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Diagnosis, Comorbidities and Management of Irritable Bowel Syndrome in Patients in a Large Health Maintenance Organization

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Abstract

Background—Irritable bowel syndrome (IBS) imposes significant clinical and economic burdens. We aimed to characterize patterns of practice for patients with IBS who were members of a large health maintenance organization, analyzing point of diagnosis, testing, comorbidities and treatment.

Methods—Members of Kaiser Permanente Northern California who were diagnosed with IBS were matched to controls by age, sex, and period of enrollment. We compared rates of testing, comorbidities and interventions.

Results—From 1995 to 2005, IBS was diagnosed in 141,295 patients (mean age 46, SD 17 years; 74% female). Internists made 68% of diagnoses, gastroenterologists 13%, and others 19%. Lower endoscopy did not usually precede IBS diagnosis. Patients with IBS were more likely than controls to have blood, stool, endoscopic and radiologic tests, and to undergo abdominal or pelvic operations (ORs 1.5–10.7, all $P < 0.0001$). Only 2.7% were tested for celiac disease and only 1.8% were eventually diagnosed with inflammatory bowel disease. Chronic pain syndromes, anxiety and depression were more common among IBS patients than controls (ORs 2.7–4.6, all $P < 0.0001$). Many patients with IBS were treated with anxiolytics (61%) and antidepressants (55%). Endoscopic and radiologic testing were most strongly associated with having IBS diagnosed by a gastroenterologist. Psychotropic medication use was most strongly associated with female sex.

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Conclusions—In a large, managed care cohort, most diagnoses of IBS were made by generalists, often without endoscopic evaluation. Patients with IBS had consistently higher rates of testing, chronic pain syndromes, psychiatric comorbidity and operations than controls. Most patients with IBS were treated with psychiatric medications.

Keywords

functional gastrointestinal disorders; therapy; population; epidemiology

INTRODUCTION

Irritable bowel syndrome (IBS) affects between 10%–20% of the US population and accounts for \$1.6 billion in direct and \$19.2 billion in indirect costs annually.^{1–3} IBS is a symptom-based diagnosis, and concepts about the appropriate investigation in patients with suspected IBS have evolved over time. For example, celiac disease has been recognized in a minority of patients with IBS, and recent guidelines on the diagnosis and treatment of IBS recommend a limited diagnostic work-up including screening for celiac disease.^{4–10} IBS treatment remains challenging, with few directed therapies available. Numerous studies suggest a potential role of antidepressants in IBS.^{11–17}

Practice patterns in the community relating to the diagnosis and management of IBS are not well described. The extent to which IBS is diagnosed by generalists as opposed to specialists, and the reliance on invasive tests such as endoscopy to rule out other diseases are not well characterized. Several studies have highlighted that patients with IBS undergo more diagnostic testing and operations than their non-IBS counterparts,^{18–22} but detailed accounting across the spectrum of care is usually not available. Although both psychiatric comorbidity in IBS as well as the potential benefit of antidepressants in non-depressed IBS patients are well recognized, it is not clear to what extent psychotropic medications are used in IBS patients in general practice.

Our aims were to characterize practice patterns relating to the diagnosis and management of IBS in community practice, with attention to point of diagnosis and associated tests, comorbidities and medication use. We performed an observational study of persons diagnosed with IBS and controls without an IBS diagnosis in Kaiser Permanente Northern California (KPNC), a large health maintenance organization.

MATERIALS AND METHODS

General Study Design

In this large observational study, we investigated practice patterns associated with the diagnosis and management of IBS, and comorbidities associated with IBS in members of KPNC. Medical databases were searched to identify subjects who received a diagnosis of IBS. Controls were matched by age, gender, and length and time of insurance coverage by KPNC. Databases were queried to determine group demographics, medical visits and testing, comorbidities, medication use, and surgical interventions. The University of California, San Francisco Committee of Human Research, and the KPNC Institutional Review Board approved the study.

Aims and Hypotheses

The study addressed two aims: 1) characterize practice patterns surrounding the diagnosis and management of IBS; and 2) explore resource utilization, comorbidities and medical

interventions in patients with IBS compared to patients without IBS in general medical practice.

We hypothesized that: 1) most IBS diagnoses occur in the primary care setting; 2) many IBS diagnoses are made without extensive use of medical tests; 3) patients with IBS undergo more laboratory tests, endoscopies, and surgical interventions than patients without IBS; 4) patients with IBS suffer from psychiatric comorbidities and chronic pain conditions at higher rates than patients without IBS; 5) patients diagnosed initially with IBS are rarely diagnosed later with a different gastrointestinal disorder that could explain their symptoms; 6) patients with IBS are treated with psychiatric medications at higher rates than patients without IBS; 7) patients diagnosed with IBS by gastroenterologists undergo more intensive testing and treatment and suffer more comorbidities than patients diagnosed by non-gastroenterologists.

Source of Study Population and Clinical Setting

From 1995 to 2005, 2.4–3.2 million people (51% female, 75% adult) were enrolled in Kaiser Permanent Northern California. This member population is demographically representative of the general population of Northern California. Physicians from The Permanente Medical Group, Inc. provide nearly all care to Kaiser Permanente members in Northern California. Before 2006, physicians entered diagnoses on scannable sheets at the end of a visit. Since 2006, they have entered diagnoses into the electronic medical record.

In 2011, there were approximately 1,400 clinicians (96% physicians and the rest nurse practitioners and physician assistants), including approximately 120 gastroenterologists, providing adult medicine care in KPNC. KPNC does not have guidelines for IBS testing or management.

Data Sources

The Kaiser Permanent Northern California databases that were searched consisted of those recording outpatient visits and diagnoses, outpatient procedures, inpatient visits and diagnoses, inpatient procedures, laboratory tests, medications, and radiology studies. Datasets for the identified IBS patients and controls were merged for final analysis.

Identification of IBS patients and Controls

Databases recording outpatient and inpatient diagnoses were searched in order to identify all patients who received a diagnosis of IBS on at least one encounter from 1995–2005. The three KPNC labels linked to ICD-9 code 564.1 for IBS are “Irritable bowel syn.,” “Irritable bowel syndrome,” and “Irritable bowel syndrome (IBS).” Demographic characteristics for these IBS patients were then determined, including gender, age, and period of coverage by KPNC.

The same databases were then searched to identify controls, defined as patients who never received a diagnosis of IBS. Controls were matched to subjects by gender, date of birth, first year of KPNC membership, last year of KPNC membership, and number of years of KPNC membership. For dates and time periods, matching was performed within 1 year, and if no match was found for all parameters, then within 2 years.

Matching for length of coverage was performed in order to have comparable periods of observation in both groups in which diagnoses could have been made, tests undertaken, medications prescribed, and interventions performed. Matching for calendar period of coverage was performed in order to minimize differences between patients that could be

attributed to secular trends in practice patterns or resource utilization. Follow-up was available through 2007.

Variables Studied

Demographics and Factors Related to the Diagnosis of IBS—We summarized demographic characteristics for IBS patients and controls, and compared race and ethnicity, since no matching was performed for these variables. We determined the period of coverage before and after IBS diagnosis, ascertained what fraction of IBS diagnoses were made in the primary vs. the secondary care setting, and determined the rates of lower endoscopy and whether endoscopy preceded the diagnosis of IBS.

Medical Tests—We determined the proportions of patients who underwent the following tests at least once:

- 1) Laboratory tests: complete blood count, sedimentation rate, electrolytes and renal chemistries (blood urea nitrogen and creatinine), liver chemistries (alanine and aspartate aminotransferases, alkaline phosphatase, bilirubin), thyroid function tests (thyroid stimulating hormone and thyroxine levels), celiac disease antibodies (antigliadin and tissue transglutaminase), and *H. pylori* antibodies.
- 2) Stool tests: fecal leukocytes, fecal occult blood testing, fecal fat.
- 3) Endoscopic tests: sigmoidoscopy, colonoscopy, upper endoscopy, endoscopic retrograde cholangiopancreatography.
- 4) Radiologic tests: abdominal film, barium enema, abdominal sonogram, computed tomography of the abdomen and/or pelvis, magnetic resonance imaging of the abdomen and/or pelvis, upper gastrointestinal series, small bowel follow-through study.

For sigmoidoscopy and colonoscopy, we ascertained the timing of the test with respect to the first diagnosis of IBS in order to clarify whether the test might have been performed as part of the pre-diagnosis evaluation, reasoning that tests performed after a diagnosis of IBS was coded could not to have been part of the pre-diagnosis investigation. We did not find adequately coded information to determine rates of stool testing for parasites.

Comorbidities and Other Gastrointestinal Diagnoses—We determined the proportions of IBS patients and controls who received the following diagnoses at least once, including the multiple possible KPNC labels for each ICD-9 code associated with each diagnosis:

- 1) Psychiatric: anxiety, depression, bipolar affective disorder, psychosis.
- 2) Somatic pain: migraine, fibromyalgia, chronic pain syndrome.
- 3) Metabolic: diabetes.
- 4) Gastrointestinal: celiac disease, colitis, Crohn's disease, inflammatory bowel disease, colorectal cancer.

Medication Use—We determined the proportions of patients who were prescribed the following medications at least once:

- 1) Antidiarrheals: loperamide, diphenoxylate/atropine.
- 2) IBS medications: alosetron, tegaserod.
- 3) Antispasmodics: dicyclomine, hyosciamine

- 4) Anxiolytics: benzodiazepines.
- 5) Antidepressants: tricyclic antidepressant (TCA), selective serotonin reuptake inhibitor (SSRI), other antidepressant.

We attempted to determine the rates of use of fiber and laxatives, but did not find adequately coded information in the databases.

Surgical Interventions—We determined the proportions of patients who were underwent the following types of surgical interventions at least once: esophageal, gastric, intestinal, rectal, biliary, gynecologic.

Patients Diagnosed by Gastroenterologists vs. Non-Gastroenterologists—We contrasted diagnostic and management practices among patients diagnosed with IBS by gastroenterologists vs. non-gastroenterologists.

Statistical Analysis

Analyses were performed in SAS 9.1 (SAS Institute Inc., Cary, NC). Summary statistics were calculated. Data from IBS patients and controls, and from patients diagnosed by gastroenterologists and non-gastroenterologists, were compared with t-tests or chi-squared tests, and odds ratios were calculated with 95% confidence intervals. Predictors of test utilization and treatment, including demographic information and diagnosis by gastroenterologists or non-gastroenterologists, were analyzed by multivariable logistic regression analysis.

RESULTS

Study Patients

From 1995 to 2005, IBS was diagnosed in 141,295 individuals. The mean age at diagnosis was 46 years, SD 17.0 years, and the majority were women (Table 1). There were more caucasian and Hispanic or Latino persons among IBS patients than controls, but race and ethnicity was more often coded as unknown in controls than in IBS patients, limiting the ability to reach conclusions about different distributions of race and ethnicity between groups (Table 1). The mean time of enrollment in KPNC prior to IBS diagnosis was 4.1 years, SD 3.2 years, and the mean time of enrollment after IBS diagnosis was 4.7 years, SD 3.3 years.

Point of Diagnosis and Use of Endoscopy

Among the 83% of patients for whom provider specialty was known, non-gastroenterologist internists made 68% of IBS diagnoses, gastroenterologists 13%, and other physicians 19%. Among non-gastroenterologist internists, 87% of IBS diagnoses were made by general internists, 6% by hospitalists, 1% each by endocrinologists and rheumatologists, and the remainder by other subspecialists. Among other physicians, 68% of IBS diagnoses were made by family practitioners, 2% by pediatricians, <1% each by surgeons, gynecologists and psychiatrists, and the remainder by other specialists.

In the majority of cases, an IBS diagnosis was coded without a preceding lower endoscopic procedure. The IBS diagnosis was preceded by sigmoidoscopy in 29,159 patients (20.6% of IBS patients, 5.1 sigmoidoscopies/100 person-years, accounting for 49.6% of sigmoidoscopies in IBS patients) and by colonoscopy in 7,497 patients (5.3% of IBS patients, 1.3 colonoscopies/100 person-years, accounting for 37.4% of colonoscopies in IBS patients).

Blood and Stool Tests

IBS patients were significantly more likely than controls to undergo common laboratory blood tests (Table 2). A small minority of IBS patients underwent stool testing for white cells, blood or fat, but the proportion was higher than among controls (Table 2). Testing for celiac disease was rare among IBS patients (2.7%), but more common than among controls (OR 10.7, 95% CI 9.62–11.9). All of the celiac disease tests in patients with IBS occurred after 2001.

Endoscopic and Radiologic Tests

IBS patients were significantly more likely than controls to undergo endoscopic testing including sigmoidoscopy, colonoscopy, upper endoscopy, and endoscopic retrograde cholangiopancreatography, as well as all categories of abdominal and pelvic imaging (Table 2).

Comorbidities and Other Gastrointestinal Diagnoses

IBS patients were significantly more likely than controls to be diagnosed with chronic pain syndromes and psychiatric comorbidities (Table 3). Very few IBS patients went on to receive other gastrointestinal diagnoses that potentially could explain abdominal pain and altered defecation (Table 3). The mean time until another gastrointestinal diagnosis was made was 1.7 (SD 1.8) years for inflammatory bowel disease, 2.5 (SD 2.8) years for colitis, 2.4 (SD 2.6) years for Crohn's disease, and 2.8 (SD 3) years for celiac disease. The prevalence of diabetes was slightly lower in IBS patients than in controls (9.6% vs. 10.4%, OR 0.91, 95% CI 0.89–0.93).

Medication Use

IBS patients were often prescribed antidiarrheal and antispasmodic medications (Table 4). IBS patients were significantly more likely than controls to be prescribed anxiolytics and antidepressants (Table 4), with 38% of prescriptions for psychotropics made after and 62% before IBS diagnosis. Nearly half of all IBS patients were treated at one point with an anxiolytic, and over half of all IBS patients were treated at one point with an antidepressant, with TCAs and SSRIs each used in approximately one third of IBS patients (Table 4).

Among IBS patients treated with anxiolytics, 45% did not have a diagnosis of anxiety, 30% received anxiolytics before a diagnosis of anxiety, and 25% after a diagnosis of anxiety. Among controls treated with anxiolytics, the respective fractions were 66%, 18% and 16%.

Among IBS patients treated with antidepressants, 37% did not have a diagnosis of depression, 34% received antidepressants before a diagnosis of depression, and 29% after a diagnosis of depression. Among controls treated with antidepressants, the respective fractions were 45%, 26% and 29%.

Surgical Interventions

The rate of abdominal and pelvic surgery during the study period was low in both groups, but IBS patients were more likely than controls to undergo an operation in all of the categories assessed (Table 5).

Patients Diagnosed by Gastroenterologists vs. Non-Gastroenterologists

Patients diagnosed with IBS by gastroenterologists demonstrated patterns of more intensive testing, greater comorbidity, and more intensive treatment than patients diagnosed by non-gastroenterologists (Tables 2–5).

Predictors of Testing and Treatment

In multivariable logistic regression models, having IBS diagnosed by a gastroenterologist had the strongest association with endoscopic and radiologic testing. For example, in a model with Caucasian as the reference race/ethnicity, the adjusted ORs for undergoing a colonoscopy were 1.035 (95% CI 1.033–1.036) per 1-year increase in age, 0.82 (95% CI 0.79–0.86) for women *vs.* men, 0.79 (95% CI 0.73–0.85) for African Americans, 0.81 (95% CI 0.76–0.86) for Hispanics/Latinos, 0.79 (95% CI 0.74–0.85) for Asian Americans, 1.20 (95% CI 0.98–1.48) for Native Americans, and 2.82 (95% CI 2.71–2.94) for having IBS diagnosis by a gastroenterologist *vs.* non-gastroenterologist. The ORs for undergoing any sigmoidoscopy were of similar magnitude as those for colonoscopy, but non-Caucasians were more likely to undergo sigmoidoscopy than Caucasians. Overall, the strengths of the associations with radiologic testing were similar to those with endoscopic testing, but women were more likely than men to undergo pelvic imaging.

In contrast, sex was the variable with the strongest association with psychotropic medication use. For example, the adjusted ORs for receiving an antidepressant prescription were 1.014 (95% CI 1.013–1.015) per 1-year increase in age, 1.86 (95% CI 1.81–1.91) for women *vs.* men, 0.77 (95% CI 0.74–0.82) for African Americans, 0.81 (95% CI 0.78–0.86) for Hispanics/Latinos, 0.40 (95% CI 0.38–0.42) for Asian Americans, 1.10 (95% CI 0.93–1.31) for Native Americans, and 1.36 (95% CI 1.31–1.41) for having IBS diagnosis by a gastroenterologist *vs.* non-gastroenterologist. The results for anxiolytics were very similar to those for antidepressants, except that African Americans were more likely than Caucasians to receive an anxiolytic prescription (OR 1.08, 95% CI 1.02–1.13).

DISCUSSION

In this large observational study, we investigated practice patterns associated with the diagnosis and management of IBS and comorbidities associated with IBS in members of a large health maintenance organization. Although our observations may not be generalizable to all practice settings, they provide insight into the point of diagnosis, testing, management and comorbidities of IBS patients across the spectrum of care in general medical practice, with medium-term follow-up.

In our cohort, the majority of IBS diagnoses were made in the primary care setting, and usually without preceding lower endoscopy. Having IBS diagnosed by a gastroenterologist was the variable with the strongest association with endoscopic and radiologic testing. This is notable in light of prior studies suggesting that primary care physicians may be more likely than gastroenterologists to view IBS as a diagnosis of exclusion.²³ Although we could not ascertain what the indications were for tests or interventions, IBS patients were more likely than controls to undergo all of the common blood, stool, endoscopic and radiologic tests, and all of the types of abdominal and pelvic operations that we studied. These findings are consistent with several prior studies that report increased health care resource utilization among patients with IBS.^{19–22, 24} Most of these previous studies did not examine the specific types of tests or interventions in detail. Our study provides a detailed accounting over a reasonably long period of follow-up.

Although celiac disease testing was performed more frequently in patients diagnosed with IBS than in controls, it was still uncommon in the IBS group, and occurred only after 2001, when the presence of celiac disease among a minority of IBS patients became well recognized. Admittedly, recommendations that patients with suspected IBS be tested for celiac disease are relatively recent.^{9, 10} The proportion of patients with IBS in our cohort who went on to receive other gastrointestinal diagnoses that could potentially explain their symptoms was very low, which is consistent with reports by other investigators.

As has been observed previously, patients with IBS in our cohort had higher comorbidities of somatic pain syndromes including fibromyalgia, migraine, and chronic pain, and psychiatric comorbidity than controls, including high rates of anxiety and depression. The rates of psychiatric comorbidity in IBS vary widely in the literature, ranging from 18% of IBS patients in the community to up to 94% of those referred to specialty centers.²⁵ The rates of anxiety and depression observed in this study are consistent with previously reported data on IBS patients presenting to outpatient clinics.^{26, 27} Fibromyalgia has been reported previously in over 30% of patients with IBS,^{28, 29} in contrast with the 5.9% observed in our cohort. This may reflect differences in study populations, as our cohort reflects the general membership of a large health maintenance organization and not selected patients in referral settings, but it may also reflect under-recognition of fibromyalgia in clinical practice in the absence of an active effort to ascertain its prevalence. The prevalence of migraine of 36.7% in our IBS cohort was significantly higher than the rate of 6% previously reported in a large IBS cohort,³⁰ and it is more consistent with the prevalence of “headache” reported in IBS patients.^{31–33}

As would be expected, IBS patients commonly received prescriptions for antispasmodic and antidiarrheal medication. It is likely that the use of antidiarrheal medication, laxatives and fiber was substantially higher than was recorded in the databases, as over the counter use was not captured. The use of anxiolytic and antidepressant medications was substantial in both IBS patients and controls, but significantly higher in IBS patients. Sex was the variable with the strongest association with psychotropic medication use, with women being more likely than men to receive these medications. Of note, the majority of antidepressants were prescribed before IBS diagnosis, possibly reflecting the high prevalence of depression and other chronic pain syndromes in patients with IBS.

The strengths of this study include its large size and the inclusion of controls matched for age, gender, and length of enrollment in KPNC. The time period of observation before and after IBS diagnosis is reasonably long. The study provides novel data on the proportion of IBS diagnoses made in the primary care setting, the rates of lower endoscopy and whether endoscopy preceded the IBS diagnosis, and the percentage of psychotropic medications prescribed before vs. after IBS diagnosis. While other studies have emphasized the importance of screening for celiac disease in patients with IBS,^{4–8} we are not aware of other large studies reporting the frequency with which practitioners have actually screened for celiac disease in an IBS population, or the proportion of IBS patients eventually diagnosed as having celiac disease. Finally, it has been suggested that diabetes may exacerbate IBS symptoms,^{34, 35} but the comparable prevalence of diabetes in IBS patients and controls in our study suggests that IBS-type symptoms were unlikely to be explained by diabetes in most cases.

Our study has limitations. First, the results may not be generalizable to practice settings that are different from KPNC. Although KPNC does not have guidelines for the management of IBS, it is possible that patterns of specialty encounters and testing differ between KPNC and other settings. Although the KPNC population is demographically representative of the general population of Northern California, it may not be representative of the U.S. as a whole, and it is an insured population that could differ from non-insured populations. Second, the study was retrospective and relied on queries of multiple databases. There was no standardized set of clinical criteria for arriving at a diagnosis of IBS. Rather, the results reflect the concept of IBS as used in clinical practice. IBS diagnoses were not confirmed by chart review or patient questionnaire. Third, the symptoms associated with the diagnosis for IBS patients in this study could not be ascertained. Thus, although IBS patients underwent more testing than their non-IBS counterparts, it is unclear how many IBS patients had “alarm symptoms” such as weight loss or rectal bleeding that may have warranted further

testing even if patients met clinical criteria for IBS. Fourth, we did not assess all comorbidities that have been reported to occur more frequently in IBS patients, including chronic fatigue,³² functional dyspepsia,^{36–39} somatization disorder,^{40–43} temporomandibular joint pain,^{32, 44} and dyspareunia.²⁸ We did not explore in detail the overlap between IBS and pelvic pain, including visits to gynecologists.^{45, 46} Although we observed high rates of diagnoses of anxiety and depression, we were not able to elucidate more specifically the types of anxiety or depression observed in IBS patients (*i.e.* generalized anxiety disorder, panic, single episode *vs.* recurrent major depression, dysthymia, etc.). Further delineation of the type of anxiety or depression, as well as ascertainment of the prevalence of personality disorders in IBS *vs.* non-IBS patients, could potentially guide the use of psychiatric treatments in patients with IBS and comorbidities. Fifth, we could not determine the indications for tests and treatments, including colorectal cancer screening and surveillance. Sixth, we did not gather information on general health care-seeking patterns for use as a covariate in our analyses, or total number of visits before and after IBS diagnosis. Specifically, we did not gather data on the total number of contacts per patient in the KPNC system, and it is possible that some of the differences between patients diagnosed by a gastroenterologist *vs.* non-gastroenterologist could reflect differences in the opportunities to have tests, diagnoses and treatments. Finally, no information was available on the use of non-prescription medication, including pro-biotic preparations.^{47–49}

In conclusion, in this large observational study, the majority of IBS diagnoses were made by generalists and usually without preceding lower endoscopy. Other chronic pain syndromes and psychiatric comorbidities were significantly more common in patients with IBS than in controls, and subsequent diagnosis of another gastrointestinal illness was rare. Patients with IBS demonstrated uniformly higher rates of medical testing than controls, as well as higher rates of all types of abdominal and pelvic surgical interventions. Psychiatric medications were used in a majority of IBS patients but usually before IBS diagnosis. Our study provides a detailed accounting of the diagnosis and management of IBS across the spectrum of care in a large population in general medical practice.

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Abbreviations

(IBS)	irritable bowel syndrome
(TCA)	tricyclic antidepressant
(SSRI)	selective serotonin reuptake inhibitor

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Table 1

Demographic characteristics of study subjects.

		IBS	Control	IBS vs. Control, P-value	IBS diagnosed by GI*	IBS diagnosed by non-GI*	IBS diagnosed by GI vs. non-GI, P-value
		N=141,295	N=141,294		N=14,640	N=102,187	
		53.0 (17.4)	53.0 (17.4)	NA	55.9 (16.0)	53.0 (17.5)	NA
	Mean Age (SD) in 2007, years						
	Gender						
	Women	104,047 (73.6%)	104,037 (73.6%)	NA	11,184 (76.4%)	74,552 (73.0%)	NA
	Men	37,237 (26.4%)	37,247 (26.4%) ^	NA	3,455 (23.6%)	27,626 (27.0%)	NA
	Race and Ethnicity						
	Caucasian	74,635 (52.8%)	60,882 (43.1%)	<0.0001	8,592 (58.7%)	53,383 (52.2%)	<0.0001
	African American	7,861 (5.6%)	8,405 (5.9%)		1,140 (7.8%)	5,526 (5.4%)	
	Asian	8,896 (6.3%)	12,471 (8.8%)		857 (5.9%)	6,730 (6.6%)	
	Hispanic or Latino	11,668 (8.3%)	9,904 (7.0%)		1,159 (7.9%)	8,542 (8.4%)	
	Native American	732 (0.5%)	557 (0.4%)		99 (0.7%)	507 (0.5%)	
	Mixed	4,973 (3.5%)	3,927 (2.8%)		586 (4.0%)	3,532 (3.5%)	
	Other	533 (0.4%)	660 (0.5%)		61 (0.4%)	398 (0.4%)	
	Unknown	31,997 (22.6%)	44,488 (31.5%)		2,146 (14.7%)	23,569 (23.1%)	
	Mean coverage period (SD), years	8.0 (3.4)	8.0 (3.4)	NA	8.5 (3.2)	8.0 (3.4)	NA
	Mean coverage period before IBS diagnosis coded (SD), years	4.1 (3.2)	NA		4.5 (3.1)	4.4 (3.2)	
	Mean coverage period after IBS diagnosis coded (SD), years	4.7 (3.3)	NA		4.7 (3.2)	4.4 (3.1)	

IBS: Irritable bowel syndrome; GI: gastroenterologist; SD: Standard deviation; NA: Not applicable

* Provider specialty known for 83% of IBS patients

Table 2

Laboratory and stool tests in IBS patients vs. controls.

	IBS	Control	IBS vs. Control, Odds Ratio (95%CI)	P-Value	IBS diagnosed by GI*	IBS diagnosed by non-GI*	IBS diagnosed by GI vs. non-GI, Odds Ratio (95%CI)	P-Value
<i>Blood Tests</i>								
<i>Any complete blood count</i>	134,688 (95.3%)	116,065 (82.1%)	4.43 (4.31–4.56)	<0.0001	14,438 (98.6%)	97,468 (95.4%)	3.46 (3.00–3.99)	<0.0001
<i>Any sedimentation rate</i>	67,961 (48.1%)	37,700 (26.7%)	2.55 (2.51–2.59)	<0.0001	8,992 (61.4%)	48,216 (47.2%)	1.78 (1.72–1.85)	<0.0001
<i>Any renal chemistry panel</i>	124,901 (88.4%)	102,687 (72.7%)	2.86 (2.81–2.92)	<0.0001	13,883 (94.8%)	90,838 (88.9%)	2.29 (2.12–2.47)	<0.0001
<i>Any glucose</i>	129,328 (91.5%)	109,556 (77.5%)	3.13 (3.06–3.20)	<0.0001	14,022 (95.8%)	93,964 (92.0%)	1.99 (1.83–2.16)	<0.0001
<i>Any liver function tests</i>	123,200 (87.2%)	94,276 (66.7%)	3.40 (3.33–3.46)	<0.0001	13,799 (94.3%)	89,589 (87.7%)	2.31 (2.15–2.48)	<0.0001
<i>Any thyroid function tests</i>	124,292 (88.0%)	101,011 (71.5%)	2.92 (2.86–2.97)	<0.0001	13,642 (93.2%)	90,417 (88.5%)	1.78 (1.66–1.90)	<0.0001
<i>Any celiac disease tests</i>	3,825 (2.7%)	366 (0.3%)	10.71 (9.62–11.93)	<0.0001	758 (5.2%)	2,713 (2.7%)	2.00 (1.84–2.17)	<0.0001
<i>Any H.pylori serology test</i>	1,487 (1.1%)	371 (0.3%)	4.04 (3.60–4.53)	<0.0001	257 (1.8%)	841 (0.8%)	2.15 (1.87–2.48)	<0.0001
<i>Stool Tests</i>								
<i>Any stool white cells test</i>	6,933 (4.9%)	1,995 (1.4%)	3.60 (3.43–3.79)	<0.0001	1,009 (6.9%)	4,690 (4.6%)	1.54 (1.43–1.65)	<0.0001
<i>Any fecal occult blood test</i>	29,517 (20.9%)	18,148 (12.8%)	1.79 (1.76–1.83)	<0.0001	3,869 (26.4%)	21,472 (21.0%)	1.35 (1.30–1.40)	<0.0001
<i>Any fecal fat test</i>	2,369 (1.7%)	265 (0.2%)	9.07 (7.99–10.31)	<0.0001	534 (3.6%)	1,504 (1.5%)	2.53 (2.29–2.80)	<0.0001
<i>Endoscopic Tests</i>								
<i>Sigmoidoscopy</i>	58,788 (41.6%)	31,411 (22.2%)	2.49 (2.45–2.53)	<0.0001	8,795 (60.1%)	41,607 (40.7%)	2.19 (2.11–2.27)	<0.0001
<i>Colonoscopy</i>	20,069 (14.2%)	8,746 (6.2%)	2.51 (2.44–2.58)	<0.0001	4,421 (30.2%)	13,134 (12.9%)	2.93 (2.82–3.05)	<0.0001
<i>Upper endoscopy</i>	19,942 (14.1%)	6,592 (4.7%)	3.36 (3.26–3.46)	<0.0001	4,635 (31.7%)	12,760 (12.5%)	3.25 (3.12–3.38)	<0.0001
<i>Endoscopic retrograde cholangiopancreatography</i>	784 (0.6%)	326 (0.2%)	2.41 (2.12–2.75)	<0.0001	183 (1.3%)	493 (0.5%)	2.61 (2.20–3.10)	<0.0001
<i>Radiologic Tests</i>								
<i>Abdominal X-ray</i>	30,249 (21.4%)	12,791 (9.1%)	2.74 (2.68–2.80)	<0.0001	4,596 (31.4%)	21,327 (20.9%)	1.73 (1.67–1.80)	<0.0001
<i>Barium enema</i>	23,960 (17.0%)	5,767 (4.1%)	4.80 (4.66–4.94)	<0.0001	3,625 (24.8%)	17,663 (17.3%)	1.57 (1.51–1.64)	<0.0001
<i>Computed tomography, pelvis</i>	27,900 (19.7%)	12,666 (9.0%)	2.50 (2.44–2.56)	<0.0001	4,659 (31.8%)	19,870 (19.4%)	1.93 (1.86–2.01)	<0.0001
<i>Computed tomography, abdomen</i>	32,206 (22.8%)	14,671 (10.4%)	2.55 (2.49–2.60)	<0.0001	5,397 (36.9%)	22,871 (22.4%)	2.02 (1.95–2.10)	<0.0001
<i>Magnetic resonance imaging, pelvis</i>	699 (0.5%)	449 (0.3%)	1.56 (1.38–1.76)	<0.0001	102 (0.7%)	497 (0.5%)	1.44 (1.16–1.78)	0.0009

	IBS	Control	IBS vs. Control, Odds Ratio (95%CI)	P-Value	IBS diagnosed by GI* %	IBS diagnosed by non-GI* %	IBS diagnosed by GI vs. non-GI, Odds Ratio (95%CI)	P-Value
<i>Magnetic resonance imaging, abdomen</i>	675 (0.5%)	317 (0.2%)	2.13 (1.87–2.44)	<0.0001	127 (0.9%)	476 (0.5%)	1.87 (1.54–2.28)	<0.0001
<i>Ultrasound, pelvis</i>	36,797 (26.0%)	21,194 (15.0%)	2.00 (1.96–2.03)	<0.0001	4,824 (33.0%)	26,454 (25.9%)	1.41 (1.36–1.46)	<0.0001
<i>Ultrasound, abdomen</i>	49,857 (35.3%)	22,440 (15.9%)	2.89 (2.84–2.94)	<0.0001	7,477 (51.1%)	35,461 (34.7%)	1.96 (1.90–2.03)	<0.0001
<i>Upper gastrointestinal series</i>	18,734 (13.3%)	5,334 (3.8%)	3.90 (3.78–4.02)	<0.0001	3,232 (22.1%)	13,166 (12.9%)	1.92 (1.83–2.00)	<0.0001
<i>Small bowel follow-through</i>	5,903 (4.2%)	1,065 (0.8%)	5.74 (5.38–6.13)	<0.0001	1,503 (10.3%)	3,650 (3.6%)	3.09 (2.90–3.29)	<0.0001

IBS: Irritable bowel syndrome; GI: gastroenterologist; SD: Standard deviation; NA: Not applicable

* Provider specialty known for 83% of IBS patients

Table 3

Comorbidities in IBS patients vs. controls.

	IBS	Control	IBS vs. Control, Odds Ratio (95%CI)	P-Value	IBS diagnosed by GI*	IBS diagnosed by non-GI*	IBS diagnosed by GI vs. non-GI, Odds Ratio (95%CI)	P-Value
<i>Other Pain Syndromes</i>								
<i>Migraine</i>	51,886 (36.7%)	28,380 (20.1%)	2.31 (2.27–2.35)	<0.0001	6,108 (41.7%)	37,534 (36.7%)	1.23 (1.19–1.28)	<0.0001
<i>Fibromyalgia</i>	8,288 (5.9%)	1,900 (1.3%)	4.57 (4.35–4.81)	<0.0001	1,179 (8.1%)	6,070 (5.9%)	1.39 (1.30–1.48)	<0.0001
<i>Chronic Pain</i>	26,467 (18.7%)	10,568 (7.5%)	2.85 (2.78–2.92)	<0.0001	3,781 (25.8%)	19,217 (18.8%)	1.50 (1.44–1.56)	<0.0001
<i>Psychiatric Comorbidities</i>								
<i>Anxiety</i>	51,452 (36.4%)	21,724 (15.4%)	3.15 (3.10–3.21)	<0.0001	5,745 (39.2%)	37,773 (37.0%)	1.10 (1.06–1.14)	<0.0001
<i>Depression</i>	55,117 (39.0%)	27,507 (19.5%)	2.65 (2.60–2.69)	<0.0001	6,308 (43.1%)	39,994 (39.1%)	1.18 (1.14–1.22)	<0.0001
<i>Bipolar</i>	4,585 (3.2%)	1,894 (1.3%)	2.47 (2.34–2.61)	<0.0001	594 (4.1%)	3,261 (3.2%)	1.28 (1.17–1.40)	<0.0001
<i>Psychosis</i>	662 (0.5%)	379 (0.3%)	1.75 (1.54–1.99)	<0.0001	106 (0.7%)	463 (0.5%)	1.60 (1.30–1.98)	<0.0001
<i>Other Medical Diagnoses</i>								
<i>Diabetes</i>	13,558 (9.6%)	14,730 (10.4%)	0.91 (0.89–0.93)	<0.0001	1,759 (12.0%)	9,643 (9.4%)	1.31 (1.24–1.38)	<0.0001
<i>Celiac Disease</i>	136 (0.1%)	26 (0.0%)	5.23 (3.44–7.96)	<0.0001	28 (0.2%)	100 (0.1%)	1.96 (1.29–2.98)	0.0014
<i>Crohn's Disease</i>	954 (0.7%)	221 (0.2%)	4.34 (3.75–5.02)	<0.0001	313 (2.1%)	499 (0.5%)	4.45 (3.86–5.13)	<0.0001
<i>Colitis</i>	2,723 (1.9%)	774 (0.5%)	3.57 (3.29–3.87)	<0.0001	685 (4.7%)	1,577 (1.5%)	3.13 (2.86–3.43)	<0.0001
<i>Inflammatory Bowel Disease</i>	1,560 (1.1%)	246 (0.2%)	6.40 (5.59–7.32)	<0.0001	373 (2.5%)	937 (0.9%)	2.83 (2.50–3.19)	<0.0001

IBS: Irritable bowel syndrome; GI: gastroenterologist; SD: Standard deviation; NA: Not applicable

* Provider specialty known for 83% of IBS patients

Table 4

Medications prescribed to IBS patients vs. controls.

	IBS	Control	IBS vs. Control, Odds Ratio (95%CI)	P-Value	IBS diagnosed by GI*	IBS diagnosed by non-GI*	IBS diagnosed by GI vs. non-GI, Odds Ratio (95%CI)	P-Value
<i>IBS Prescriptions</i>								
<i>Antispasmodics</i>	80,205 (56.8%)	13,112 (9.3%)	12.83 (12.57–13.10)	<0.0001	9,032 (61.7%)	58,106 (56.9%)	1.22 (1.18–1.27)	<0.0001
<i>Prescription Antidiarrheal</i>	21,573 (15.3%)	6,767 (4.8%)	3.58 (3.48–3.69)	<0.0001	3,163 (21.6%)	15,080 (14.8%)	1.59 (1.52–1.66)	<0.0001
<i>Prescription Laxative</i>	4,122 (2.9%)	2,736 (1.9%)	1.52 (1.45–1.60)	<0.0001	698 (4.8%)	2,733 (2.7%)	1.82 (1.67–1.98)	<0.0001
<i>Prescription Fiber</i>	125 (0.1%)	94 (0.1%)	1.33 (1.02–1.74)	0.0361	14 (0.1%)	87 (0.1%)	1.12 (0.64–1.98)	0.6863
<i>Alosetron</i>	133 (0.1%)	2 (0.0%)	66.56 (16.47–268.9)	<0.0001	34 (0.2%)	92 (0.1%)	2.58 (1.74–3.83)	<0.0001
<i>Tegaserod</i>	748 (0.5%)	21 (0.0%)	35.80 (23.20–55.24)	<0.0001	178 (1.2%)	508 (0.5%)	2.46 (2.08–2.92)	<0.0001
<i>Psychiatric medications</i>								
<i>Anxiolytics</i>	62,844 (44.5%)	37,863 (26.8%)	2.19 (2.15–2.22)	<0.0001	7,927 (54.1%)	44,991 (44.0%)	1.50 (1.45–1.55)	<0.0001
<i>Any Antidepressant</i>	77,563 (54.9%)	41,446 (29.3%)	2.93 (2.89–2.98)	<0.0001	9,477 (64.7%)	56,005 (54.8%)	1.51 (1.46–1.57)	<0.0001
<i>Tricyclic Antidepressant</i>	46,656 (33.0%)	19,551 (13.8%)	3.07 (3.01–3.13)	<0.0001	6,473 (44.2%)	33,312 (32.6%)	1.64 (1.58–1.70)	<0.0001
<i>Selective Serotonin Reuptake Inhibitor</i>	50,714 (35.9%)	25,050 (17.7%)	2.60 (2.55–2.64)	<0.0001	6,028 (41.2%)	36,741 (36.0%)	1.25 (1.20–1.29)	<0.0001
<i>Other Antidepressant</i>	37,439 (26.5%)	18,371 (13.0%)	2.41 (2.37–2.46)	<0.0001	4,913 (33.6%)	26,914 (26.3%)	1.41 (1.36–1.47)	<0.0001

IBS: Irritable bowel syndrome; GI: gastroenterologist; SD: Standard deviation; NA: Not applicable

* Provider specialty known for 83% of IBS patients

Table 5

Operations in IBS patients vs. controls.

	IBS	Control	IBS vs. Control, Odds Ratio (95%CI)	P-Value	IBS diagnosed by GI*	IBS diagnosed by non-GI*	IBS diagnosed by GI vs. non-GI, Odds Ratio (95%CI)	P-Value
<i>Esophageal</i>	221 (0.2%)	172 (0.1%)	1.29 (1.05–1.57)	0.0134	52 (0.4%)	130 (0.1%)	2.80 (2.03–3.86)	<0.0001
<i>Gastric</i>	1,262 (0.9%)	734 (0.5%)	1.73 (1.58–1.89)	<0.0001	257 (1.8%)	809 (0.8%)	2.24 (1.94–2.58)	<0.0001
<i>Rectal</i>	1,936 (1.4%)	1,083 (0.8%)	1.80 (1.67–1.94)	<0.0001	286 (2.0%)	1,354 (1.3%)	1.48 (1.30–1.69)	<0.0001
<i>Intestinal</i>	6,921 (4.9%)	3,864 (2.7%)	1.83 (1.76–1.91)	<0.0001	1,134 (7.7%)	4,734 (4.6%)	1.73 (1.62–1.85)	<0.0001
<i>Abdominal</i>	3,147 (2.2%)	1,376 (1.0%)	2.32 (2.17–2.47)	<0.0001	505 (3.4%)	2,057 (2.0%)	1.74 (1.58–1.92)	<0.0001
<i>Biliary</i>	8,266 (5.9%)	4,094 (2.9%)	2.08 (2.00–2.16)	<0.0001	1,190 (8.1%)	5,825 (5.7%)	1.46 (1.37–1.56)	<0.0001
<i>Gynecologic</i>	12,154 (8.6%)	8,489 (6.0%)	1.47 (1.43–1.52)	<0.0001	1,547 (10.6%)	8,543 (8.4%)	1.30 (1.22–1.37)	<0.0001

IBS: Irritable bowel syndrome; GI: gastroenterologist; SD: Standard deviation; NA: Not applicable

* Provider specialty known for 83% of IBS patients