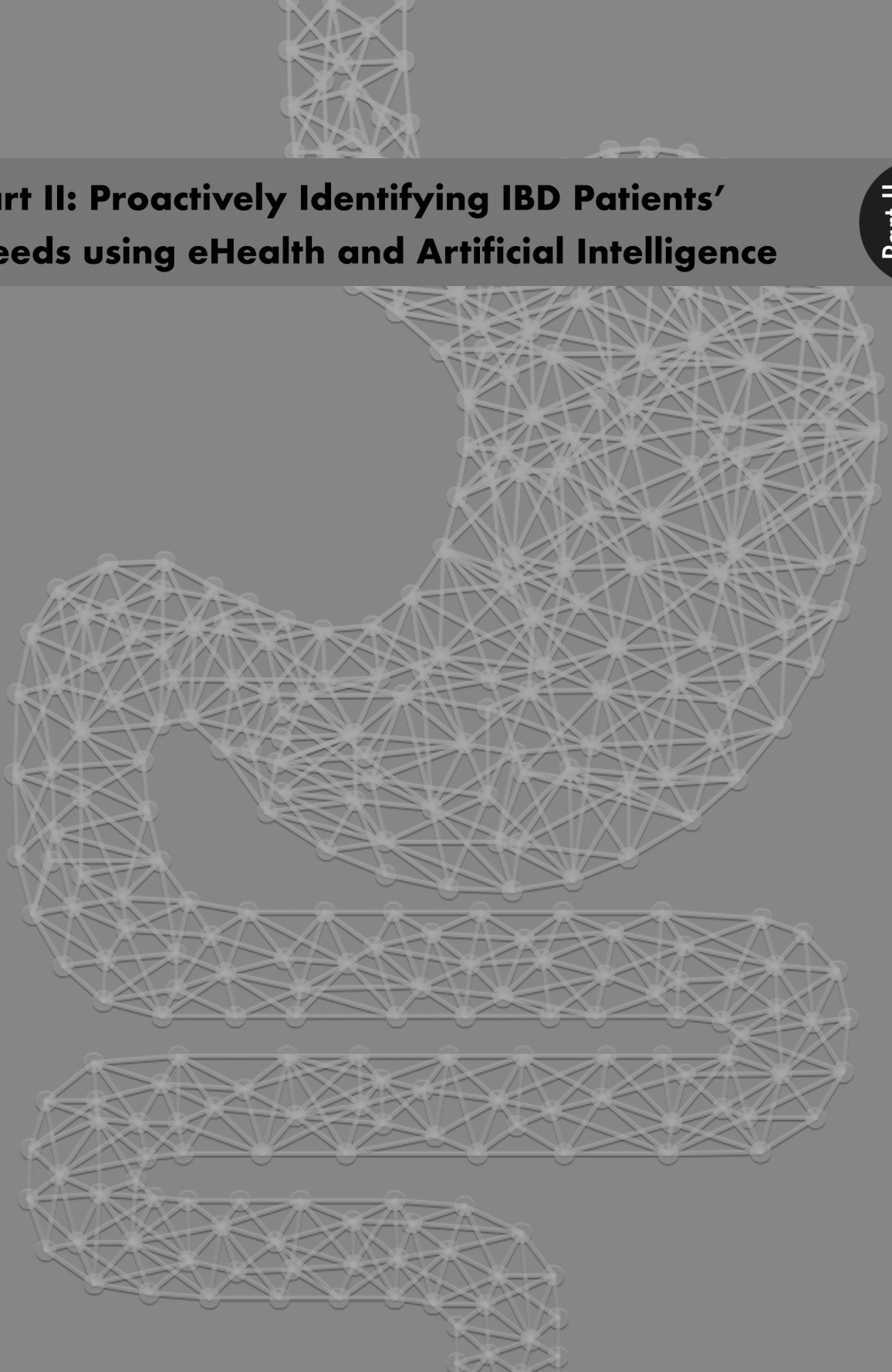
Artificial intelligence and e-health for inflammatory bowel diseases: the quest to enhance patient experiences, outcomes and costs

Zand, A.

Part II: Proactively Identifying IBD Patients' Needs using eHealth and Artificial Intelligence



CHAPTER 4

The Development of a Screening Tool to Identify and Classify Non-adherence in Inflammatory Bowel Disease

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A. Zand[1,2], A. Nguyen[1], Z. Stokes[1], W.K. van Deen[3], C. Reynolds[1], M. Dimitrova[1], A. Khandadash[1], M. Dvorsky[1], J. Sauk[1], E. Esrailian[1], D.W. Hommes[1,2]

[1] UCLA Center for Inflammatory Bowel Diseases, Vatche and Tamar Manoukian Division of Digestive Diseases, David Geffen School of Medicine, University of California at Los Angeles, CA, USA
[2] Leiden University Medical Center, Department of Digestive Diseases, Leiden, the Netherlands
[3] Cedars-Sinai Center for Outcomes Research and Education, Division of Health Services Research, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Abstract

Background

Medication non-adherence is a challenge in chronic disease management. Tools that can both determine adherence levels and analyze patient-specific reasons for non-adherence are lacking.

Methods

Our tool was developed using 23 patient-reported items and its predictive performance was compared to the most widely used instrument in the literature.

Results

133 IBD patients were included, 44 (33%) were nonadherent and 89 (67%) were adherent. Our screening question, with 87% sensitivity and 64% specificity was followed by a 9-item survey for patients qualified as nonadherent.

Conclusions

Quantifying reasons for non-adherence can lead to more effective and personalized interventions for nonadherent patients.

Introduction

Medication non-adherence remains a major challenge in chronic disease management. In the US, about 117 million adults have at least one chronic disease[1] and 50% do not take their medications as prescribed[2]. For inflammatory bowel diseases (IBD), one study showed a non-adherence rate of 33%, of which 34% experienced at least one relapse after stopping treatment[3]. Although the rate of non-adherence in IBD varies in many studies[4], the vast majority of literature reports non-adherence in the range of 30-45%[5].

Medication non-adherence is also associated with increased costs of healthcare utilization and negative health outcomes. It is estimated that non-adherence causes between one-third and two-thirds of all medication-related hospitalizations[6] and at least 10% of all hospitalizations in the US[7]. The resultant indirect and direct healthcare costs of non-adherence in chronic diseases are estimated to be between $100 billion and $300 billion annually in the US,[8] contributing between 10% and 30% of the overall estimated wasteful healthcare spending per year ($910 billion)[9]. Medication non-adherence has further been shown to be significantly correlated with increased disability in IBD patients[10].

Various solutions addressing non-adherence have been identified. Electronic-health (eHealth) technologies including web-based interventions for IBD management and mobile applications can improve short-term adherence[11]. Similarly, programs such as the TELE-IBD trial has suggested the promising potential and feasibility of telemedicine for improving health outcomes and disease monitoring[12,13]. Patients receiving daily short message service reminders to take medications have shown a significantly reduced rate of missed doses compared to those with no message reminders[14]. Motivational interviewing interventions have also been shown to improve adherence in chronic disease patients within a 6-month follow-up period[15].

To successfully improve adherence, however, the reasons behind a patient's non-adherence must first be identified so the most effective solution can be applied. The literature describes two main categories of reasons for non-adherence: intentional/intrinsic and unintentional/extrinsic factors, differentiated by their underlying cognitive processes[16–19]. Intrinsic non-adherence can arise due to a fear of side effects[20], lack of patient involvement in the treatment decision-making process[21], and a lack of understanding medication[22]. The extrinsic category can be divided into subcategories including poor health literacy[23], forgetfulness[24], inadequate funds[6], and disruptions in daily routine[25], In IBD the most

frequent intrinsic reason for non-adherence occurs when patients stop treatment after their symptoms resolve (42.7%), which indicates a lack of understanding of treatment regimens[3]. Meanwhile, the most frequent extrinsic reason for non-adherence in IBD is forgetfulness (5.2%)[3]. These non-adherence factors are especially crucial to address in IBD due to the complicated nature and lifelong management of the disease. IBD patients have noted complex treatment regimens, dose amount, and dose frequency as factors affecting their adherence[26]. The form of medication administration (oral or infusion) may also be burdensome to IBD patients and affect adherence levels[27]. With many factors to consider, monitoring of adherence is critical.

Several self-report assessment tools are used to measure adherence (i.e., 8-Item Morisky Medication Adherence Scale (MMAS-8)[28–31], Self-Efficacy for Appropriate Medication Use Scale (SEAMS)[25], the Medication Adherence Rating Scale (MARS[32]). However, these scales do not assess the intrinsic and extrinsic reasons behind non-adherence, such as patient access to resources or problems in the patient-physician relationship. In addition, many of these questionnaires are lengthy, which limits their use in clinical settings due to respondent fatigue[33]. Therefore, we aimed to develop a brief screening tool to identify non-adherence levels and reasons for non-adherence in IBD.

Materials and Methods

Study Design & Questionnaire Development

We performed a cross-sectional study to develop a screening tool that accurately screens for medication adherence in IBD patients and assesses the reasons for non-adherence to help guide medical providers in their management. Our tool was developed using patient self-reported measures and its predictive performance was compared to the widely used MMAS-8[28–30,34].

Eligible IBD patients filled out questionnaires assessing factors of non-adherence commonly identified in literature on medication adherence in IBD (Table, Supplementary Data Content 1)[3,5]. We compiled 25 questions drawn from previously validated adherence questionnaires (SEAMS[25], MARS[32]) and based on literature review of common non-adherence factors, including recommended questions from the World Health Organization[6] and questions assessing patient-physician interactions[35,36].

In total, 2 open-ended questions related to the types of medication used and 23 closed-ended questions related to adherence (Table, Supplementary Data Content 1) were included. The questions were categorized as either 1) intrinsic: measuring lack of understanding of disease/medication, lack of involvement in the treatment decision-making process, and fear of side effects; 2) extrinsic: measuring dose frequency, inadequate health literacy, forgetfulness, poor patient-physician communication, lack of funds, disruption in daily routine; or 3) general questions: neither intrinsic nor extrinsic factors.

In addition, we asked each patient the 8 questions included in the MMAS-8 (Table 1), a copyrighted tool for which a license was obtained and which served as our gold standard comparison. A total of 33 questions were therefore administered to participants. The online Morisky Widget[28–31] was used to score our results of the MMAS-8 as either adherent (score ≥6) or nonadherent (score <6).

Population & Data Collection

IBD patients 18 years and older were recruited via email or during clinic visits to the University of California, Los Angeles (UCLA) Center for IBD between June 2017 and November 2017. Patients with an underlying diagnosis of bipolar affective disorder, schizophrenia, substance abuse/dependence, pregnancy, terminal illness, and psychosis according to chart review were excluded. Chart review was performed to confirm the patients' IBD diagnosis and to collect patient characteristics such as race, ethnicity, marital status, smoking history, insurance type, comorbidities and to collect a list of current medications. For medications, we excluded medications that patients only used as needed or that were available over the counter (even if prescribed).

Software

Study data were collected on encrypted iPads using the Research and Electronic Data Capture (REDCap) tools hosted at UCLA[37]. Excel 2010 and RStudio V3.4.3 were used for statistical analysis.

Statistical Objectives and Analysis

Our primary goal was to find a subset of the 23 adherence questions that most accurately predict medication adherence in IBD patients. Our secondary goal was to develop a supplementary questionnaire that determines why nonadherent patients do not take their medication based on the 10 extrinsic or intrinsic reasons described in the literature. Furthermore, we conducted a post-hoc analysis to determine if patient characteristics were associated with non-adherence using the MMAS-8 outcomes. We tested if adherence is

associated with patients' age, gender, race, Hispanic ethnicity, marital status, smoking status, insurance type, IBD subtype, number of medical conditions requiring a prescription medication, the number of prescription medications, and whether the patient was prescribed a self-injection (such as Adalimumab) or infusion medication (Infliximab). Table 1 shows the complete list of patient characteristics assessed.

Normal distribution of data was tested using a Normal-QQ-Plot. Fisher's exact test (two-sided) or the $\chi 2$ tests were used to explore differences of categorical data in adherent and nonadherent groups and the T-test was used to explore associations of parametric numerical data. A p-value <0.05 was considered statistically significant.

Model Building

Initially a simple logistic regression of each question was performed to understand their individual performance in predicting adherence as defined by the MMAS-8. Questions with a p-value <0.3 were selected for inclusion in a multiple logistic regression model with stepwise selection. The stepwise regression model adds questions if its benefit to the model does not overcome the penalty of having an extra question as defined by the Akaike information criterion[38]. Questions with low occurrence to one or more of the possible responses were omitted (<10 patients selecting one of the responses) due to the low predictive power and the potential to cloud the effects of the other questions in the model. We fit the multiple logistic model with the selected questions and obtained the coefficients. From the model coefficients we developed scores by dividing each by the smallest coefficient and rounding to obtain integer-value scores. The performance of the score was measured by the specificity, and sensitivity. The cutoff for every question was obtained from the model coefficients.

To get a complete overview of potential reasons for non-adherence in patients shown to be nonadherent, questions were added for all intrinsic and extrinsic categories that were not included in the questions selected by the stepwise regression model. These questions only need to be completed by those patients shown to be nonadherent in the prediction model. From each category the question with the highest predictive power based on the simple logistic regression model was included.

Ethical Considerations

All patients gave consent to participate in this study. This study was approved by the institutional review board at UCLA, under protocol number IRB#17-000602.

Table 1. Morisky Medication Adherence Scale-8 (MMAS-8) Items
The following 8 items were used as the gold standard comparison.

	Question
1	Do you sometimes forget to take your pills? - Yes - No
2	Over the past 2 weeks, were there any days when you did not take your medicine? - Yes - No
3	Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it? - Yes - No
4	When you travel or leave home, do you sometimes forget to bring along your medications? - Yes - No
5	Did you take your medications yesterday? - Yes - No
6	When you feel like your symptoms are under control, do you sometimes stop taking your medicine? - Yes - No
7	Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan? - Yes - No
8	How often do you have difficulty remembering to take all your medications? - All the time - Usually - Sometimes - Once in a while - Never/rarely

Ref: Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive Validity of a Medication Adherence in an Outpatient Setting. J Clin Hypertens. 2008;10(5):348-354.
The MMAS (8-item) content, name, and trademarks are protected by US copyright and trademark laws. Permission for use of the scale and its coding is required. A license agreement is available from Donald E. Morisky, ScD, ScM, MSPH, MMAS Research LLC., 294 Lindura Ct. Las Vegas NV 89138-4632, USA; dmorisky@gmail.com.

Results

Patient Characteristics

We included 133 (63 UC and 67 CD, 3 indeterminate colitis) patients in this study (Figure 1). Our study population was primarily Caucasian, non-Hispanic, non-smoking and privately insured (Table 2). Fewer than 10% of patients had other significant comorbidities. Nearly 40% of patients were taking an IBD medication delivered by infusion, and about

half as many were taking an IBD medication requiring self-injection. On average, patients were taking 2-3 prescription medications at the time of our survey according to chart review.

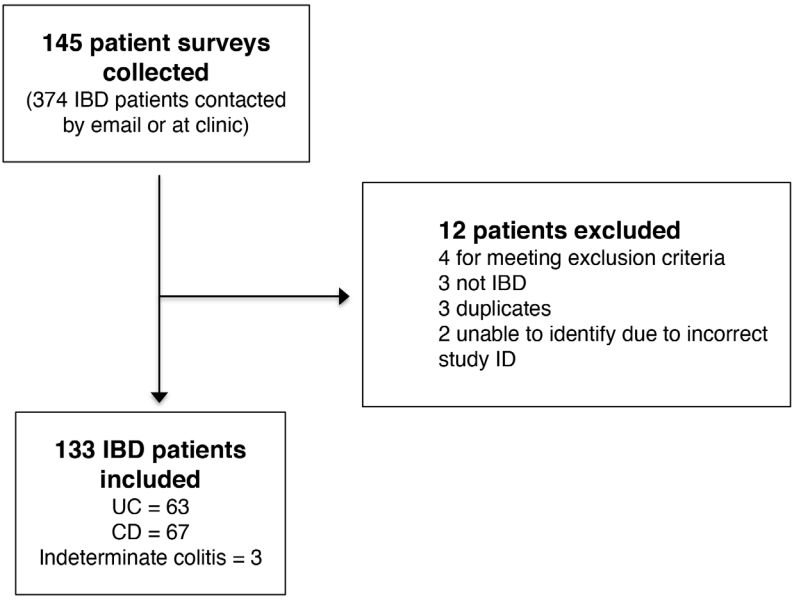

Figure 1. Patient flowchart for inclusion/exclusion.
Out of 145 total respondents, 133 met inclusion criteria and were included in the analysis.

Adherence Levels

Of the 133 patients, 44 (33%) were nonadherent (MMAS-8 score <6) and 89 (67%) were adherent (MMAS-8 score ≥6). There was no significant difference in patient demographics between these two groups (Table 2). Frequent reasons for non-adherence were: not being as careful about taking medications (29%; Question 1) and missing taking medication (41.4%; Question 13) (Table 3). In relation to patient-physician communication, a majority of patients indicated that their physician offers them choices in medical care (84%; Question 3), discusses the pros and cons of these choices with them (89%; Question 4), and considers their preferences when making treatment decisions (90%; Question 6) (Table 3).

Analysis, Interpretation and Final Questionnaire

Figure 2 outlines our questionnaire development. Out of 23 questions (excluding the 2 open-ended items), 10 provided little to no predictive power due to the low occurrence to

Table 2. Patient demographics of adherent vs nonadherent population (n=133).

Variable	89 (67%) Adherent	44 (33%) Nonadherent	p-value
Female gender	41 (46%)	21 (48%)	1.0
Age (mean)	42.4	40.1	0.41
Disease Type	CD 42 (47%) UC 45 (51%) Indeterminate colitis 2 (2%)	CD 25 (57%) UC 18 (41%) Indeterminate colitis 1 (2%)	0.57
Race			0.75
Caucasian	66 (74%)	30 (68%)	
Asian	2 (2%)	2 (5%)	
Black	2 (2%)	2 (5%)	
Other or not declared	19 (21%)	10 (23%)	
Hispanic Ethnicity	4 (4%)	1 (2%)	0.88
Education			
Less than high school	0 (0%)	0 (0%)	
Some high school	2 (2%)	0 (0%)	
High school graduate	6 (7%)	4 (9%)	
Some College	14 (16%)	11 (25%)	
College Graduate	33 (37%)	20 (45%)	
Post-College Degree	33 (37%)	9 (21%)	
Other	1	0 (0%)	
Married	39 (44%)	19 (43%)	1.0
Current Smoker	5 (6%)	2 (5%)	1.0
Insurance			0.36
Private HMO, PPO	68 (76%)	29 (66%)	
Medicaid	5 (6%)	5 (11%)	
Medicare	11 (12%)	4 (9%)	
Self	2 (2%)	2 (5%)	
Other or unknown	3 (3%)	4 (9%)	
Comorbidities			0.57
Diabetes mellitus	3 (3%)	2 (5%)	
Chronic Kidney Disease	2 (2%)	0 (0%)	
COPD or asthma	4 (4%)	3 (7%)	
Organ transplant	1 (1%)	1 (1%)	
Congestive Heart Failure	0 (0%)	0 (0%)	
HIV/AIDS	0 (0%)	1 (1%)	
Receiving Medication by Infusion (i.e., Infliximab, Vedolizumab)	34 (38%)	15 (34%)	0.79
Receiving Medication by Self-Injection (i.e., Adalimumab, Ustekinumab)	20 (22%)	7 (16%)	0.51

one or more of the possible answers and were thus omitted. Out of the remaining 13 questions our univariate model found questions 1, 3, 4, 5, 7, 15, 17, and 18 to have a p-value <0.3 (Table 3). After running our multiple logistic regression model with stepwise selection, question 1 and 17 remained significant (p-value <.05). The associated sensitivity and

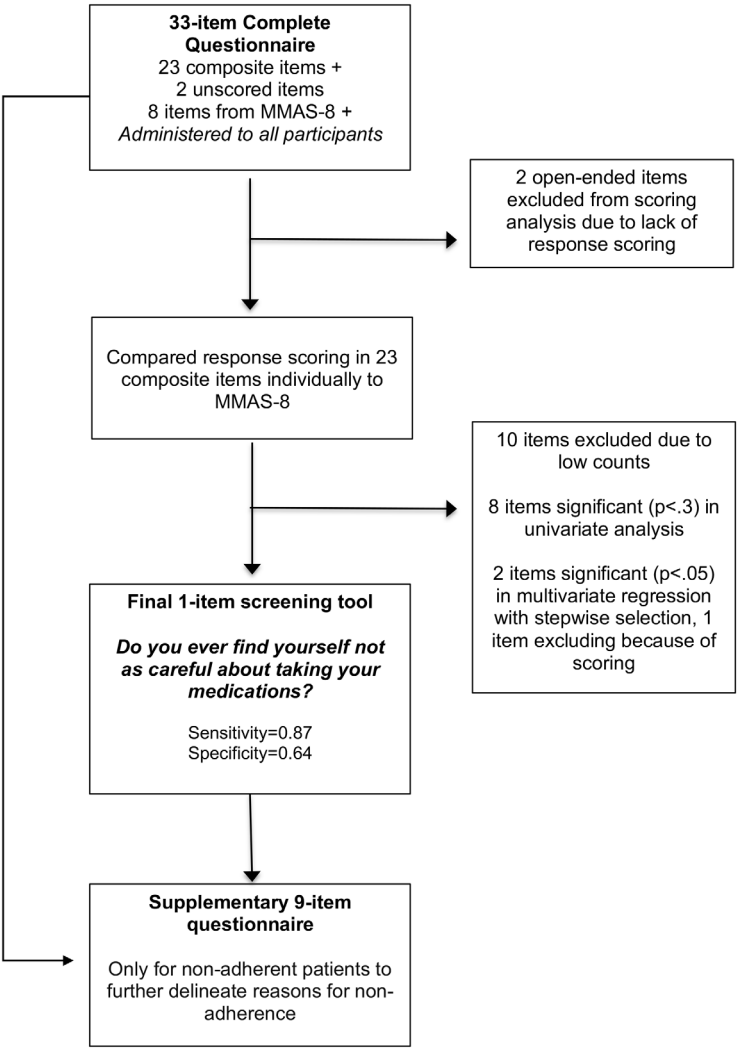

Figure 2. Flowchart of questionnaire development.
The initial 33-item questionnaire assessed extrinsic and intrinsic factors of nonadherence. Simple logistic regression analysis and multiple logistic regression with stepwise selection ultimately yielded a 1-item screening tool complemented by a 9-item scale

specificity of this model were 87% and 64%, respectively. However, the optimal cut off to classify a patient as adherent was 1.5 points, while the scoring assigned 2 points for question 1 alone and 1 point for question 17. In practical terms this meant that question 1 was all decisive on whether patient is adherent or not and question 17 effectively had no impact on the outcome. Looking at the questions separately, question 1 alone had a better sensitivity and specificity ratio to predict adherence (87% sensitivity; 64% specificity) than question 17 alone (90% sensitivity; 23% specificity). Therefore, we opted to use question 1 alone as a screening question to assess adherence.

Thus, our final screening survey included only question 1 ("*Do you ever find yourself not as careful about taking your medications?*").

Reasons for Non-adherence

Question 1 represents 1 category: general adherence. We assembled an additional 9-item survey to be administered to patients determined as "nonadherent" based on this question. The questions with the highest predictive power within each of the 9 remaining categories of non-adherence reasons (side effects, poor patient-physician communication, frequency of medication regimen, lack of understanding of disease/medication, forgetfulness, lack of involvement in the treatment decision-making process, inadequate health literacy, lack of funds and disruptions in daily routine) were included in the additional survey (Table 4).

Table 3. Outcomes of Patients (n=133)

	Question	Total n (%)	Ln (OR) (95% CI) for underlined answers	p-value
1	Do you ever find yourself not as careful about taking your medications?		2.49 (1.64-3.34)	* & ** p<.01
*	- Yes	39 (29.3%)		
**	- No	94 (70.7%)		
2	Do you understand how to take your medications?		0	N/A
++	- Yes	132 (99.2%)		
	- No	1 (0.8%)		
3	Does your physician offer choices in medical care?		0.74 (-0.17-1.64)	
*	- Yes	112 (84.2%)		p=.11
	- No	21 (15.8%)		
4 *	Does your physician discuss pros and cons of each choice with you?		0.94 (-0.09-1.96)	
	- Yes	118 (88.7%)		p=.07
	- No	15 (11.3%)		
5	Does your physician get you to state which choice or option you prefer?			
*	- Yes	113 (85%)	0.74 (-0.17-1.64)	p=.11
	- No	20 (15%)		
6	Does your physician take your preferences into account when making treatment decisions?			
	- Yes	120 (90.2%)	0.6 (-0.55-1.75)	p=.30
	- No	13 (9.8%)		
7 *	How confident are you that you can take your medicines correctly when they cause some side effects?			p=.25
	- Not confident	15 (11.3%)		
	- Somewhat confident	28 (21.1%)		
	- Very confident	90 (67.7%)	0.1 (0.97-1.43)	
8	Have you noticed any adverse effects from your medications?			
	- Yes	51 (38.3%)	0.18 (-0.54-0.9)	p=.62
	- No	82 (61.7%)		
9 ++	How confident are you that you can take your medicines correctly when you take medicines more than once a day?			
	- Not confident	10 (7.5%)		
	- Somewhat confident	28 (21.1%)	0.47 (1.48-1.92)	N/A
	- Very confident	95 (71.4%)		

Table 3. Continued

	Question	Total n (%)	Ln (OR) (95% CI) for underlined answers	p-value
10	How confident are you that you can take your medicines correctly when you are not sure how to take the medicine?			
	- Not confident	18 (13.5%)		
	- Somewhat confident	52 (39.1%)	-0.36 (0.46-1.01)	p=.34
	- Very confident	63 (47.4%)		
11	How confident are you that you can take your medicines correctly when you get a refill of your old medicines and some of the pills look different than usual?			
	- Not confident	13 (9.8%)		
	- Somewhat confident	33 (24.8%)	-0.21 (0.54-1.02)	p=0.8
	- Very confident	87 (65.4%)		
12	How confident are you filling out medical forms by yourself?			
++	- Not confident	3 (2.3%)		
	- Somewhat confident	24 (18%)	-0.8 (-0.36-0.1)	N/A
	- Very confident	106 (79.7%)		
13	I know it must be difficult to take all your medications regularly. How often do you miss taking them?			
++	- All the time	0 (0%)		
	- Usually	0 (0%)		
	- Sometimes	11 (8.3%)	0.97 (3.49-3.93)	N/A
	- Once in a while	44 (33.1%)		
	- Never/rarely	78 (58.6%)		
14	How often do you not take medication X? (address each medication individually)			
++	- All the time	21 (15.8%)		
	- Usually	1 (0.8%)		
	- Sometimes	10 (7.5%)	0.33 (2.2-2.68)	N/A
	- Once in a while	32 (24.1%)		
	- Never/rarely	69 (51.9%)		
15 *	Does your physician tell you everything?		0.54 (-0.46-1.55)	p=.28
	- Yes	116 (87.2%)		
	- No	17 (12.8%)		
16	Does your physician let you know test results when promised?			N/A
++	- Yes	128 (96.2%)	0.3 (-1.53-2.12)	
	- No	5 (3.8%)		

Table 3. Continued

	Question	Total n (%)	Ln (OR) (95% CI) for underlined answers	p-value
17	Does your physician explain treatment alternatives?			
*	- Yes	114 (85.7%)	1.06 (0.1-2.02)	* & ** p=.03
**	- No	19 (14.3%)		
18	Does your physician explain side effects of medications?			
*	- Yes	111 (83.5%)	0.76 (-0.12-1.64)	p=.09
	- No	22 (16.5%)		
19	Does your physician tell you what to expect from your disease or treatment?			
++	- Yes	125 (94%)	2.09 (0.47-3.7)	N/A
	- No	8 (6.2%)		
20	Do you ever delay a refill or skip a dose of your medication for financial reasons?			
	- Yes	16 (12%)	0 (-1.05-1.05)	N/A
	- No	117 (88%)		
21	Do you plan on rationing or sharing your medication for financial reasons?			
++	- Yes	6 (4.5%)	0.73 (-0.91-2.37)	N/A
	- No	127 (95.5%)		
22	How confident are you that you can take your medicines correctly when you are away from home?			
++	- Not confident	5 (3.8%)	1.14 (2.18-2.6)	N/A
	- Somewhat confident	23 (17.3%)		
	- Very confident	105 (78.9%)		
23	How confident are you that you can take your medicines correctly when your normal routine gets messed up?			
++	- Not confident	5 (3.8%)	0.6 (2.07-2.52)	N/A
	- Somewhat confident	41 (30.8%)		
	- Very confident	87 (65.4%)		

Table 4. Additional Targeted Questions for Nonadherent Patients
These questions are intended to assist providers in identifying specific, individualized reasons for nonadherence.

Question	Response Score	Type	Specific Factor
2. Do you understand how to take your medications?[2]	Yes No	General	Lack of understanding of disease/medication
3. Does your physician offer choices in medical care?[2]	Yes No	Intrinsic	Lack of involvement in the treatment decision-making process
7. How confident are you that you can take your medicines correctly when they cause some side effects?[1]	Very Confident: Somewhat Confident Not Confident	Intrinsic	Side Effects
9. How confident are you that you can take the medication correctly when you need to take it more than once a day?[1]	Not confident Somewhat confident Very confident	Extrinsic	Frequency of medication regimen
13. I know it must be difficult to take all your medications regularly. How often do you miss taking them?[3]	Yes No	Extrinsic	Forgetfulness
17. Does your physician explain treatment alternatives?[2]	Yes No	Extrinsic	Poor Patient-Physician Communication
20. Do you ever delay a refill or skip a dose of your medication for financial reasons?[3]	Yes No	Extrinsic	Lack of funds
22. How confident are you that you can take your medicines correctly when you are away from home?[1]	Not confident Somewhat confident Very confident	Extrinsic	Disruptions in daily routine
* How confident are you that you understand how to take all your medications correctly?[1,4]	Not confident Somewhat confident Very confident	Extrinsic	Inadequate health literacy

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Discussion

To address the significant impact of non-adherence in IBD, we assessed what questions can most accurately assess medication adherence and developed a 1-item screening tool based on a patient-reported outcome measurement (PRO) that is easy to administer. Our final predictive question identifies non-adherence with a sensitivity of 87% and a specificity of 64% and our supplementary survey assesses the leading extrinsic and intrinsic factors in the nonadherent population. The 1-item screening tool together with the 9-item survey can be used for managing adherence in IBD patients. Where a lot of studies have addressed non-adherence, few have adequately specified the reasons for non-adherence in IBD necessary for proper management.

Our study found that non-adherence was present in 33% of IBD patients, which is consistent with prior findings indicating non-adherence ranging from 30-45%[5]. However, while prior studies suggested a lack of understanding and poor patient-physician relationships, we were not able to confirm this. In our sample, most patients reported they had a good understanding of their disease or medication. This suggests that a lack of understanding was not a large contributor to non-adherence in our sample population, despite it being the most frequent intrinsic contributor to non-adherence in IBD overall[3]. This discrepancy could be explained by the fact that our sample is primarily white and highly educated (Table 2), or the strength of the patient-physician relationship in our study. In fact, patients who reported being involved in the decision-making process and who reported good patient-physician communication had higher odds of being adherent. This is consistent with previous work in which it was shown that when a physician is a strong communicator, the odds of a patient being adherent is 2.16 times better[24]. Physician communication is crucial to adherence because it enables more effective transmission of important clinical information, allows for discussion of barriers to adherence, and encourages patient involvement in the decision-making process[24].

Importantly, the accuracy of the 1-item screening tool we found is comparable to currently existing scales. A study validating the MMAS-8 in an outpatient setting of primarily low-income hypertensive patients estimated a sensitivity of 93% and specificity of 53%[34]. The MMAS-4 was shown to have a sensitivity and specificity of 81% and 44%, respectively[39]. A review of medication adherence measures discussed the pros and cons of several scales[40]. For example, the 10-item MARS examines behavior and attitude towards medication-taking, but is limited to use in patients with psychiatric illness[40]. The 13-item SEAMS

demonstrates good reliability in both low and high literacy populations and is useful for chronic disease management, but difficult to administer due to its length[40].

A limitation of this study is the potential for recall bias. When completing the survey, patients were expected to recall when they had last taken their medications and if certain measures of non-adherence (i.e., forgetting to take pills, whether or not their physician had given them treatment alternatives) had occurred. In addition, as patients were recruited from a tertiary IBD referral center, our sample is likely homogenous, potentially limiting the generalizability of our study to other IBD patient populations. Lastly, our model was not validated in an independent sample, so the results presented are from the development of the screening tool.

Although the 1-item screening tool has not yet been tested in an independent sample, we found a relatively high sensitivity and specificity for our final 1-item model of 87% and 64%, respectively. With only 1 question, our tool is short and simple to administer, making it useful for clinical and remote monitoring. This is particularly important as studies have repeatedly shown the negative associations between response rates and questionnaire length[41,42]. The benefits of a 1-item screening tool[43] to screen for non-adherence can help minimize respondent fatigue and open the conversation for providers to follow-up with patients on specific reasons for non-adherence, distinguishing it from previous adherence tools. Use of the 1-item screening tool complemented with the 9-item survey allows practitioners the opportunity to further inquire about all the major categories of factors causing non-adherence and trigger potential solutions—all of which are important for creating patient-tailored interventions[19].

Our study was designed to provide an optimal screening method that monitors non-adherence both inside and outside the clinical setting. Integration of our tool into mobile technologies, for example, could have promising implications for IBD monitoring and management, as users may take the survey on the accessible platform of their mobile phone at a convenient time and show their results to providers to inform future interventions.

Conclusion

We developed a novel screening tool for management of medication non-adherence in IBD. To our knowledge, our adherence tool is the first that enables healthcare providers to screen

for non-adherence in IBD and further identify the specific reasons for non-adherence so they may offer more tailored solutions. The use of this survey could allow for continuous monitoring of medication adherence. With IBD being a prototypic chronic disease, this tool can potentially be adapted for monitoring adherence in other chronic disease populations. Future studies should validate it in an independent and more heterogenous population and assess the effect of remote monitoring of adherence on medication adherence levels, patient satisfaction, and health care costs.

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Supplementary Table

Supplementary Data Content 1. Adherence Data Model Complete Questionnaire (25 questions)

Type of Nonadherence	Factors	Questions
General Adherence Questions		0. When was the last time you took medication X? Include the most recent dates for each medication that you have taken. (Answer format: medication name, date taken)
		0. Of all the medications prescribed to you, which ones are you taking? List all.
		1. Do you ever find yourself not as careful about taking your medications?
I. Intrinsic (Intentional)	I.1: Lack of Understanding of Disease/Medication	2. Do you understand how to take your medications?
	I.2: Lack of Involvement in the Treatment Decision–making Process	3. Does your physician offer choices in medical care?
		4. Does your physician discuss pros and cons of each choice with you?
		5. Does your physician get you to state which choice or option you prefer?
		6. Does your physician take your preferences into account when making treatment decisions?
	I.3: Side Effects	7. How confident are you that you can take your medicines correctly when they cause some side effects?
		8. Have you noticed any adverse effects from your medications?
II. Extrinsic (Unintentional)	II.1: Frequency	9. How confident are you that you can take your medicines correctly when you take medicines more than once a day?
	II.2: Inadequate Health Literacy	10. How confident are you that you can take your medicines correctly when you are not sure how to take the medicine?
		11. How confident are you that you can take your medicines correctly when you get a refill of your old medicines and some of the pills look different than usual?
		12. How confident are you filling out medical forms by yourself?
	11.3 Forgetfulness	13. I know it must be difficult to take all your medications regularly. How often do you miss taking them?
		14. How often do you not take Medication X?
	II.4: Poor Patient-physician Communication	15. Does your physician tell you everything?

Scoring (1 = good, 0 = bad)	Source
N/A	Medication Adherence: WHO Cares? Mayo Clinic Proceedings.[1]
N/A	Medication Adherence: WHO Cares? Mayo Clinic Proceedings.
yes = 0, no = 1	Medication Adherence Clinical Reference - American College of Preventive Medicine (Web. 20 July 2016.)[2]
yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management[3]
yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
A: not confident/somewhat confident/ very confident	Development and Psychometric Evaluation of the Self-Efficacy for Appropriate Medication Use Scale (SEAMS) in Low-Literacy Patients With Chronic Disease[4]
yes = 0, no = 1	Medication Adherence: WHO Cares? Mayo Clinic Proceedings.
not confident = 0, somewhat confident = 0.5, very confident = 1	Development and Psychometric Evaluation of the Self-Efficacy for Appropriate Medication Use Scale (SEAMS) in Low-Literacy Patients With Chronic Disease
not confident = 0, somewhat confident = 0.5, very confident = 1	Development and Psychometric Evaluation of the Self-Efficacy for Appropriate Medication Use Scale (SEAMS) in Low-Literacy Patients With Chronic Disease
not confident = 0, somewhat confident = 0.5, very confident = 1	Development and Psychometric Evaluation of the Self-Efficacy for Appropriate Medication Use Scale (SEAMS) in Low-Literacy Patients With Chronic Disease
not confident = 0, somewhat confident = 0.5, very confident = 1	BRIEF REPORT: Screening Items to Identify Patients with Limited Health Literacy Skills[5]
all the time = 0, usually = 0.25, sometimes = 0.5, once in a while = 0.75, never/rarely = 1	Medication Adherence: WHO Cares? Mayo Clinic Proceedings.
all the time = 0, usually = 0.25, sometimes = 0.5, once in a while = 0.75, never/rarely = 1	Medication Adherence: WHO Cares? Mayo Clinic Proceedings.
yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management

Supplementary Data Content 1. Continued

Type of Nonadherence	Factors	Questions
		16. Does your physician let you know test results when promised?
		17. Does your physician explain treatment alternatives?
		18. Does your physician explain side effects of medications?
		19. Does your physician tell you what to expect from your disease or treatment?
	II.5: Lack of Funds	20. Do you ever delay a refill or skip a dose of your medication for financial reasons?
		21. Do you plan on rationing or sharing your medication for financial reasons?
	II.6: Disruptions in Daily Routine	22. How confident are you that you can take your medicines correctly when you are away from home?
		23. How confident are you that you can take your medicines correctly when your normal routine gets messed up?

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	Scoring (1 = good, 0 = bad)	Source
	yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
	yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
	yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
	yes = 1, no = 0	The Relative Importance of Physician Communication, Participatory Decision Making, and Patient Understanding in Diabetes Self-Management
	yes = 0, no = 1	Medication Adherence: WHO Cares? Mayo Clinic Proceedings.
	yes = 0, no = 1	Medication Adherence: WHO Cares? Mayo Clinic Proceedings
	not confident = 0, somewhat confident = 0.5, very confident = 1	Development and Psychometric Evaluation of the Self-Efficacy for Appropriate Medication Use Scale (SEAMS) in Low-Literacy Patients With Chronic Disease
	not confident = 0, somewhat confident = 0.5, very confident = 1	Development and Psychometric Evaluation of the Self-Efficacy for Appropriate Medication Use Scale (SEAMS) in Low-Literacy Patients With Chronic Disease