DETERMINANTS OF PATIENT RESPONSE TO SATISFACTORY RELIEF IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Determinants of Patient Response to Satisfactory Relief In Patients with 

Irritable Bowel Syndrome

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BACKGROUND: Treatment trials for Irritable Bowel Syndrome (IBS) commonly report satisfactory relief of symptoms as an outcome measure at the end of a trial. It is unclear what predicts a response to this multidimensional construct.

AIMS: (1) Assess if the following primary independent variables predict satisfactory relief of bowel symptoms: patient reported effectiveness of treatment, patient report severity of side effects, and patient satisfaction with initial physician visit. (2) Determine if these independent variables differ among patients taking prescription versus non-prescription medications for IBS relief. (3) Determine if satisfactory relief is predicted by baseline scores on the Irritable Bowel Syndrome Symptom Severity Scale (IBS-SS) or the Brief Symptom Inventory (BSI). (4) Test if the independent variables predict satisfaction with treatment.

METHODS: A total of 835 patients (78% females, average age 52 yr) who had a medical diagnosis of IBS and satisfied Rome II criteria, were recruited from Group Health Cooperative of Puget Sound. The initial questionnaire assessed baseline symptom severity (IBS-SS) and
psychological distress (BSI). The follow-up questionnaire, administered after 6 months, assessed responses to the satisfactory relief outcome measured on a binary scale, satisfaction with treatment outcome measured on an ordinal scale, and responses to patient reported effectiveness of treatment, patient report severity of side effects, and patient satisfaction with initial physician visit.

RESULTS: Greater patient reported treatment effectiveness predicted satisfactory relief for prescription drug users (OR = 3.1) and nonprescription drug users (OR = 2.3). Lesser side effect severity to prescription drugs was a statistically significant predictor of satisfactory relief for prescription drugs (OR = 0.65) but not nonprescription drugs. Patient satisfaction with initial physician visit had a negligible predictive value for the satisfactory relief outcome after adjusting for other independent variables. Responses to the secondary outcome, satisfaction with treatment measured on an ordinal scale, were largely congruent with satisfactory relief for all primary variables tested. Neither baseline psychological distress nor baseline symptom severity significantly predicted satisfactory relief after multivariable adjustment, although the results suggest that a larger sample may show significant trends.

CONCLUSIONS: These data from an observational study suggest that patient’s perceptions of drug effectiveness and side effect severity with prescription medications are significant predictors of satisfactory relief, while physician-patient interaction does not significantly predict satisfactory relief. These results may help in the future design of clinical trials for IBS.
Introduction:

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder (FGID) with a complex pathophysiologic basis but largely diagnosed by exclusion of organic disease. IBS is commonly encountered in general medical practices with prevalence rates in the United States estimated to be 10 – 15%\(^1\). Known physiologic determinants include colonic dysmotility, intestinal hypersensitivity, changes in bacterial flora, mucosal immune dysregulation, and alteration of the CNS-ENS pathway. Using symptom-based criteria, the Rome III committee define IBS to include pain associated with a change in bowel habits, and suggests that it differs from other FGIDs including functional diarrhea and functional constipation\(^2\).

IBS Treatment Efficacy

The FDA has declared a preference that investigators state, \textit{a priori}, what defines a responder to treatment in clinical trials of IBS\(^3\). A responder should be defined by a change in symptoms that gives clear evidence that a patient has experienced clinically meaningful benefit from treatment. IBS studies should report the proportion of subjects who are considered responders. However, controversy exists over what constitutes a clinically meaningful improvement for IBS relief, and studies have used multiple definitions to identify a responder including responses to symptom-based questionnaires, health-related quality of life instruments, health care costs, and global measurements that use non-specific outcome targets such as responses to "satisfactory relief" or "adequate relief."\(^4\) A consensus on IBS endpoints has proven difficult given the diversity of endpoints employed in trials, use of both clinician and
patient-centered responses, and measurement of responses on various response scales including
categorical scales, visual analogue scales, numerical scales, and global assessment scales²⁻⁹.

The latest recommendation by the Rome III committee recognizes that two global
measures of symptomatology, “adequate relief” and “satisfactory relief,” are the current standard
for assessing efficacy in clinical trials of IBS. In addition, a validated symptom questionnaire,
like the Irritable Bowel Syndrome Symptom Severity Scale (IBS-SS), can serve as a primary
outcome measure². However, classifying an IBS patient as a responder in clinical trials has
proved especially difficult for multiple reasons. By definition, IBS is a clinically diagnosed
condition and no single biological marker exists.¹⁰ Moreover, few effective therapies are
available or are robust, and thus responsiveness can only be assessed under subtherapeutic
states⁴. Since the disease is generally not fatal, conventional analytic methods, like survival
analysis, are not applicable.

The adequate relief endpoint has often been used as a global measure in assessing
treatment efficacy. The FDA approved this outcome measure in testing alosetron for IBS relief¹¹⁻¹⁴. The original wording was phrased, “In the past 7 days have you had adequate relief of your
IBS pain and discomfort,” and responses were a dichotomous yes/no answer. Similarly,
satisfactory relief was used in treatment trials of tegaserod¹⁵,¹⁶, and patients offered a yes/no
response to the question, “Over the past week, do you consider that you have had satisfactory
relief from your IBS symptoms.”

A recent FDA report entitled “Patient-Reported Outcome Measures: Use in Medical
Product Development to Support Labeling Claims” describes proper validation of patient
reported measures. Important properties of a well devised patient-reported outcome (PRO) instrument include the ability to reliably measure the concepts it was designed to assess (reliability), the ability to address all the relevant symptoms related to the disorder (content validity), the ability to generate comparable results from a similar but independent instrument (construct validity), the ability to detect a change in symptoms when one has occurred (responsiveness), and the ability to detect the smallest difference between treatment groups that is considered clinically important (interpretability)

Although the psychometric properties of global assessment endpoints of IBS have been studied to a certain extent, the validity of these endpoints has been in question recently. A study by Whitehead and colleagues investigated if baseline symptom severity (classified as mild, moderate, or severe by a validated questionnaire) is linked to the probability of reporting satisfactory relief. The authors concluded that satisfactory relief was confounded by baseline symptom severity. Although patients with mild symptoms at baseline were more likely to report satisfactory relief, they were less likely to have a large reduction in IBS symptom severity compared to patients with severe symptoms at baseline. A recent review challenged these results citing an unpublished abstract of a phase II trial. Although the study showed similar response to adequate relief among patients with mild, moderate, and severe pain at baseline, the review did not report how baseline severity was measured (and likely not with a validated questionnaire like the IBS-SS since pain was the only symptom measured) nor did it report a response to adequate relief in a way that is currently used in IBS trials. Bijkerk and colleagues recommend the adequate relief question when measuring global symptomatology in IBS studies,
but identified specific psychometric and methodological properties requiring further validation including reliability and generalizability to the primary care population⁴.

Determining a minimum clinically important difference between responders and nonresponders has also been a challenge in IBS clinical trials that use global assessment endpoints. Corriziari and colleagues recommend defining a responder to include a 50% improvement in the global assessment measure¹⁹. While this definition has shown to be able to establish efficacy in some clinical trials, further validation is needed to determine if a 50% improvement is the most clinically appropriate threshold. An additional issue is properly classifying patients as responders and nonresponders over time. Clinical trials of tegaserod measured satisfactory relief at one week intervals and labeled patients as responders or nonresponders during each interval. At the end of the trial, patients were classified as overall responders if they reported satisfactory relief for at least 50% of the weeks. Reviewers suggested that more statistical modeling and analyses are needed to establish thresholds for response over time². Supporters of the adequate relief endpoint state that this measure allows patient to integrate all relevant symptoms of IBS related to their own reference standard⁹. However the adequate relief question commonly used in clinical trials only asks about relief from IBS pain and discomfort and excludes other critical symptoms including change in the frequency and consistency of stools. The current wording of this global assessment tool could fail to recognize efficacy of treatments that improve bowel function.

IBS Treatment Side Effects
Tolerability is an important issue in the evaluation of investigational treatment for IBS. IBS is a heterogeneous condition often subdivided into constipation predominant, diarrhea predominant, and alternating predominant subtypes. Treatments often target one specific subgroup for relief of symptoms (e.g. promotility therapy for constipation-predominant disease) and thus could adversely impact other patient populations (e.g. diarrhea predominant disease). Limited published data exists on the tolerability of pharmacologic agents used in the treatment of IBS compared to measures of efficacy. A recent systematic review concluded that there is insufficient evidence to assess the impact of side effects of newer IBS agents as well as older therapies including non-prescription medications\textsuperscript{20}. Furthermore, many of the therapies used are non-prescription medications that have not been evaluated for IBS in large trials.

Surveys have shown a correlation between level of dissatisfaction with IBS medications and treatment side effects\textsuperscript{21}. However, given the similarities between IBS symptoms and side effects of the medications given to treat IBS symptoms, such as abdominal cramps, bloating, and diarrhea, difficulties arise in distinguishing between lack of efficacy and presence of side effects in treatment trials. In a survey by the International Foundation for Functional Gastrointestinal Disorders (IFFGD), over 50\% of patients reported some degree of side effects related to prescription medication. Patients reporting side effects with treatment were also more likely to be dissatisfied with the remedy and suffer adverse events including hospitalizations, emergency room visits, and missed days at work and school\textsuperscript{22}. However, one limitation of the IFFGD survey was that it analyzed patients normally excluded from clinical trials of IBS including those with inflammatory bowel disease, diverticulitis, and other organic diseases.
Doctor-Patient Relationship

Psychosocial variables are important determinants of global wellbeing, and a strong doctor-patient relationship is an important aspect of successful treatment of IBS. A physician approach that addresses a patient’s psychological and social status, adopts a positive and encouraging attitude that is patient-centered, addresses patient concerns, and involves the appropriate prescription of medications and referrals to mental health professionals are all identified as ways to help patients cope with IBS symptoms. Furthermore, a positive physician-patient interaction has been shown to be associated with fewer return visits for IBS. However, IBS patients have reported an unsympathetic attitude from their medical provider, and other studies have characterized doctors as often being intolerant towards their IBS patients.

The patient-physician relationship is a difficult dimension to study because the quality of a medical visit is difficult to assess, details of the initial observation are often not recorded in medical charts, and patients who seek therapy for IBS have different characteristics from those who don’t seek therapy including greater severity of disease and higher rates of anxiety and depression. A systematic review by Dhaliwal and colleagues explored the doctor-patient interaction and consequences of IBS. They concluded that IBS patients in the primary care setting commonly experience negative attitudes and dissatisfaction in the interaction with their physicians, but due to limitations in the review, this may not be generalizable to all IBS patients. The study recognized a need for further understanding of the doctor-patient relationship in order to better meet and manage a patient’s needs.
Study Aims

The patient-reported outcomes used in clinical trials attempt to capture attitudes, behaviors, and events associated with IBS treatment. A patient’s perspective of how well a treatment works, the severity of side effects associated with a treatment, and level of satisfaction with the physician may determine if a patient is a responder or nonresponder for global endpoints in clinical trials of IBS. The Rome III guidelines identifies a number of priorities for future research in the design of treatment trials for IBS that include: examining the influence of disease modifiers (predictors) on outcome measures, examining the impact of baseline observations on treatment response, further validating “satisfactory relief” as a primary endpoint, and further evaluating the definitions of a treatment responder.

Determining predictors of treatment satisfaction may be useful in further validating current endpoints used in IBS trials as well as identifying potential gaps in the current design of treatment trials. If determinants of treatment satisfaction vary by class of medication, this may suggest the need to refine the outcome measures depending on the type of intervention being tested. Identifying factors that predict lower rates of treatment satisfaction may also uncover patient groups in need of additional resources and attention.

The aims of this study were (1) to assess if the following primary independent variables predict satisfactory relief of bowel symptoms: patient reported effectiveness of treatment, patient reported severity of side effects, and patient satisfaction with the initial physician visit; (2) to determine if these independent variables differ among patients taking prescription versus non-prescription medication for IBS relief; (3) to determine if satisfactory relief is predicted by
baseline scores on the Irritable Bowel Syndrome Symptom Severity Scale (IBS-SS) or the Brief Symptom Inventory (BSI) scale that measures psychological symptoms; (4) to test if the independent variables predict satisfaction with treatment, a novel outcome measure that measures response on an ordinal scale.

Methods:

Setting:

This survey was conducted between December 4, 2001 and September 12, 2002 at the Group Health Cooperative of Puget Sound (GHC). This large health maintenance organization serves 400,000 members in Seattle, Washington. The demographics of this patient population are similar to the demographics of the Seattle area, except for less representation of the highest and lowest income groups. In comparison to the rest of the United States, GHC and the Seattle area have a higher proportion of Asians and a lower proportion of African Americans and Hispanics. The demographic makeup of the GHC membership is otherwise similar to the United States population.

Subjects:

Investigators prospectively screened all patient encounter forms submitted by 353 primary care physicians and 16 gastroenterologists to identify patients with a clinical diagnosis of IBS (564.0), abdominal pain (789.X), constipation (564.0), and diarrhea (787.91). Patients from these groups who fulfilled the Rome II criteria for IBS were included in the analysis. Patients also had to be aged 18-75, enrolled in GHC for at least 1 year, and have no treatment
record for ulcerative colitis or Crohn’s disease. Sampling was stratified with the goal of enrolling 500 patients with IBS from primary care clinics and 300 patients with IBS from gastroenterology clinics. Among the 1770 patients who participated in the study, the final analysis included a total of 835 patients meeting Rome II criteria for IBS with no diagnosis of organic disease.

**Design:**

Subjects who met eligibility criteria were mailed an invitation to participate, an informed consent statement, and the initial questionnaires within 1 week of receipt of their clinical encounter forms by the administrative offices of GHC. In the invitation to participate, subjects were told to telephone or write the survey team at GHC if they chose not to participate. They were also informed that if they neither returned the questionnaires nor refused to participate, they would be telephoned after approximately 2 weeks to remind them to complete the questionnaires. At least six attempts were made to contact each participant.

Participants who returned the initial set of questionnaires were re-contacted 6 months later to collect updated information and to complete follow-up questionnaires. Further details of the recruitment process are summarized in Figure 1. A 10 dollar incentive was offered for completing the initial survey and a second $10 incentive for completing the follow-up survey. The survey was initially designed to describe usual medical care for IBS\textsuperscript{32}, and the type of treatment prescribed was decided by each individual patient’s primary care physician or gastroenterologist. This study was reviewed and approved by the institutional boards of GHC, the University of Washington, and the University of North Carolina at Chapel Hill.
Questionnaires:

The primary outcome measure assessed patient reported satisfactory relief with a yes/no response to the question: "In the past 7 days, have you had satisfactory relief of your bowel symptoms?" Bowel symptoms were defined in a footnote to include abdominal pain and discomfort, bloating, constipation, and diarrhea. Separate analyses were performed for prescription users and nonprescription users. A second, novel, outcome measure assessed patient response to satisfaction with treatment. The question asked: "How satisfied or dissatisfied are you with the relief you are experiencing from the prescription, non-prescription, herbal remedies or other/alternative treatments you are taking for your bowel symptoms (abdominal pain and discomfort, bloating, constipation, diarrhea)?” Responses to prescription and non-prescription medication were assessed on the following 5-point Likert scale: 1 = extremely dissatisfied; 2 = a little dissatisfied; 3 = somewhat satisfied; 4 = very satisfied; 5 = extremely satisfied. Rating of herbal remedies and alternative treatments are not included in this report.

The first primary independent variable tested was patient-reported effectiveness of usual treatment. This potential predictor variable was assessed in the follow-up survey, six months following the index visit, with the following question: “To what extent has the prescription, non-prescription, herbal remedies, or other/alternative treatments you have taken been effective in relieving your bowel symptoms (abdominal pain and discomfort, bloating, constipation, diarrhea)?” Only responses to prescription and non-prescription medication were assessed on a 5-point Likert scale: 1 = not at all effective; 2 = a little effective; 3 = somewhat effective; 4 = very effective; 5 = extremely effective.
The second primary independent variable tested was patient-reported side-effect severity of usual treatment. Patients responded to the following question in the follow-up survey: “Please tell us whether you experienced any side effects from these treatments?” Responses for the following 9 categories of treatment were categorized as prescription treatment (anti-spasmodic drugs, anti-diarrheal drugs, and psychotropic medications) or non-prescription treatment (laxatives, stool softeners, fiber supplements, and OTC drugs for gas relief, anti-diarrhea, and pain). Responses were assessed on a 4-point Likert scale: 1 = no side effects; 2 = mild side effects; 3 = moderate side effects; 4 = severe side effects.

The third primary independent variable tested was patients’ response to satisfaction with their initial physician visit. The initial survey asked the following question using a numerical scale: “How satisfied were you with the care you received at your last visit? Rate your satisfaction from 0% (very dissatisfied) to 100% (very satisfied). A rating of 50% would mean that you were neither dissatisfied nor satisfied with the clinic visit but are waiting to see.” The “last visit” refers to the index visit with either the primary care physician or gastroenterologist.

The initial survey also included the following integrative symptom questionnaires: (1) Rome questionnaire to determine if subjects met Rome II criteria for IBS\textsuperscript{31}. (2) The Irritable Bowel Symptom Severity Scale (IBS-SS) to assess overall severity of IBS symptoms. (3) The Brief Symptom Inventory-18 (BSI) to assess psychological symptoms. Additional questionnaires which are not included in this study were also administered; see prior report\textsuperscript{32}. 
**IBS-SS**

The impact of baseline symptom severity on patient-reported satisfaction with treatment was assessed using the IBS-SS scale. This validated questionnaire contains five questions which address (1) typical severity of abdominal pain over the last 10 days, (2) frequency of abdominal pain, (3) severity of abdominal distension, (4) dissatisfaction with bowel habits, and (5) impact of IBS symptoms on everyday activities. All questions contribute equally to the total score, which ranges from 0 to 500. In accordance with previously validated cutoffs\(^3\), patients were categorized as having mild baseline symptom severity if they reported scores below 175, moderate symptom severity if reported scores were between 175 and 300, and severe symptom severity if reported scores were greater than 300.

The IBS-SS was cited as the only validated integrative symptom questionnaire by the Rome III committee\(^2\). It has been tested in hypnosis trials\(^34,35\) and in a study of usual care for IBS\(^32\). Furthermore, the IBS-SS was not confounded by initial symptom severity when used to define a responder as having a 50% reduction in symptoms\(^18\). However, a review by Camilleri and colleagues recommends further validation of the psychometric properties and scoring algorithm of this scale specifically related to internal consistency, construct validity, and factor structure. They point out that the IBS-SS gives equal weight to all five items comprising the scale, and thus may not accurately capture the clinical heterogeneity of each patient’s disease process\(^9\). To further validate this scale and assess for confounding effects, we tested if baseline scores on the IBS-SS predicted response to the outcome measures.
BSI

The impact of psychological distress and psychiatric illness on patient-reported satisfaction with treatment was assessed using the BSI-18 scale. The full BSI measures distress with 53 items that contain nine subscales and 3 global scales. The BSI-18 is an abridged scale that measures the primary dimensions of psychological distress including somatization, depression, and anxiety. It is written at a 6th grade level and requires 5 to 7 minutes to complete. For analysis, the raw scores were first transformed to T-scores to allow males and females to be pooled together. Patients with T-scores of 63 or higher were classified as abnormal, i.e., reflective of clinically significant psychological distress.

Data Analysis:

Qualitative analysis involved a comparison of the three primary independent variables (patient reported severity of treatment side effect, patient reported effectiveness of treatment effectiveness, and patient satisfaction with initial physician visit) with the ordinal dependent variable (patient satisfaction with treatment) using bar graphs. Separate bar graphs were shown for prescription and nonprescription drug users, and median values were calculated for responses to the primary independent variables measured on an ordinal scale. The physician satisfaction rating was measured on a continuous scale (from 0 – 100), and scores were divided equally into quintiles when comparing this independent variable to the primary endpoint, satisfaction with treatment, on the bar graphs.

A nonparametric correlation coefficient, Kendall tau-b, was computed to test correlations between (a) the primary independent variables and the outcome measures and between (b)
baseline scores on the integrative symptom questionnaires (IBS-SS and BSI) and the outcome measures. Separate correlations were performed for responses to satisfaction with prescription and nonprescription treatment, and p values less than 0.05 were considered statistically significant.

A binary logistic regression analysis was used to test the hypothesis that the primary independent variables and baseline symptom scores predict responses to patient reported satisfactory relief. The 1st model tested if the primary independent variables predicted responses to satisfactory relief of symptoms after adjusting for demographic characteristics. Demographic characteristics included age, gender, education status (dichotomized as college graduate and greater vs. less than college graduate), and race (Caucasian vs. non-Caucasian). The 2nd model tested if the primary independent variables predicted responses to satisfactory relief of symptoms after adjusting for baseline symptom scores on the IBS-SS (categorized as mild, moderate, and severe) and BSI (treated as a continuous variable) scales.

The secondary outcome measure, ordinal response to patient satisfaction with treatment, was evaluated with an ordinal logistic regression analysis. A similar modeling strategy was performed for the secondary outcome measure as was performed for the binary satisfactory relief of symptoms outcome. The 1st model tested whether the primary independent variables predicted satisfaction with treatment after adjusting for demographic characteristics, and the 2nd model tested whether the primary independent variables predicted satisfaction with treatment after adjusting for baseline symptom scores.
For all regression models, separate analyses were carried for users of prescription treatment and nonprescription treatment. All analyses were conducted with Stata Statistical Software: Release 9.0 (College Station, TX), and results from logistic regression models were reported using odds ratios and 95% confidence intervals.

Results:

Patient Characteristics

Table 1 shows the demographic characteristics of participants, median baseline scores on the integrated symptom questionnaires, and median satisfaction rating with the index physician visit. The study participants were largely white and female. Asians and blacks were the next most commonly represented minority groups, comprising 4% of the study population each.

A similar number of patients self reported using prescription and nonprescription medication. In contrast to non-prescription users, prescription users appeared to have greater symptom severity at baseline (IBS-SS score of 277.7 vs. 257.3) and were less likely to be college graduates (40.5% vs. 44.7%). Otherwise the two groups appeared similar. No statistical comparisons of demographic characteristics were made between groups in Table 1 because some patients reported taking both prescription and nonprescription medications.

Among the 835 patients diagnosed with IBS by Rome II criteria, 215 had missing responses for the outcome measure, patient satisfaction with prescription or nonprescription treatment (Table 1). Although subjects with missing responses were more likely to be Hispanic
and non-college graduates, they otherwise appeared similar to those using prescription and nonprescription drugs that responded to the outcome measure.

**Treatment Side Effect Severity**

Table 2 shows a statistically significant and negative correlation between side effect severity and satisfactory relief of symptoms for users of prescription and nonprescription medications. As side effect severity increased, satisfactory relief of symptoms decreased. Similar correlation coefficients were seen between side effect severity and the secondary outcome measure, satisfaction with treatment measured by an ordinal scale, for prescription and nonprescription users (Table 3).

Multivariate regression analysis was performed to determine if severity of side effects to treatment predict satisfactory relief after adjusting for potential covariates. Table 4 shows that the odds of reporting satisfactory relief of symptoms decreased as patients experienced greater side effect severity with prescription drugs after adjusting for patient characteristics (Table 4, Model I) or baseline symptom severity (Table 4, Model II). Similarly, for the second outcome measure, patients with greater side effect severity to prescription drugs were less likely to report satisfaction with treatment after adjusting for patient characteristics (Table 6, Model I) or baseline symptom severity (Table 6, Model II).

Different trends were noted for side effect severity to nonprescription drugs, compared to prescription drugs, for the outcome measures. As side effect severity with nonprescription drugs increased, the odds of reporting satisfactory relief of symptoms decreased after adjusting for
patient characteristics (Table 5, Model I). However, side effect severity was no longer a statistically significant predictor of satisfactory relief after adjusting for baseline symptom severity (Table 5, Model II). In contrast, side effect severity remained a statistically significant predictor for the satisfaction with treatment outcome after adjusting for patient characteristics (Table 7, Model I) and baseline symptom severity (Table 7, Model II).

**Treatment Effectiveness**

Table 2 shows a positive and statistically significant correlation between treatment effectiveness and satisfactory relief of symptoms for users of prescription and nonprescription medications (Table 2). Similar correlation coefficients were seen between treatment effectiveness and the secondary outcome measure, satisfaction with treatment (Table 3).

In Figures 2 and 3, bar graphs describe the median number of patients reporting satisfaction with treatment for categories of treatment effectiveness. The abscissa divides all patients into 5 groups based on their reports of treatment effectiveness, and the ordinate shows median satisfaction with treatment for the various subgroups. The bar graphs support the positive trends suggested by the correlations: as patients report increasing effectiveness of treatment, satisfaction with treatment increases. The trend appears to be similar for prescription and nonprescription treatments.

The odds ratios reported in the logistic regression models for prescription treatment effectiveness (Table 4) confirmed this variable as a strong predictor of satisfactory relief. After
adjusting for patient characteristics (Table 4, Model I) and baseline symptom severity (Table 4, Model II), the odds of reporting satisfactory relief of IBS symptoms increased as effectiveness of prescription medication increased. For the second outcome measure, effectiveness of prescription medications was a strong predictor of satisfaction with prescription treatment after adjusting for patient demographics (Table 6, Model I) and baseline symptom severity (Table 6, Model II).

Increased effectiveness of nonprescription medication was also a strong predictor of satisfactory relief. As patient reported increased effectiveness of nonprescription treatment, odds of reporting satisfactory relief of IBS symptoms increased significantly after adjusting for patient characteristics (Table 5, Model I) and baseline symptom severity (Table 5, Model II). Similarly, patient reported effectiveness of nonprescription drugs was a strong predictor of the secondary outcome measure, satisfaction with treatment, after adjusting for patient characteristics (Table 7, Model I) and baseline symptom severity (Table 7, Model II).

Satisfaction with Physician Visit

For both prescription and nonprescription users, the correlation between satisfaction with initial physician visit and satisfactory relief of IBS symptoms six months later were statistically significant and support a positive trend: as satisfaction scores with physician visit increased on a continuous scale, binary response to satisfactory relief of symptoms increased (Table 2). Similar correlation coefficients were seen between satisfaction with physician visit and the secondary outcome measure, satisfaction with prescription and nonprescription medications (Table 3).
In Figures 4 and 5, bar graphs describe the median number of patients reporting satisfaction with medications for categories of physician satisfaction. The abscissa divides prescription and nonprescription drug users into 5 equal quintiles based on the satisfaction rating with their physician. The ordinate shows median satisfaction with treatment for subgroups differing in physician satisfaction ratings. For prescription drug users, the bar graph (Figure 4) shows a positive trend that supports the correlation coefficient. However, patients in quintiles representing scores from 20 to 80 reported moderate levels of treatment satisfaction regardless of their physician visit. For nonprescription drug users, the bar graph suggests a relatively weak positive trend where patients report moderate levels of treatment satisfaction except those in the lowest quintile (Figure 5).

Although the odds ratios for the initial satisfaction rating with physician visit and satisfactory relief of symptoms were statistically significant (Table 4 and 5), the point estimates were very close to one suggesting that the doctor visit had a negligible effect on any response to the outcome measure. Similarly, satisfaction with physician visit does appear to meaningfully contribute to a response to the secondary outcome measure, satisfaction with treatment (Table 6 and 7), after adjusting for other independent variables, patient demographics, and baseline symptom scores.

**Baseline IBS-SS**

Lower baseline symptom severity (categorized as mild, moderate, and severe on the IBS-SS) was correlated with satisfactory relief of IBS symptoms on the binary scale (Table 2) and satisfaction with treatment on the ordinal scale (Table 3) for both users of prescription and
nonprescription medication. After adjusting for the three primary independent variables and baseline psychological distress (BSI), baseline symptom severity was not a statistically significant predictor of satisfactory relief of IBS symptoms for prescription drug users (Table 4, Model II) or nonprescription drug users (Table 5, Model II). For the secondary outcome measure, lower baseline symptom severity was a statistically significant predictor of satisfaction with prescription treatment (Table 6, Model II) but not nonprescription treatment (Table 7, Model II).

**Baseline BSI**

Lower scores on the psychological distress scale, measured at baseline, were significantly correlated with satisfactory relief of IBS symptoms (Table 2) and satisfaction with treatment (Table 3). However, after adjusting for the primary independent variables and baseline symptom scores, lower baseline scores on the BSI did not predict satisfactory relief of IBS symptoms for users of prescription drugs (Table 4, Model II) or nonprescription drugs (Table 5, Model II). Similarly, lower baseline psychological distress was not a significant predictor of satisfaction with prescription (Table 6, Model II) or nonprescription treatment (Table 7, Model II) after adjusting for other variables.

**Discussion:**

Global endpoints that ask patients whether they received satisfactory or adequate relief of IBS symptoms are considered the current standard for assessing efficacy of IBS treatment in clinical trials. However, classifying a patient as a responder in clinical trials has proven difficult,
and the use of global endpoints has been a topic of controversy in recent literature. Recognizing this, members of the Rome III committee recommended further validation of satisfactory and adequate relief outcome measures during clinical trials. Specific suggestions for future research included determining predictors of response to IBS symptom relief, evaluating the impact of baseline symptoms on treatment response, and further characterizing the multidimensional construct of satisfactory and adequate relief.

In an effort to address these recommendations, we hypothesized that a patient’s rating of treatment effectiveness, severity of side effects with medication, and satisfaction with the physician visit predicts response to satisfactory relief of IBS symptoms. Based on results from a previous study, we also hypothesized that lower baseline symptom severity would predict satisfactory relief, but baseline psychological distress would not have a significant effect on this outcome measure18.

Predictive Value of the Primary Independent Variables:

The data presented in this study shows that when patients with a Rome diagnosis of IBS believe their treatment is effective, they are much more likely to report satisfactory relief of their IBS symptoms after 6 months. The odds ratios reported in Table 4 and Table 5 shows that (1) patient reported treatment effectiveness is the strongest predictor of satisfactory relief compared to any other independent variable tested and (2) the predictive value of treatment effectiveness is stronger for prescription medication (OR ~ 3.0) compared to nonprescription medication (OR ~ 2.0). This second finding implies that high effectiveness ratings of prescription drugs are more likely to predict satisfactory relief with IBS symptoms compared to similar ratings of
nonprescription drugs, and this is concordant with previous survey results\textsuperscript{22}. The effectiveness of herbal remedies and alternative treatments was not assessed in this study.

After adjustment for correlations among the independent variables, the regression analyses (Table 4-7) show that severity of side effects to IBS treatment is the next strongest predictor of response to satisfactory relief of IBS symptoms. The odds ratios reported in Table 4 are for categories of side effect severity. For every one level increase on the ordinal scale of side effect severity to prescription drugs (e.g. moderate side effects → severe side effects), patients have about half the odds (OR ~ 0.65) of reporting satisfactory relief with IBS symptoms. Compared to prescription drugs, side effect severity with nonprescription drugs is a weaker predictor of satisfactory relief and becomes statistically non-significant after adjusting for other variables (Table 5, Model II). The differences between prescription and nonprescription drugs are logical as side effects of prescription drugs are associated with greater levels of distress and adverse events\textsuperscript{22} and thus require a physician consultation. Several possible explanations may exist as to why severity of side effects to prescription drugs, but not nonprescription drugs, predicts satisfactory relief. First, given the similarities between side effects of treatment and symptoms of IBS, patients taking prescription drugs may have greater severity of disease compared to those taking nonprescription drugs. By adjusting for baseline symptoms scores, we hoped to control for some of this effect. Second, a severe side effect to a prescription drug may differ compared to a severe side effect to a nonprescription drug. However, specific side effects to medication were not addressed in this study.
Previous studies suggest that the doctor-patient interaction can be beneficial or detrimental depending on the physician’s approach to the patient’s disease process. The simple correlations shown in Tables 2 and 3 support this association. However, after adjusting for the correlations among variables by multivariate regression analysis (Tables 4-7), patient satisfaction was no longer a significant predictor of treatment satisfaction. Although the odds ratios for prescription and nonprescription drug users are statistically significant, the point estimates are close to one and therefore probably should be considered negligible. It is important to note that all three primary predictor variables were adjusted for each other in the multivariable logistic regression analyses. Therefore, while a positive patient-physician interaction alone may predict satisfaction with IBS relief, the joint effect of treatment effectiveness and side effect severity may no longer make the patient-physician interaction a significant predictor of satisfactory relief. Additionally, all patient satisfaction scores were pooled together in the analysis regardless of whether the provider was a primary care physician or gastroenterologist. Therefore, the impact of the doctor-patient relationship on satisfactory relief may differ based on provider type, but this potential difference was not assessed in the analysis.

Validation of Satisfactory Relief with a Novel Endpoint

We also tested if treatment effectiveness, side effect severity, and satisfaction with physician predicted response to a second, novel outcome measure, satisfaction with treatment measured on an ordinal scale. We found similar results from the ordinal logistic regression models using the satisfaction with treatment endpoint (Table 6 and 7) when compared to the binary logistic regression models using the satisfactory relief with symptoms endpoint (Table 4 and 5). However, notable differences were observed. First, effectiveness of prescription and
nonprescription drugs is a much stronger predictor of satisfaction with treatment (OR \sim 10-20) compared to satisfactory relief of IBS symptoms (OR \sim 2-3). Conceptually, effectiveness of treatment is more closely related to satisfaction with treatment than it is to satisfactory relief of symptoms and may be one reason to account for differences between endpoints.

Second, lower severity of side effects to nonprescription drugs is a significant predictor of satisfaction with treatment (Table 7) but not a predictor of satisfactory relief of IBS symptoms (Table 5, Model II). The choice of the response scale used may in part explain why side effect severity to nonprescription drugs is a statistically significant predictor of one endpoint and not the other. An advantage of measuring response on an ordinal scale, compared to a binary scale, is that it increases sensitivity and specificity due to a greater number of response options. Therefore, the binary scale may not be equipped to detect a statistically significant difference in yes/no responses to satisfactory relief based on severity of side effect to nonprescription drugs. However, it is important to note that these two endpoints distinctly differ (satisfaction with symptoms vs. satisfaction with treatment) and thus evaluating different concepts altogether.

The use of a second, novel outcome measure lends construct validity and reliability to the results for the satisfactory relief endpoint. The FDA report on validation of PRO instruments recommends that the primary instrument show convergent results with a similar but independent secondary instrument\textsuperscript{38}. Construct validity was demonstrated as results from satisfactory relief endpoint compared favorably with results from the satisfaction with treatment endpoint, a similar but independent measure. Confirmation with an ordinal scale measure also adds reliability due to the greater number of response options.
Baseline Symptom Severity

A previous study reported that satisfactory relief is confounded with initial IBS symptom severity, and patients with lower baseline symptom severity were more likely to report satisfactory relief compared to patients with higher baseline symptom severity\textsuperscript{18}. Simple correlations (Table 2 and 3) are consistent with this earlier report. However, after adjustment for the correlations among variables by multivariate regression analysis, baseline symptom severity did not significantly predict satisfactory relief of symptoms for prescription (Table 4) or nonprescription (Table 5) drug users. Although the influence of baseline symptom severity on satisfactory relief is statistically non-significant in this study, the point estimates for the odds ratios for users of prescription drugs (OR = 0.636) support previously reported results. Furthermore, the relative proximity of the upper confidence limit to 1.0 suggests that lower baseline symptom severity may predict satisfactory relief in a larger sample size. Additionally, lower baseline symptom severity was a significant predictor of the secondary outcome measure, satisfaction with prescription treatment (Table 6, Model II). Increased sensitivity and specificity of this ordinal measure suggests a lack of power to detect a statistically significant difference for the binary satisfactory relief endpoint. Further confirmation with a clinical trial is needed.

Baseline psychological distress, as measured by the BSI scale, does not predict satisfactory relief after adjusting for IBS symptom severity and the primary independent variables, and these results are concordant with a prior report\textsuperscript{18}.
Limitations:

Out of 835 patients in the final study analysis, there were 215 missing responses to the satisfactory relief outcome measure. From Table 1, patients with missing responses appear more likely be Hispanic and have lower education status than non-missing responders. One possibility is that missing responders may not have understood wording of the instructions or scaling of the response options. Otherwise, patients with missing responses did not seem to systematically differ from patients with non-missing responses based on pertinent demographic and baseline characteristics.

All concepts and domains measured in the study are based on patient-reported responses to outcome measures as well as to questionnaires assessing treatment effectiveness, side effect severity, and satisfaction ratings with physician visit. Any undue physical, emotional, or cognitive strain on patients can decrease the quality of reported data\textsuperscript{38}. Additionally, any degree of administrator burden including how questionnaires are distributed, administered, and analyzed can undermine the validity of results. However, the integrity of the questionnaires used in this study have been examined\textsuperscript{30} and results from the questionnaires have been published in prior reports\textsuperscript{18,32}.

This study was not a clinical trial but an observational study of patients receiving usual medical care for IBS. As such, limitations are present given the study design including the way patients were selected to be in the study and the influence of factors, other than the independent variables identified, on the outcome measures. To minimize selection bias, we provided eligibility criteria consistent with recommendations by the Rome III committee on design on IBS.
studies\textsuperscript{2}, and included a flow diagram (Figure 1) explicitly stating how patients were enrolled in the study and junctures where dropouts occurred. We recognize that satisfactory relief is a multidimensional construct, and responses to this outcome are predicted by variables other than those identified in this study. Furthermore results from this population of patients receiving treatment for IBS in an outpatient, managed care setting may not be generalizable to all IBS patients. However, we extended the generalizability of these results by including usual care given by primary care physicians and gastroenterologists, in contrast to other studies that report only one provider type.

This study is the first to assess predictors of response to satisfactory relief of IBS symptoms. The results show that a patient's perception of drug effectiveness is a significant predictor of satisfactory relief, a commonly used endpoint in clinical trials of IBS treatment. We also show that tolerability to prescription medication, but not nonprescription drugs, is an important predictor of treatment efficacy and that the initial patient-doctor interaction has little effect on satisfactory relief after adjusting for other variables. The results from this study may help in the future design of clinical trials of IBS.
Figure 1. Flow diagram of recruitment

3024 Initial Surveys Mailed

1770 Completed (59%)
1240 Not Completed
14 Ineligible/Unable to Contact

1639 Follow-Up Surveys Mailed
131 Excluded (refused follow-up survey or labeled as controls for a previous study)

1261 Completed (77%)
373 Not Completed
5 Indigible

635 Rome II Diagnosed IBS
421 Other FGID
5 Organic Disease

620 Responses to Primary Endpoint: Satisfaction with Treatment
215 Missing Responses to Primary Endpoint

323 Report Using Prescription Drugs
297 Report Not Using Prescription Drugs
359 Report Using Nonprescription Drugs
261 Report Not Using Prescription Drugs
<table>
<thead>
<tr>
<th></th>
<th>Prescription (n=323)</th>
<th>Non-Prescription (n=359)</th>
<th>Missing Responses (n=215)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>52.2 ± 14.4</td>
<td>52.0 ± 14.7</td>
<td>50.0 ± 15.4</td>
</tr>
<tr>
<td>Gender: % female</td>
<td>78.6</td>
<td>79.1</td>
<td>72.9</td>
</tr>
<tr>
<td>Race: % Caucasian</td>
<td>88.6</td>
<td>88.1</td>
<td>84.5</td>
</tr>
<tr>
<td>Ethnicity: % Hispanic</td>
<td>3.3</td>
<td>3.3</td>
<td>7.3</td>
</tr>
<tr>
<td>Education: % College</td>
<td>40.5</td>
<td>44.7</td>
<td>36.1</td>
</tr>
<tr>
<td>IBS-QOL: mean score</td>
<td>69.6 ± 20.6</td>
<td>72.7 ± 18.7</td>
<td>67.7 ± 22.3</td>
</tr>
<tr>
<td>IBS-SS: mean score</td>
<td>277.7 ± 104.5</td>
<td>257.3 ± 104.1</td>
<td>264.1 ± 111.6</td>
</tr>
<tr>
<td>BSI: mean T-score</td>
<td>55.5 ± 10.4</td>
<td>54.7 ± 10.1</td>
<td>56.6 ± 10.5</td>
</tr>
<tr>
<td>Satisfaction w/ index visit</td>
<td>66.1 ± 26.8</td>
<td>67.5 ± 26.3</td>
<td>66.0 ± 26.5</td>
</tr>
</tbody>
</table>
### Table 2. Correlations between Binary Satisfactory Relief and Independent Variables

<table>
<thead>
<tr>
<th></th>
<th>Treatment Effectiveness</th>
<th>Treatment Side-Effects</th>
<th>Satisfaction with Physician Visit</th>
<th>Baseline IBS-SS</th>
<th>Baseline BSI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prescription Users:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Satisfactory Relief</td>
<td>0.4028 (p &lt; 0.0001)</td>
<td>-0.1630 (p = 0.0039)</td>
<td>0.3036 (p &lt; 0.0001)</td>
<td>-0.2449 (p = 0.0002)</td>
<td>-0.1250 (p = 0.0270)</td>
</tr>
<tr>
<td><strong>Nonprescription Users:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Satisfactory Relief</td>
<td>0.3201 (p &lt; 0.0001)</td>
<td>-0.1701 (p = 0.0001)</td>
<td>0.2562 (p &lt; 0.0001)</td>
<td>-0.2278 (p &lt; 0.0001)</td>
<td>-0.1048 (p = 0.0272)</td>
</tr>
</tbody>
</table>

(All correlations performed with Kendall's tau-b)

### Table 3. Correlations between Ordinal Satisfaction with Treatment and Independent Variables

<table>
<thead>
<tr>
<th></th>
<th>Treatment Effectiveness</th>
<th>Treatment Side-Effects</th>
<th>Satisfaction with Physician Visit</th>
<th>Baseline IBS-SS</th>
<th>Baseline BSI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Satisfaction with Prescription Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7398 (p &lt; 0.0001)</td>
<td>-0.1905 (p = 0.0013)</td>
<td>0.2329 (p &lt; 0.0001)</td>
<td>-0.2675 (p &lt; 0.0001)</td>
<td>-0.1882 (p &lt; 0.0001)</td>
</tr>
<tr>
<td><strong>Satisfaction with Non-Prescription Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.6993 (p &lt; 0.0001)</td>
<td>-0.1678 (p = 0.0009)</td>
<td>0.2066 (p &lt; 0.0001)</td>
<td>-0.1685 (p = 0.0005)</td>
<td>-0.1160 (p = 0.0050)</td>
</tr>
</tbody>
</table>

(All correlations performed with Kendall's tau-b)
Figure 2: Satisfaction with Treatment vs. Treatment Effectiveness (*Prescription*)

Figure 3: Satisfaction with Treatment vs. Treatment Effectiveness (*Nonprescription*)
Figure 4: Satisfaction with Treatment vs. Physician Satisfaction (*Prescription*)

Figure 5: Satisfaction with Treatment vs. Physician Satisfaction (*Nonprescription*)
Adjusted Odds Ratios Comparing Binary Response to Satisfactory Relief with Independent Variables.

**Table 4: Prescription Drug Users**

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Model I</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness (5-point ordinal)</td>
<td>3.080</td>
<td>2.103 - 4.511</td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity (4-point ordinal)</td>
<td>0.648</td>
<td>0.438 - 0.958</td>
</tr>
<tr>
<td>Patient Satisfaction with Physician (1-point)</td>
<td>1.028</td>
<td>1.014 - 1.043</td>
</tr>
<tr>
<td><strong>Model II</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness (5-point ordinal)</td>
<td>2.963</td>
<td>1.988 - 4.415</td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity (4-point ordinal)</td>
<td>0.651</td>
<td>0.432 - 0.981</td>
</tr>
<tr>
<td>Patient Satisfaction with Physician (1-point)</td>
<td>1.029</td>
<td>1.013 - 1.045</td>
</tr>
<tr>
<td>IBS-SS (3-point ordinal)</td>
<td>0.636</td>
<td>0.378 - 1.069</td>
</tr>
<tr>
<td>BSI (1 point)</td>
<td>1.009</td>
<td>0.972 - 1.047</td>
</tr>
</tbody>
</table>

*Model I is based on logistic regression model; each variable adjusted for other variables listed and patient demographics (age, race, gender, and education); none were statistically significant (95% CI = NS)

*Model II is based on logistic regression model; each variable adjusted for other variables listed and baseline symptom scales.
### Table 5: Nonprescription Drug

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model I</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness (5-point ordinal)</td>
<td>2.254</td>
<td>1.652 - 3.076</td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity (4-point ordinal)</td>
<td>0.712</td>
<td>0.535 - 0.948</td>
</tr>
<tr>
<td>Patient Satisfaction with Physician (1-point)</td>
<td>1.020</td>
<td>1.010 - 1.031</td>
</tr>
<tr>
<td><strong>Model II</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness (5-point ordinal)</td>
<td>2.087</td>
<td>1.530 - 2.847</td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity (4-point ordinal)</td>
<td>0.774</td>
<td>0.575 - 1.041</td>
</tr>
<tr>
<td>Patient Satisfaction with Physician (1-point)</td>
<td>1.019</td>
<td>1.008 - 1.031</td>
</tr>
<tr>
<td>IBS-SS (3-point ordinal)</td>
<td>0.743</td>
<td>0.505 - 1.094</td>
</tr>
<tr>
<td>BSI (1 point)</td>
<td>0.988</td>
<td>0.961 - 1.016</td>
</tr>
</tbody>
</table>

*Model I is based on logistic regression model; each variable adjusted for other variables listed and patient demographics (age, race, gender, and education); none were statistically significant (95% CI = NS).

*Model II is based on logistic regression model; each variable adjusted for other variables listed and baseline symptom scales.*
Adjusted Odds Ratios Comparing Ordinal Response to Satisfaction with Treatment with Independent Variables.

**Table 6: Prescription Drug Users**

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness</td>
<td>11.892</td>
<td>7.590 - 18.633</td>
</tr>
<tr>
<td>(5-point ordinal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity</td>
<td>0.607</td>
<td>0.430 - 0.856</td>
</tr>
<tr>
<td>(4-point ordinal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Satisfaction with Physician</td>
<td>1.024</td>
<td>1.012 - 1.036</td>
</tr>
<tr>
<td>(1-point)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness</td>
<td>10.393</td>
<td>6.524 - 16.555</td>
</tr>
<tr>
<td>(5-point ordinal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity</td>
<td>0.577</td>
<td>0.400 - 0.834</td>
</tr>
<tr>
<td>(4-point ordinal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Satisfaction with Physician</td>
<td>1.022</td>
<td>1.010 - 1.035</td>
</tr>
<tr>
<td>(1-point)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBS-SS (3-point ordinal)</td>
<td>0.633</td>
<td>0.404 - 0.993</td>
</tr>
<tr>
<td>BSI (1 point)</td>
<td>0.985</td>
<td>0.955 - 1.016</td>
</tr>
</tbody>
</table>

\(^1\)Model I is based on ordinal logistic regression model; each variable adjusted for other variables listed and patient demographics (age, race, gender, and education); none were statistically significant (95% CI = NS)

\(^2\)Model II is based on ordinal logistic regression model; each variable adjusted for other variables listed and baseline symptom scales.
Table 7: Nonprescription Drug Users

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model I</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness (5-point ordinal)</td>
<td>16.054</td>
<td>10.205 - 25.256</td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity (4-point ordinal)</td>
<td>0.626</td>
<td>0.468 - 0.836</td>
</tr>
<tr>
<td>Patient Satisfaction with Physician (1-point)</td>
<td>1.020</td>
<td>1.009 - 1.031</td>
</tr>
<tr>
<td><strong>Model II</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Reported Treatment Effectiveness (5-point ordinal)</td>
<td>18.040</td>
<td>11.078 - 29.376</td>
</tr>
<tr>
<td>Patient Reported Side Effect Severity (4-point ordinal)</td>
<td>0.684</td>
<td>0.502 - 0.932</td>
</tr>
<tr>
<td>Patient Satisfaction with Physician (1-point)</td>
<td>1.022</td>
<td>1.022 - 1.034</td>
</tr>
<tr>
<td>IBS-SS (3-point ordinal)</td>
<td>1.188</td>
<td>0.796 - 1.771</td>
</tr>
<tr>
<td>BSI (1 point)</td>
<td>0.983</td>
<td>0.956 - 1.012</td>
</tr>
</tbody>
</table>

*Model I is based on ordinal logistic regression model; each variable adjusted for other variables listed and patient demographics (age, race, gender, and education); none were statistically significant (95% CI = NS)

*Model II is based on ordinal logistic regression model; each variable adjusted for other variables listed and baseline symptom scales.
References:


