Revealing the Puzzle of Nonadherence in IBD—Assembling the Pieces

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Background: Adherence is generally associated with improved treatment outcomes in inflammatory bowel disease (IBD) patients. Different components of the patient profile have an impact on patient adherence. Capturing nonadherent patients by identifying modifiable risk factors in daily practice still remains a challenge. The objective of this study was to identify modifiable and nonmodifiable risk factors for nonadherence in IBD patients.

Methods: Patients filled out questionnaires including demographic, clinical, and socioeconomic information and accessibility to gastrointestinal services. Psychological features were assessed using the Sense of Coherence, Hospital Anxiety and Depression Scale, IBD–Self Efficacy, and Brief Illness Perception (BIPQ) questionnaires. Adherence to treatment was evaluated using the Morisky score.

Results: The study included 311 patients: 62.4% females, median age 34.78 years, 70.4% Crohn's disease (CD). Multivariate analysis was done in 3 sections: demographic and disease characteristics, communication with medical staff, and psychological aspects; all included sex and disease type. Ulcerative colitis (UC) patients were less adherent (odds ratio [OR], 1.792; OR, 1.915; OR, 1.748; respectively). Females were less adherent in 2 sections (OR, 1.841; OR, 1.751; respectively). Employment (OR, 2.449), low score in on the BIPQ–understanding of disease (OR, 0.881), and poor communication with the gastroenterologist (OR, 1.798) were also predictors of low adherence.

Conclusions: Nonmodifiable characteristics such as female sex and UC are associated with low adherence. Good communication with the treating physician and understanding the disease are modifiable factors associated with high adherence. Early intervention might improve patients' adherence.

Key Words: adherence, inflammatory bowel disease

INTRODUCTION

Inflammatory bowel diseases (IBDs) are chronic conditions with periods of remission alternating with unpredictable periods of exacerbation. Medical therapy remains at the center of management. To induce and maintain remission over time, it is essential to use an appropriately prescribed medication tailored by an expert IBD gastroenterologist.[1]

Several controlled trials[2–5] have shown the benefit of maintenance therapy in lowering the risk of clinical recurrence, hospitalization, cancer, and surgery.

However, success of treatment depends on adherence to medical therapy. Nonadherent behavior can lead to worse disease activity and higher rates of complications.

IBD, as a chronic disease, is a clinical condition with a tendency toward high risk for nonadherence.[2] Adherence in IBD patients was evaluated by several studies in the past,[6–7] which reported that nonadherence rates range from 35% to 87% in all treatments and from 17% to 45% regarding treatment with anti–tumor necrosis factor agents.[1, 8] Identifying causes and risk factors of nonadherence is important as it will enable the caretaking team to interfere and prevent failure of treatment due to nonadherence.

The most widely used method to assess medication adherence in clinical practice is by patient self-report. Morisky et al.[9] developed and published the Morisky Medication Adherence scale (MMAS8), an 8-item screening tool of a self-reporting survey that was validated in IBD patients in previous studies.[10]

Some studies have reported the effect of sociodemographic characteristics,[11] such as younger age, higher educational level, and being single as predictors for low adherence. Others reported the type of therapy as a predictor of adherence, stating that mesalamine is a risk factor for low adherence and biological treatment is correlated with high adherence.[6, 12]

Good communication with the treating physician and trust were also found to improve adherence.[13]

Psychological aspects of the patient with IBD, such as depression, anxiety, and illness perceptions have also been able to predict adherence.[14] Although other studies have emphasized the importance of other psychological parameters such as IBD Self-Efficacy[15] and Sense of Coherence,[16] to our knowledge their influence on patient adherence have not been investigated in any IBD study.

In addition, previous studies explored only certain aspects and did not correlate all different possible elements that may be associated with nonadherence.

In our study, we aimed to evaluate the mutual influence of many different aspects of patient adherence using sociodemographic characteristics, disease-related characteristics, relationship with the medical staff, and psychological aspects.

METHODS

Study Design

Between November 2015 and May 2017, adult (age ≥ 18 years) ambulatory patients with an established diagnosis of IBD were invited to participate in this study. Patients were recruited from 3 university hospitals, Assaf Harofeh, Meir, and Shaare Zedek in Israel. Patients not receiving any medical treatment were not included.

All patients completed questionnaires including demographic data, disease parameters, relationship with the medical staff, and psychological profile, as described below. Adherence to treatment was assessed using MMAS8.

The study was approved by the Ethics Committee of each of the 3 hospitals. All patients signed an informed consent.

Factors Investigated for Nonadherence

Potential risk factors to nonadherence in IBD patients were divided into 3 categories:

Demographic risk factors

Demographic risk factors included age, sex, origin (Ashkenazi, Sepharadi, other Jewish origin, or Arab), belief (secular, orthodox, and ultraorthodox), education (divided to 12 or more years of education and less than 12 years), relationship status (divided into in a relationship, single, or past relationship), employment, level of income (divided into low, medium, or high), working hours per week, and smoking status (current smoker, ex-smoker, and nonsmoker).

Clinical risk factors included type of disease, duration of disease, number of concomitant medications for the treatment of other diseases (less than 3 or 3 or more), presence of perianal disease, disease extension, presence of stoma (current, past stoma, or no stoma), past surgery, past hospitalization, type of medical therapy (5-aminosalicylic acid [5-ASA], steroids, immunomodulators, and biological treatment), cannabis use, and alternative medicine use (none, conservative, or alternative alone).

Assessment of disease severity. Clinical disease severity was calculated by modification from a study by the GETAID group.[17] The first score was calculated from an average of disease severity, as reported by the physician. The score was graded on a scale between 0 and 5 (0 = no symptoms; 1 = mild symptoms; 2 = medium symptoms; 3 = active disease; 4 = hospitalization in the past year; 5 = surgery in the past year or current stoma). Another component of severity was based on medical treatment summing up a scale varying from 0 to 5 (0 = no treatment; 1 = 5-ASA or antibiotics; 2 = steroid dose of less than 10 mg per day; 3 = steroids in a regular dose; 4 = immunomodulatory treatment; 5 = biological treatment).These scales were calculated for each of the last 3 years. The final score was the average of the score given each year over the last 3 years.

Additionally, the disease was considered severe if the score was 3 and greater in the past 3 years, if the patient had more than 1 surgery in the past, or if there was a stoma currently or in the past. All the other patients were considered "not severe disease" according to this scale.

Communication with the medical team. Relationship with the medical team was evaluated by a questionnaire of 7 parameters (Appendix 1).

Psychological factors

Psychological factors included illness perceptions, IBD self-efficacy, depression and anxiety, and sense of coherence.

Illness perceptions were assessed by the Brief Illness Perception Questionnaire[18]. This 9-item questionnaire explores the cognitive and emotional representations of illness across 8 dimensions: Consequences, Timeline, Personal Control, Treatment Control, Identity, Concerns, Understanding, and Emotional Response. Items were assessed on an 11-point Likert scale (0 = not affecting my life at all; 10 = severely affecting my life). Self-Efficacy was evaluated using the IBD Self-Efficacy scale.[14, 15, 19] It is a 29-item scale developed by Keefer et al. based on patient interview, validated self-efficacy measures for other diseases, and self-efficacy theory. The instrument assesses the level of confidence in managing various disease-related "tasks," with item scores ranging from 1 to 10 (1 = not at all; 10 = totally). Higher scores reflect greater disease self-management efficacy. Items were grouped conceptually into 4 subscales: Managing Stress and Emotions, Managing Medical Care, Managing Symptoms and Disease, and Maintaining Remission. Sense of coherence was assessed according to the Sense of Coherence (SOC)[16]–Orientation to Life score. The SOC-13 scale measures the degree to which an individual views the world as comprehensible (5 items), manageable (4 items), and meaningful (4 items) using a 7-point Likert scale. The total SOC-13 score is the sum of the items, ranging from 13 to 91, with the higher scores reflecting a better sense of coherence. We received the author's permission to use this scale in our study.

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Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS).[20] This is a 14-item scale assessing anxiety (7 items) and depression (7 items) in patients with organic pathology. A higher score corresponds to higher severity of emotional stress. We used the cutoff of a score above 10 in each of the parameters (anxiety or depression) as a marker for anxiety or depression, respectively.[21, 22]

Adherence Measure

Adherence to medical treatment was measured by the 8-item self-reported Morisky score. Patients were divided to 3 groups: low adherence (MMS8 score 1–6), medium adherence (MMS8 score 6–<8), and high adherence (MMS8 score ≥8).[9, 10]

Statistical Analysis

Categorical variables were described using frequency and percentage. Continuous variables were evaluated for normal distribution using histograms and Q-Q plots. Normally distributed continuous variables were described using mean and standard deviation, and not normally distributed were expressed as median and interquartile range. The Kruskal Wallis test, analysis of variance, and Mann-Whitney test were used to compare continuous variables between categories. Categorical variables were compared between categories using the chi-square test or Fisher exact test. Correlation between continuous variables was evaluated using Spearman's rank correlation coefficient test.

Multivariate analysis was performed using multinominal regression. The low-adherence group (Morisky score < 6) and the moderate-adherence group (Morisky score ≥ 6 and < 8) were compared with the high-adherence group (Morisky score = 8), which was considered the reference group; age, sex, type of disease, and variables that were associated with adherence with a *P* value of less than 0.2 in the univariate analysis (employment, number of medications, hospitalization, stoma, surgeries, 5-ASA, prednisone, biologics, Gastroenterologist (GE) follow-up, number of GEs, accessibility of GE, trust GE, communication with GE, assist IBD nurse, depression, SOC, treatment will help, understanding of disease, management of medications, keeping remission, total severity score) were included in the multivariate analysis. Age, sex, and type of disease were forced into the regression model whereas all the other parameters were selected to the final model using the backward stepwise likelihood ratio method. As there was no difference between those who were completely adherent (Morisky = 8) and those who showed good adherence (Morisky ≥ 6 and < 8), these 2 groups were analyzed together vs those who were nonadherent using logistic regression. We used the same criteria for variable selection, and the regression model included 2 blocks; the first included age, sex, and type of disease, the second all the other parameters (demographic characteristics: education, employed, number of medications, surgeries, hospitalization, and stoma. Communication with the medical staff characteristics: GE follow-up, accessibility of GE, trust in GE,

communication with GE; psychological parameters: depressed, feel symptoms, treatment will help, understanding of disease), using backward stepwise likelihood ratio methods. All the regression models were analyzed 3 times: once against disease characteristics, once against communication with medical staff, and once against psychological aspects. As we had data from 3 different medical centers as a sensitivity analysis, we reperformed all the logistic regression using a generalized estimating equation model to control for possible effects. Because the participating hospitals were all secondary care public hospitals delivering the same service under the same regulations to all the patients, we did not believe that there would be a difference between the hospitals; however, to exclude this possibility, we did a sensitivity analysis, which did show equal results in all 3 hospitals. All statistical tests were 2-tailed. A *P* value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS (IBM SPSS Statistics for Windows, version 23.0; IBM Corp., Armonk, NY, USA).

RESULTS

Patient Population

Between November 2015 and May 2017, we interviewed 311 consecutive IBD patients attending outpatient clinics in

TABLE 1: Demographic Characteristics of Study Participants

Characteristic	Patients (All) (n = 311)
Age, median (IQR), y	34.78 (27.44–44.91)
Sex, No. (%)	
Male	117 (37.6)
Female	194 (62.4)
Education, No. (%)	
Not university graduate	134 (43.6)
University graduate	173 (56.4)
Relationship status, No. (%)	
In a relationship	203 (66.1)
Single	83 (27)
Past relationship	21 (6.8)
Employment, No. (%)	
Currently employed	230 (74.9)
Unemployed	77 (25.1)
Level of income, No. (%)	
Low	182 (60.7)
Medium	50 (16.7)
High	68 (22.7)
Type of disease, No. (%)	
Crohn	219 (70.4)
UC	81 (26)
IBDU	11 (3.5)

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TABLE 2: Adherence According to Demographic Characteristics

Characteristic	Low Adherence	Medium Adherence	High Adherence	*P*
Age, median (IQR), y	33.6 (27.4–42.5)	34.8 (27.4–45.1)	39.4 (28.4–54.3)	0.125
Sex, No. (%)				0.255
Male	41 (35)	39 (33.3)	37 (31.6)	
Female	85 (43.8)	61 (31.4)	48 (24.7)	
Education, No. (%)				0.214
Not university graduate	48 (35.8)	43 (32.1)	43 (32.1)	
University graduate	77 (44.5)	54 (31.2)	42 (24.3)	
Relationship status, No. (%)				0.775
In a relationship	83 (40.9)	65 (32)	55 (27.1)	
Single	31 (37.3)	27 (32.5)	25 (30.1)	
Past relationship	11 (52.4)	6 (28.6)	4 (19)	
Employment, No. (%)				0.002
Currently employed	106 (46.1)	63 (27.4)	61 (26.5)	
Unemployed	19 (24.7)	35 (45.5)	23 (29.9)	
Level of income, No. (%)				0.842
Low	73 (40.1)	59 (32.4)	50 (27.5)	
Medium	24 (48)	14 (28)	12 (24)	
High	26 (41)	24 (35.3)	18 (26.5)	
Working h per wk, median (IQR)	40 (18.5–45)	24.5 (0–44.4)	36 (0–45)	0.008
Smoking, No. (%)				0.726
Never	95 (41.5)	70 (30.6)	64 (27.9)	
Current	17 (37.8)	14 (31.1)	14 (31.1)	
Ex-smoker	13 (38.2)	14 (41.2)	7 (20.6)	

3 participating hospitals: 129 (41.5%) from Assaf-Harofe, 119 (38.3%) from Meir, and 63 (20.3%) from Shaare-Zedek. Relevant demographic and clinical characteristics are shown in Table 1.

Adherence

All participants filled the MMS8. Low adherence was documented in 126 (40.5%), medium adherence in 100 (32.1%), and high adherence in 85 (27.3%) patients.

Risk Factors for Nonadherence

The results of the univariate analysis are shown in Tables 2–5. Independent risk factors for low adherence according to the Morisky scale were employment (*P* = 0.002), greater number of working hours per week (*P* = 0.008), and use of 5-ASA tablets (*P* < 0.001). High adherence was correlated with biological treatment (*P* < 0.001), more severe disease (*P* = 0.013), and higher trust in the gastroenterologist (*P* = 0.012).

Lower adherence was associated with lower SOC-13 score (*P* = 0.025), BIPQ-understanding of disease (*P* = 0.043), and IBD self-efficacy management of medication (*P* = 0.001). No correlation was found between anxiety or depression and adherence.

The results of the multivariate analysis are shown in Table 6. The multivariate analysis was done in 3 sections: demographic and disease characteristics, communication with the medical staff, and psychological aspects. In all 3 sections, UC patients had a lower adherence compared with Crohn's and inflammatory bowel disease unclassified patients (odds ratio [OR], 1.792; 95% confidence interval [CI], 1.037–3.098; OR, 1.915; 95% CI, 1.082–3.386; OR, 1.748; 95% CI, 1.005–3.042; respectively). Female patients were less adherent than male patients in the second and third sections, but only trended toward statistical significance in the first section (OR, 1.572; 95% CI, 0.951–2.604; OR, 1.841; 95% CI, 1.075–3.154; OR, 1.751; 95% CI, 1.042–2.941; respectively). Employment (OR, 2.449; 95% CI, 1.331–4.506) and low score in BIPQ–understanding of disease (OR, 0.881; 95% CI, 0.787–0.987) were also associated with low adherence. Poor communication with the treating gastroenterologist correlated with low adherence as well (OR, 1.798; 95% CI, 1.219–2.651).

DISCUSSION

Our study is unique in applying a comprehensive approach to explore many different aspects associated with adherence in IBD patients. We used several questionnaires addressing different aspects of patients: psychological profile,

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TABLE 3: Adherence According to Disease Characteristics

Characteristic	Low Adherence, No. (%)	Medium Adherence, No. (%)	High Adherence, No. (%)	P
Total No. medications				0.158
<3	99 (43.4)	73 (32)	56 (24.6)	
≥3	27 (33.3)	26 (32.1)	28 (34.6)	
Type of disease				0.143
Crohn's	80 (36.5)	71 (32.4)	68 (31.1)	
UC	41 (50.6)	25 (30.9)	15 (18.5)	
IBDU	5 (45.5)	4 (36.4)	2 (18.2)	
Perianal disease	107 (43.5)	77 (31.3)	62 (25.2)	0.91
Hospitalization	81 (37.2)	77 (35.3)	60 (27.5)	0.067
Stoma				0.166
No	122 (41.5)	95 (32.3)	77 (26.2)	
Yes	1 (10)	3 (30)	6 (60)	
Past	3 (42.9)	2 (28.6)	2 (28.6)	
Surgeries	32 (32.7)	33 (33.7)	33 (33.7)	0.117
Medication use				
Topical 5-ASA	13 (41.9)	12 (38.7)	6 (19.4)	0.546
Tab 5-ASA	57 (57)	24 (24)	19 (19)	<0.001
Budesonide	7 (41.2)	5 (29.4)	5 (29.4)	0.959
Prednisone	6 (21.4)	14 (50)	8 (28.6)	0.05
Immunosuppressive drugs	38 (39.6)	32 (33.3)	26 (27.1)	0.965
Biologics	45 (29.6)	54 (35.5)	53 (34.9)	<0.001
Cannabis use	8 (30.8)	12 (46.2)	6 (23.1)	0.278
Crohn's extensive disease	28 (34.6)	30 (37)	23 (28.4)	0.507
UC extensive disease	12 (30.8)	16 (41)	11 (28.2)	0.004
Alternative medicine				0.155
No	78 (39.2)	58 (29.1)	63 (31.7)	
Together with conservative	31 (43.7)	27 (38)	13 (18.3)	
Only	9 (7.6)	8 (8.6)	3 (3.8)	
Total severity score	5.6 (3.2)	6.6 (3.5)	6.6 (2.8)	0.013
Severe disease yes/no score	18 (27.7)	24 (36.9)	23 (35.4)	0.07

5-ASA = 5-aminosalicylic acid.

patient characteristics, disease parameters, and communication with the medical team. Thus, we obtained a comprehensive profile of patient characteristics to identify modifiable risk factors associated with nonadherence in IBD patients.

Nonadherence rates in our study were similar to those reported in previous studies.[23–29] However, we focused on differentiating modifiable and nonmodifiable factors associated with adherence. The nonmodifiable factors associated with low adherence were sex and type of disease. Association of sex with adherence is controversial, as some studies have found male sex to be associated with lower adherence,[9] whereas other studies have found that females were less adherent.[12] Type of disease as a predictor of nonadherence has been described in few studies. Ediger et al. found nonadherence to be correlated with UC, but only in men.[30] In our study, we found that UC was associated with lower adherence. This finding was consistent in all examined aspects of multivariate analysis.

Our study is the first to use long-term severity of disease. As commonly used parameters of disease severity reflect activity only at a certain time point, we widened the scope by modifying a score developed by the GETAID group.[17] This score reflects disease severity over a time frame of the last 3 years. A higher severity score was correlated with better adherence in the univariate analysis. Our results are contradictory to those of the study by Trindade et al.,[16] in which a higher Harvey-Bradshaw index was associated with lower adherence. As adherence is built over a long time frame, we believe that long=term severity of disease is a better tool to assess it.

Modifiable parameters found to be correlated with adherence can be divided into 3 categories: life conditions, psychological profile, and communication with the medical staff.

Parameters reflecting life conditions included full employment and long working hours, both of which were found to be correlated with low adherence. This is in accordance with

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TABLE 4: Adherence According to Relationship with Medical Staff

Characteristic	Low Adherence	Medium Adherence	High Aderence	P
Members of IBD association, No. (%)	33 (39.3)	31 (39.3)	20 (23.8)	0.495
No. no GE follow-up (%)	11 (68.8)	3 (18.8)	2 (12.5)	0.068
No. GE, median (IQR)	2 (2–3)	2 (2–3)	2 (1–3)	0.073
Accessibility of GE score, median (IQR)	2 (1–3)	2 (1, 2)	1 (1, 2)	0.074
Trust GE score, median (IQR)	1 (1, 2)	1 (1, 2)	1 (1)	0.012
Communication with GE score, median (IQR)	1 (1, 2)	1 (1)	1 (1)	0.107
Assist IBD nurse, median (IQR)	5 (3–5)	4 (2–5)	5 (3–5)	0.032

GE = Gastroenterologist.

TABLE 5: Adherence According to Psychosocial Scales

Characteristic	Low Adherence	Medium Adherence	High Adherence	P
HADS				
Anxious, No. (%)	29 (40.8)	22 (31)	20 (28.2)	0.96
Depressed, No. (%)	7 (25)	12 (42.9)	9 (32.1)	0.182
HADS anxiety score, median (IQR)	8 (4.25–10)	7 (4–10)	7 (4–10)	0.61
HADS depression score, median (IQR)	3 (2–6)	4 (1.25–8)	4 (1–8)	0.272
Sense of coherence, mean (SD)	62 (51–69)	59 (53.5–71)	63 (57–71.75)	0.025
BIPQ, median (IQR)				
Disease influence	7 (5–9)	8 (6–9)	7 (5–8)	0.223
Duration of disease	10 (8–10)	10 (9, 10)	10 (9, 10)	0.283
Control of disease	6 (4–8)	6.5 (5–8)	6 (4–8)	0.323
Treatment will help	8 (5–9)	8 (6–9)	8 (7–9.25)	0.149
Feeling symptoms	7 (4–8)	7 (4–8)	6 (3–8)	0.192
Worry about disease	7 (5–9)	7 (5–9)	7 (4.75–9)	0.819
Understanding of disease	8 (6–8)	8 (7–9)	8 (7–10)	0.043
Emotional influence	7 (4–8)	8 (7–9)	5.6 (3.2)	0.275
BIPQ total, mean (SD)	44.6 (12.8)	43.2 (13.3)	42.4 (12.4)	0.476
Self-efficacy				
Management of feelings, median (IQR)	67.5 (56–77.25)	66 (52.5–79.75)	78 (58–79)	0.448
Management of medications, median (IQR)	72 (62.25–78)	80 (72.75–80)	80 (72.5–80)	<0.001
Management of symptoms, mean (SD)	43.8 (15.9)	44 (16.8)	44.3 (15.8)	0.875
Maintaining remission, median (IQR)	35 (25–40.5)	36 (29–44)	39 (32–43.5)	0.077
Total efficacy, median (IQR)	220 (183–244.5)	222.5 (186.25–255)	228 (191–251)	0.434

other studies.[31] Therefore, in such patients, careful monitoring of adherence is warranted.

Parameters reflecting psychological profile included sense of coherence, understanding of disease, and management of medication. Lower scores in these 3 parameters were associated with low adherence scores. Self-efficacy is the belief of the individual that he can cope with a certain task. The higher the self-efficacy is, the more effort the individual will invest in fulfilling the task. Therefore, higher self-efficacy will improve performance. Self-efficacy was found to be connected with better adherence in several chronic diseases such as diabetes and hypertension.[32–35] The self-efficacy score we used was developed especially for IBD.[15, 19] The concept of "Sense of Coherence" is used to describe a person's capacity to respond to stressful situations, such as chronic illness. The concept was introduced by the medical sociologist Antonovsky in his theory of salutogenesis, which focuses on the personal resources needed to move toward and maintain health.[36] Our study is the first to implement a sense of coherence and IBD self-efficacy in the context of adherence to treatment. We found that the confidence of the patient in the ability to self-manage his medications and higher level of Sense of Coherence were correlated with good

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TABLE 6: Multivariate Analysis of Low Adherence Vs Medium–High Adherence

	Characteristic	OR (95% CI)	*P*
Demographic and disease characteristics	Age	0.983 (0.964–1.002)	0.076
	Female vs male	1.572 (0.951–2.604)	0.078
	UC vs Crohn's	1.792 (1.037–3.098)	0.037
	Employed	2.449 (1.331–4.506)	0.004
Communication with medical staff	Age	0.984 (0.965–1.002)	0.087
	Female vs male	1.841 (1.075–3.154)	0.026
	UC vs Crohn's	1.915 (1.082–3.386)	0.026
	Bad communication with Gastroenterologist	1.798 (1.219–2.651)	0.003
	Not assisted by IBD nurse	1.168 (0.979–1.393)	0.084
Psychological aspects	Age	0.978 (0.959–0.997)	0.022
	Female vs male	1.751 (1.042–2.941)	0.034
	UC vs Crohn's	1.748 (1.005–3.042)	0.048
	Treatment will help	0.904 (0.813–1.006)	0.064
	Understanding of disease	0.881 (0.787–0.987)	0.029

adherence. Surprisingly and contrary to other studies, we could not find any correlation between anxiety and depression and adherence.

Parameters reflecting the relationship with the medical team, such as patient trust and communication with the treating gastroenterologist, were highly correlated with better adherence. These findings are in agreement with previously published data emphasizing the ability of good communication with the treating physician to improve adherence.[3, 31] In our investigation of the psychological aspects, we showed that better understanding of the disease correlates with better adherence. We also demonstrated that better communication with the gastroenterologist correlates with better adherence.

The limitations of the study are the use of self-reporting to assess adherence. Patients tend to overestimate their adherence to therapy with self-evaluation. Another limitation is the fact that patients were recruited to the study in out-patient clinics; thus our study might be subjected to selection bias because patients who adhere to clinic visits and agree to participate in the study can be expected to have higher adherence. It would be interesting to analyze patients who take their medications independently vs those who receive intravenous treatment in an outpatient clinic. Unfortunately, only a small number of the patients were treated with infliximab monotherapy; therefore, we could not differentiate these 2 groups of patients.

Obviously, if we wish to improve adherence, it is important to first identify the characteristics of the nonadherent patient, to differentiate modifiable and nonmodifiable parameters, and then to try and influence the modifiable aspects. This study first demonstrates that the communication between patients and gastroenterologists is a very important modifiable parameter impacting patient adherence. Another important

factor was the patient's understanding of the disease, as measured by the Brief Illness Perception Questionnaire, whereas better understanding is correlated with better adherence. According to these results, it is very important for the physician to be aware of these medical and psychological issues and collaborate with the patient on the different aspects of both disease understanding and medical treatment. Physicians and medical psychologists should be aware of these important nonadherence aspects, and if they are identified, appropriate interventions should be undertaken.

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APPENDIX 1

TABLE A1: Disease Severity Questionnaire

Disease Activity – Year	This Year	1 Year Ago	2 Years Ago
No symptoms – 0			
Mild symptoms – 1			
Medium symptoms – 2			
Active disease – 3			
Hospitalization – 4			
Surgery – 5			
Stoma – 5			
a. Highest score			
Treatment			
No treatment – 0			
5-Aminosalicylic acid or antibiotics – 1			
Low-dose steroids – 2			
Steroids – 3			
Immunosuppresive – 4			
Biologics – 5			
b. Sum of treatments			
Total year score (a+b)			

Communication with the medical staff questionnaire:

- a. Are you a member of the IBD association? Yes/No
- b. Do you have a permanent gastroenterologist? Yes/No
- c. How many gastroenterologists have treated you since you have been diagnosed?
- d. Do you have good accessibility to the gastroenterologist services?

  1. high accessibility
  2. good accessibility
  3. medium accessibility
  4. low accessibility
  5. extremely low accessibility

- e. Do you trust your gastroenterologist?

  1. Yes, completely
  2. Very much
  3. Medium trust
  4. Not so much
  5. Don't trust at all

- f. Do you have good communication with your gastroenterologist?

  1. Always
  2. Most of the time
  3. Sometimes
  4. Mostly not
  5. Not at all

- g. Do you use the assistance of an IBD nurse?

  1. Always
  2. Most of the time
  3. Sometimes
  4. Mostly not
  5. Not at all

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