually changed the lifestyle of these patients is unknown, as changes in diet and level of physical activity were not reported. In both studies, only patients in remission or with mildly active disease were included. As known from other studies, disease status at baseline clearly determines the room for improvement.<sup>32-34</sup> Also in our study, the participants were in remission or had only mildly active disease, which most likely explains the lack of an effect on clinical disease activity and fecal calprotectin because these were already low at baseline.

As shown in previous studies, exclusion of certain food components may reduce proinflammatory processes and thereby benefit IBD patients.<sup>10,11</sup> In our study, participants improved their diet quality and reduced the inflammatory potential of their diet by increasing their intake of products high in anti-inflammatory components, such as vegetables, fruit, whole-grain products, legumes, fish, and nuts, while decreasing their intake of products high in proinflammatory components, such as red and processed meat, sweetened beverages, and alcohol. Adherence to such an anti-inflammatory dietary pattern has the potential to prevent intestinal inflammatory processes via the gut microbiome.<sup>35</sup> Moreover, it is associated with less inflammation and a lower disease activity,<sup>36</sup> which is associated with a lower impact of disease.<sup>26</sup> Therefore, reduction of the inflammatory potential of diet might have decreased the impact of disease on daily life and fatigue in our study population, as the improvement in diet quality was followed by improvement of those disease-related outcomes. Moreover, our intervention diet is not a restrictive exclusion diet but is in line with the general dietary guidelines on healthy eating.<sup>18</sup> Therefore, the diet is more acceptable for patients, has a lower risk of nutritional deficiencies and undernutrition, and also has broader health effects.<sup>37</sup>

In contrast to the effect of our lifestyle intervention on diet quality, we found no improvement in level of physical activity. This may be explained by the limited room for improvement because a large percentage of participants already exercised regularly compared with another cohort of IBD patients.<sup>38</sup> Another explanation for the lack of improvement in level of physical activity may be the COVID-19 pandemic.<sup>39</sup> Participants reported that their possibilities to be physically active were restricted due to COVID-19 measures. Gyms and sports clubs were closed, so physical activity was generally limited to walking, cycling, running, and at-home resistance exercises. The level of physical activity might have improved if we had included supervised exercise training as was done in other physical activity interventions instead of only providing participants with recommendations and examples.<sup>33,34</sup> However, this is more difficult to implement in daily life and more expensive.

The evaluation revealed that participants were satisfied with the lifestyle intervention and would recommend it to other patients with IBD. Although we did not find changes in level of physical activity, participants found the physical activity advice more feasible and more easy to apply than the dietary advice. This can be explained by our study population already exercising regularly. Furthermore, difficulty to comply with the dietary advice may in part be explained by the social aspects of eating and drinking. Participants reported to experience difficulties with dietary adherence when going out for dinner or when having something to celebrate, as in those situations the consumed foods and drinks are generally not (fully) in line with dietary guidelines.

During the lifestyle intervention, the mean body mass index of our participants significantly decreased, which is likely the result of their healthier lifestyle. In addition to the benefits

of a reduced inflammatory potential of diet, improvement in body mass index may further decrease low-grade inflammation and is associated with broader health benefits.<sup>40</sup>

As mentioned previously, to our knowledge, this is the first study in IBD patients to examine a combined lifestyle intervention focusing on diet and physical activity. Other strengths of this study are the follow-up of 6 months, the personalized approach, and the inclusion of a representative group of IBD patients including comparable numbers of CD and UC, males and females, and patients of all ages. This study also has limitations that should be considered. We did not include a control group because there is no ideal placebo treatment. Several types of control groups were considered, but all had their drawbacks leading to bias. As a result, we could not correct for natural changes over time and we could not determine whether diet quality solely improved because of our intervention or also as a result of dietary awareness. However, dietary awareness would also be a positive result of our intervention. Furthermore, participants may have given socially desirable answers to the diet and physical activity questionnaires. However, the fact that we found a change in diet quality but not in level of physical activity suggests that the degree of social desirability is limited. Nevertheless, memory bias and estimation error may still have occurred during completion of the diet and physical activity questionnaires.<sup>41</sup> Another limitation is that we only included patients in remission or with mildly active disease, as high disease activity would require more intense pharmacological treatment or even surgery, which would distort the results of lifestyle changes. In that case, we would not be able to distinguish between medication and lifestyle effects anymore. Also, we excluded patients with a stoma or pouch in situ, as these patients might have specific dietary needs that may interfere with our dietary recommendations. As a result of this participant selection, our results cannot be extrapolated to the whole IBD population. It remains unknown whether patients with high disease activity would benefit from our lifestyle intervention. Finally, this study started just before the COVID-19 pandemic and finished during the pandemic. COVID-19 measures not only restricted the possibilities to be physically active, but also limited social activities that might have led to an underestimation of social limitations because of IBD complaints. Moreover, we can speculate about the impact of psychosocial aspects, such as anxiety and depression, on our outcomes as a result of the pandemic.

## Conclusions

We found that a combined lifestyle intervention significantly improved diet quality. This improvement in diet quality was associated with a reduction in impact of disease on daily life and fatigue in patients with IBD in remission or with mildly active disease. The level of physical activity remained the same, and no associations with disease-related outcomes were found. This combined lifestyle intervention was mainly based on general dietary and physical activity guidelines meant for healthy adults. The study results suggest that these general guidelines, when actively supervised while applying, might also benefit IBD patients. To further support these findings, future studies should be performed outside pandemic times to ensure representative daily life, in patients with a low

diet quality and level of physical activity, and in larger study populations.

## Supplementary data

Supplementary data is available at *Inflammatory Bowel Diseases* online.

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## Author Contributions

C.R.L.: study concept and design, data acquisition, data analysis and interpretation, drafted manuscript. N.M.d.R.: study concept and design, data interpretation, critical revision of manuscript. H.H.H.: study concept and design, critical revision of manuscript. L.A.v.d.W.-K.: study concept and design, critical revision of manuscript. B.J.M.W.: study concept and design, critical revision of manuscript. All authors have read and approved the final manuscript.

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## Conflicts of Interest

The authors declare that they have no conflict of interest.

## Data Availability

All data generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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