



Symptom burden and consulting behavior in patients with overlapping functional disorders in the US population

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Abstract

Background: Regulatory and treatment guidelines focus on individual conditions, yet clinicians often see patients with overlapping conditions.

Objective: This cross-sectional survey study assesses the impact of overlapping functional dyspepsia (FD), gastroesophageal reflux disease (GERD), irritable bowel syndrome with constipation (IBS-C), and chronic idiopathic constipation (CIC) on symptom burden and consulting behavior.

Methods: Survey participants met Rome III criteria for FD, IBS-C, and/or CIC, and/or reported GERD; participants answered questions about symptom frequency and bothersomeness, work and productivity, and consulting behavior.

Results: Of 2641 respondents, 1592 (60.3%) had one condition; 832 (31.5%) had two; and 217 (8.2%) had three; 57.3% of 1690 FD, 54.6% of 1337 GERD, 82.6% of 328 IBS-C, and 62.5% of 552 CIC respondents had condition overlap. Overall GI symptoms were very/extremely bothersome in 28.6% of single-condition respondents, 50.7% of two-condition, and 69.6% of three-condition respondents ($p < 0.001$, chi square). Symptom frequency and productivity losses both increased with condition overlap. Over 12 months, 43.7% of single-condition, 49.9% of two-condition, and 66.5% of three-condition respondents consulted a physician about GI symptoms ($p < 0.001$, chi square).

Conclusion: Functional GI disorders frequently overlap with each other and with GERD. Condition overlap is associated with greater symptom burden and increased physician consultations.

Keywords

Irritable bowel syndrome with constipation, IBS-C, IBS, chronic idiopathic constipation, gastroesophageal reflux disease, GERD, functional dyspepsia, FD

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Introduction

Constipation-predominant irritable bowel syndrome (IBS-C) and chronic idiopathic constipation (CIC, also called functional constipation) are functional bowel disorders, with diagnoses generally based on assessing patient-reported symptoms and excluding structural disease.¹ IBS is characterized by recurring abdominal pain or discomfort that is associated with altered bowel habits; the disease is subtyped by the predominant bowel pattern: constipation, diarrhea, mixed, or unsubtyped.¹ The sponsors of this study market a drug that is approved in North America for the treatment of IBS-C and CIC in adults and in Europe for the treatment of IBS-C in adults. The distinction between IBS-C and CIC is not always clear in clinical practice. While the well-established Rome III diagnostic criteria

maintain a clear distinction between IBS-C and CIC,¹ recent studies have shown that many CIC patients experience abdominal symptoms, that patients often migrate from one diagnosis to another over time, and that the presence of abdominal symptoms in CIC is associated with greater symptom and disease burden, approaching that of IBS-C.^{2–6}

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IBS and CIC patients also often experience symptoms associated with functional dyspepsia (FD) and gastroesophageal reflux disease (GERD).⁷⁻⁹ Beyond symptom overlap, patients often have overlapping diagnoses of IBS, FD, and/or GERD.¹⁰⁻¹³ When multiple disorders are present, the symptom profile and severity may be altered, creating challenges for treating patients and assessing treatments.

Extending existing research, the aims of this cross-sectional population-based study were to evaluate the extent of overlap among four disorders (IBS-C, CIC, FD, and GERD); evaluate patient symptom experience; and assess the impact of overlap on symptom burden and consulting behavior.

Methods

A United States (US) Web-based survey, with participants randomly drawn from the Universal Survey Opinion site consumer panel, was conducted in 2010. A group of 37,500 adults were randomly drawn from >550,000 members of the consumer panel recruited via various media (e.g. market research surveys, email lists, social networking websites, and banner ads). Sampling was stratified, based on age, sex, and ethnicity, to be representative of the demographic composition of the 2009 Current Population Survey (CPS) estimate of the US Census Bureau.¹⁴

Email invitations included a link to a 21-item screening questionnaire. Participants were screened for eligibility based on 1) absence of conflicts of interest (i.e. respondent or household member employed by advertising, marketing research, health care, or pharmaceutical companies); 2) ≥ 18 years of age; 3) absence of diagnosis of an organic gut condition (e.g. inflammatory bowel disease, ulcer or significant inflammation in the gastrointestinal (GI) tract, GI cancer); 4) having GI symptoms in the past 12 months; and 5) meeting criteria for IBS-C, CIC, FD, and/or GERD.⁴ The screening questions for IBS-C, CIC, and/or FD used in this analysis are based on the Rome III diagnostic criteria for these conditions.¹ Per Rome III criteria, IBS-C and CIC are mutually exclusive diagnoses.¹ GERD was defined as heartburn or regurgitation in the absence of treatment \geq twice/week according to the Montreal definition.¹⁵

Respondents who met the eligibility criteria completed a 31-item questionnaire, including assessments of overall and specific symptom experience (Supplementary materials). Respondents were asked to rate the frequency and bothersomeness of 16 GI symptoms: abdominal discomfort, abdominal pain, bloating, constipation, diarrhea, gas pain, hard/lumpy stool, inability to have a bowel movement (BM), incompletely emptying rectum, pellet-like stools, rectal

pain during BM, stomach cramping, straining during BM, sudden urges to have a BM, heartburn/acid reflux, and postprandial distress (feeling full too quickly).⁴ Respondents were also asked to report health-care-seeking behavior and impact of symptoms on productivity.

Overall global and individual symptom bothersomeness was reported on a five-point Likert scale (“Not at all,” “A little,” “Somewhat,” “Very,” and “Extremely”). Frequency means were calculated using the number of days corresponding to the available choices as follows: every day (365 days), four to six days per week (260 days), two to three days per week (130 days), one day a week (52 days), one to two days a month (18 days), five to ten days per year (7.5 days), and <five days (2.5 days) per year.⁴

Analysis

Demographic data from the survey did not align completely with the 2009 US adult population;¹⁴ there was a small under-representation of men and the elderly (≥ 65 years of age). Therefore, the demographic distribution from the full sample of 10,030 respondents was adjusted to match the 2009 CPS for age and sex¹⁴ by applying a weight, or constant, to each respondent and the answers given.⁴ All findings reported in this paper are based on the weighted survey data.

Binary data were summarized using the percentage of respondents with the event. Continuous data were reported using the sample size and mean.

To analyze the effect of overlapping conditions, respondents were grouped into 11 mutually exclusive diagnostic categories of those meeting the diagnostic criteria for a single condition (IBS-C, CIC, GERD, or FD), two of the conditions, and three of the conditions. No respondents could meet the criteria for all four conditions, given the diagnostic distinction between IBS-C and CIC.¹

The mean frequencies of individual symptoms were compared among the 11 independent diagnostic groups using a one-way analysis of variance (ANOVA). Statistical significance was verified using the post-hoc Tukey honest significant difference (HSD) test to minimize the opportunity for type 1 errors. The proportions of respondents reporting very or extremely bothersome symptoms were compared using chi square tests. Overall significance was tested at the $p < 0.05$ level. Statistical testing was conducted using SPSS version 22 (IBM Corp., Armonk, NY).

To identify patterns in responses via data visualization, a heat-map technique was used, force-ranking the symptom frequency and the proportion reporting very/extremely bothersome symptoms relative to the medians for each symptom.

Table 1. Patient demographics

	Respondents meeting the criteria for one or more of the conditions: GERD, FD, IBS-C, CIC (N = 2641)
Age (mean)	45.2
18-39 (%)	40.5%
40-49 (%)	21.3%
50-64 (%)	23.4%
65+ (%)	14.8%
Gender	
Male (%)	42.8%
Female (%)	57.2%
Race	
White (%)	82.0%
Black/African American (%)	9.2%
Asian/Pacific Islander (%)	3.3%
Native American (%)	0.6%
Other (%)	4.9%
Sought physician care for GI symptoms in past year (%)	47.3%

GI: gastrointestinal; CIC: chronic idiopathic constipation; IBS-C: constipation-predominant irritable bowel syndrome; FD: functional dyspepsia; GERD: gastroesophageal reflux disease.

Results

Of 10,030 adults who responded and completed the screening questionnaire, 2641 (26.3%) met the eligibility criteria, including the Rome III criteria for IBS-C, CIC, and/or FD, and/or the GERD definition. Among the 2641 meeting the study criteria, the mean age was 45.2; 57.2% were female, and 82.0% were white (Table 1). Less than half (47.3%) had sought physician care for GI symptoms in the past year.

Of the 2641 respondents meeting the criteria for at least one condition, 1049 (39.7%) had condition overlap: 832 (31.5%) had two conditions, and 217 (8.2%) had three conditions (Figure 1). Of the 328 respondents meeting the criteria for IBS-C, 271 (82.6%) had condition overlap, as did 345 (62.5%) of the 552 CIC respondents, 730 (54.6%) of the 1337 GERD respondents, and 969 (57.3%) of the 1690 FD respondents.

Symptom burden

Frequencies of the 16 individual symptoms are presented in Table 2. For 14 of the 16 symptoms, the frequency was significantly higher in the IBS-C-GERD-FD overlap group compared with each single-condition group. For 12 of the 16 symptoms, the frequency was

significantly higher in the CIC-GERD-FD overlap group compared with the respondents who had CIC, GERD, or FD as a single condition. In general, symptom frequencies were higher in the three-condition groups compared with the two-condition groups and higher in the two-condition groups compared with the single-condition groups; however, these differences did not all reach statistical significance.

Frequency comparisons for the principal symptoms of the functional disorders are presented in Figure 2. Among IBS-C respondents, mean frequencies of abdominal pain, abdominal discomfort, and bloating were more than twice as high in IBS-C-GERD-FD respondents compared with IBS-C-only respondents ($p < 0.05$ each pair) (Figure 2(a)). These abdominal symptoms were most frequent in the three-condition group, and more frequent in the two-condition groups compared with IBS-C only; not all of these differences reached statistical significance. For constipation and straining in IBS-C respondents, though the differences were not as great as those seen in the abdominal symptoms, the mean frequencies were significantly higher in IBS-C-GERD-FD respondents compared with IBS-C-only respondents ($p < 0.05$ each pair). Straining was significantly higher in IBS-C-GERD-FD respondents compared with IBS-C-FD.

Among the CIC respondents, abdominal pain, abdominal discomfort, and bloating in CIC-GERD-FD respondents were more than three-fold more frequent than in CIC-only ($p < 0.05$ each pair), more than two-fold than in CIC-GERD ($p < 0.05$ each pair), and more frequent than in CIC-FD respondents ($p < 0.05$ each pair) (Figure 2(b)). Constipation and straining also had significantly higher frequencies in CIC-GERD-FD respondents compared with CIC-only respondents ($p < 0.05$ each pair). Constipation was significantly more frequent in CIC-GERD-FD compared with CIC-FD respondents ($p < 0.05$).

Postprandial distress was experienced a mean of 121 days per year in IBS-C-GERD-FD respondents compared with 54 days per year in FD-only respondents ($p < 0.05$) (Figure 2(c)). The frequency of postprandial distress was significantly higher in all FD-overlap groups, with the exception of the FD-CIC overlap group, compared with FD only.

Heartburn was experienced a mean of 155 days per year in GERD-only respondents, compared with 175 days in GERD-FD ($p < 0.05$) and 189 days in IBS-C-GERD-FD respondents ($p < 0.05$) (Table 2). Compared with the frequency in GERD-only, the frequency of heartburn appears slightly higher in CIC-GERD, IBS-C-GERD, and CIC-GERD-FD respondents, but the differences were not statistically significant.

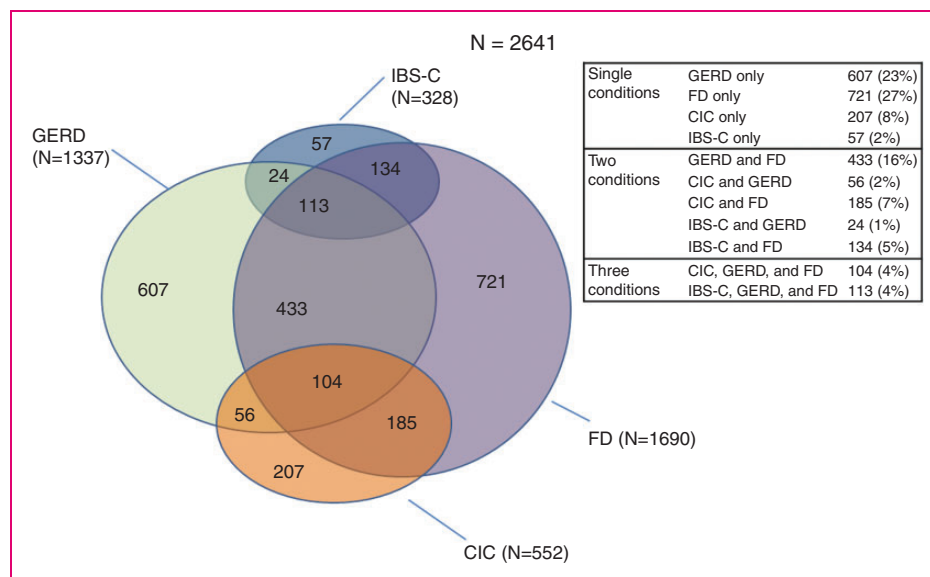


Figure 1. Overlap among common symptomatic gastrointestinal disorders. Figure not to scale.

CIC: chronic idiopathic constipation; IBS-C: constipation-predominant irritable bowel syndrome; FD: functional dyspepsia; GERD: gastroesophageal reflux disease.

Diarrhea was most frequent and most bothersome in the FD-GERD overlap group and, in general, more frequent and bothersome in respondents with FD.

Symptom bothersomeness

Overall symptom bothersomeness increased with the number of conditions: 28.6% of single-condition respondents, 50.7% of two-condition, and 69.6% of three-condition respondents reported that, overall, GI symptoms were very or extremely bothersome ($p < 0.001$, chi square test). Overall symptoms were very/extremely bothersome in 22.5% of IBS-C-only respondents and in 28.3% of GERD-only respondents. By comparison, 65.7% of IBS-C-GERD and 73.5% of IBS-C-GERD-FD respondents had very/extremely bothersome symptoms overall. The pattern of increasing bothersomeness with increasing overlap was similar for the other conditions (Figure 3).

The bothersomeness of individual symptoms by condition was also analyzed by the percentage of respondents reporting symptoms were very/extremely bothersome (Table 3). For the majority of symptoms, the highest percentages were in IBS-C-GERD-FD respondents, with CIC-GERD-FD respondents also having comparatively high percentages. For straining, hard/lumpy stool, and pellet-like stool, the percentages in IBS-C-GERD respondents were similar to those in IBS-C-GERD-FD respondents and higher than in IBS-C-FD respondents. For abdominal symptoms and constipation, the percentages were higher in IBS-C-FD compared with IBS-C-GERD respondents.

The percentage of patients reporting diarrhea to be very/extremely bothersome was highest (47.2%) in GERD-FD respondents. For BM urgency, the percentage was highest (46.3%) in IBS-C-GERD-FD respondents.

The percentage reporting heartburn or acid reflux to be very or extremely bothersome was highest (76.1%) in IBS-C-GERD-FD respondents, followed by 73.3% in CIC-GERD-FD, 68.8% in GERD-FD, and 61.1% in GERD-only respondents. For postprandial distress, the percentage was highest (37.0%) in IBS-C-GERD-FD, followed by 27.0% in FD-GERD respondents.

Ability to work

Among respondents who were working or attending school (68% of the study population), GI symptoms interfered with productivity a mean of 6.0 days per month in those with three conditions, 3.9 days in those with two conditions, and 2.3 days in those with a single condition ($p < 0.05$, all pairs). GI symptoms led to a mean of 1.4 missed days of school or work per month in those with three conditions, 0.8 days in those with two conditions, and 0.4 days in those with a single condition ($p < 0.05$, all pairs).

Consulting behavior

Of those with three overlapping conditions, 65.9% had consulted a physician in the previous year for their symptoms, compared with 49.6% of those with two overlapping conditions, and 43.5% of those with a

Table 2. Symptom Frequency: Mean days per year

Colors depict force ranking of frequencies relative to the median for each symptom											
	Lowest		median		highest						
	SINGLE CONDITIONS				TWO CONDITIONS					THREE CONDITIONS	
	GERD ONLY	FD ONLY	CIC ONLY	IBS-C ONLY	FD & GERD	CIC & GERD	CIC & FD	IBS-C & GERD	IBS-C & FD	CIC & FD & GERD	IBS-C & FD & GERD
N (total = 2641)	607	721	207	57	433	56	185	24	134	104	113
Gas pain	59.3	72.4	46.7	79.9	122.9 ^a	66.7	85.0	111.8	116.0	146.0 ^b	193.2 ^{b,c,d}
Abdominal pain	31.2	57.4	19.4	56.9	90.4 ^a	38.0	72.5	86.3	95.9	133.4 ^{b,f}	149.2 ^{b,c}
Abdominal discomfort	34.8	70.3	34.4	59.6	106.5 ^a	43.7	88.1	113.1	120.3 ^a	144.4 ^{b,g}	167.5 ^{b,f}
Stomach cramping	25.7	49.6	19.1	42.4	79 ^a	37.2	60.2	86.9	82.5	100.3 ^b	124.6 ^{b,f}
Bloating	37.9	65.1	34.7	82.7	105.8 ^a	52.2	88.5	123.9	135.4 ^a	129.1 ^e	194.9 ^{b,d,f}
Constipation	24.1	37.4	96.9	139.0	65.6 ^a	117.0	110.4	137.5	164.2	145.8 ^e	192.2 ^{b,d,g}
Straining during BM	33.6	44.4	92.7	111.8	71.6 ^a	119.7	113.6	137.8	122.5	141.5 ^e	161.0 ^b
Hard/lumpy stool	25.8	34	81.2	108.6	56.2 ^a	118.7	88.4	153.5	114.7	139.4 ^e	150.8 ^b
Pellet-like stools	17.9	22.5	48.5	79.4	42.3 ^a	76.4	56.6	105.5	61.6	70.9	91.6
Inability to have BM	11.7	24	43.3	74.9	33.6	44.2	73.6 ^a	77.0	98.8	87.4 ^e	117.5 ^{b,f}
Rectal pain during BM	11.3	21	33.7	41.0	44.6 ^a	46.0	55.1	69.2	62.8	67.4 ^e	99.2 ^{b,d,f}
Incomplete evacuation	26.7	40.3	65.4	73.7	65.6 ^a	57.8	87.6	106.7	104.8	110.3 ^e	132.6 ^{b,f}
Diarrhea	30.7	50.6	9.3	5.1	70.9 ^a	21.5	19.4	11.4	16.3	46.0	36.0
BM Urgency	35.1	52.0	20.3	25.5	82.2 ^a	28.6	47.1	42.9	61.2	74.5	86.5 ^b
Heartburn/ acid reflux	155.3	28.9	22.4	15.4	175.0 ^a	160.1	31.9	163.1	26.5	169.5	188.8 ^b
Postprandial distress	16.4	53.5	5.1	17.6	93.5 ^a	11.1	65.9	26.3	89.2 ^a	88.8 ^b	121.0 ^b

Note: Not all statistically significant comparisons are noted.

- The frequency in the 2-condition overlap group is significantly higher than in each of the 2 individual single conditions.
- The frequency in the 3-condition overlap group is significantly higher than in each of the 4 single conditions
- The frequency in the 3-condition overlap group is significantly higher than in each of the 5 double conditions
- The frequency in the 3-condition overlap group is significantly higher than in the other triple condition: CIC and FD and GERD
- The frequency in the 3-condition overlap group is significantly higher than in the single conditions, with the exception of IBS-C
- The frequency in the 3-condition overlap group is significantly higher than in the double conditions, with the exception of IBS-C & GERD
- The frequency in the 3-condition overlap group is significantly higher than in the double conditions not involving IBS-C, i.e. FD-GERD, CIC-GERD, and CIC-FD overlap

single condition ($p < 0.001$, chi square test). Following those with three conditions, respondents with GERD-FD overlap, GERD only, and CIC-GERD overlap were the most likely to have sought care (Figure 4). Respondents with CIC only, CIC-FD overlap, and FD only were the least likely to have sought physician care. The rate of consultation appeared higher in the IBS-C-only group, compared with the IBS-C-GERD and IBS-C-FD overlap groups.

Discussion

The results of this cross-sectional, population-based survey study show that GERD and functional GI disorders defined by Rome criteria can frequently overlap in individual patients. Among the 2641 respondents with at least one of the four conditions assessed—IBS-C, CIC, FD, and GERD—approximately 40% had overlapping conditions. Of the four conditions, IBS-C respondents experienced the highest rate of overlap, with 83% having IBS-C in combination with GERD and/or FD. The results of our study show that patients with overlapping conditions have more days with symptoms and report more bothersome symptoms compared with

patients without overlapping conditions. As the number of overlapping conditions increases, symptom frequency and bothersomeness increase and reduced productivity and absences from work become more frequent. Patients with overlapping disorders are also more likely to consult a doctor for their symptoms.

Clinical trials and prescribing information are focused on disease-specific outcomes, and current treatment guidelines offer disease-specific management pathways, offering little guidance to clinicians managing patients with overlapping disorders. In clinical practice, however, the treating physician is likely to be confronted with patients who have features of more than one disorder. The effectiveness of available treatments in these patients, with regard to specific symptoms and quality of life, may be different from that reported in the regulatory studies.

The increased frequency and bothersomeness of symptoms seen in overlapping conditions suggest that such overlap may confound the results of clinical trials. Clinical trial results for a single condition may be affected by the exclusion of treatments for overlapping conditions (e.g. proton pump inhibitors). Also, symptom-specific assessments may be affected.

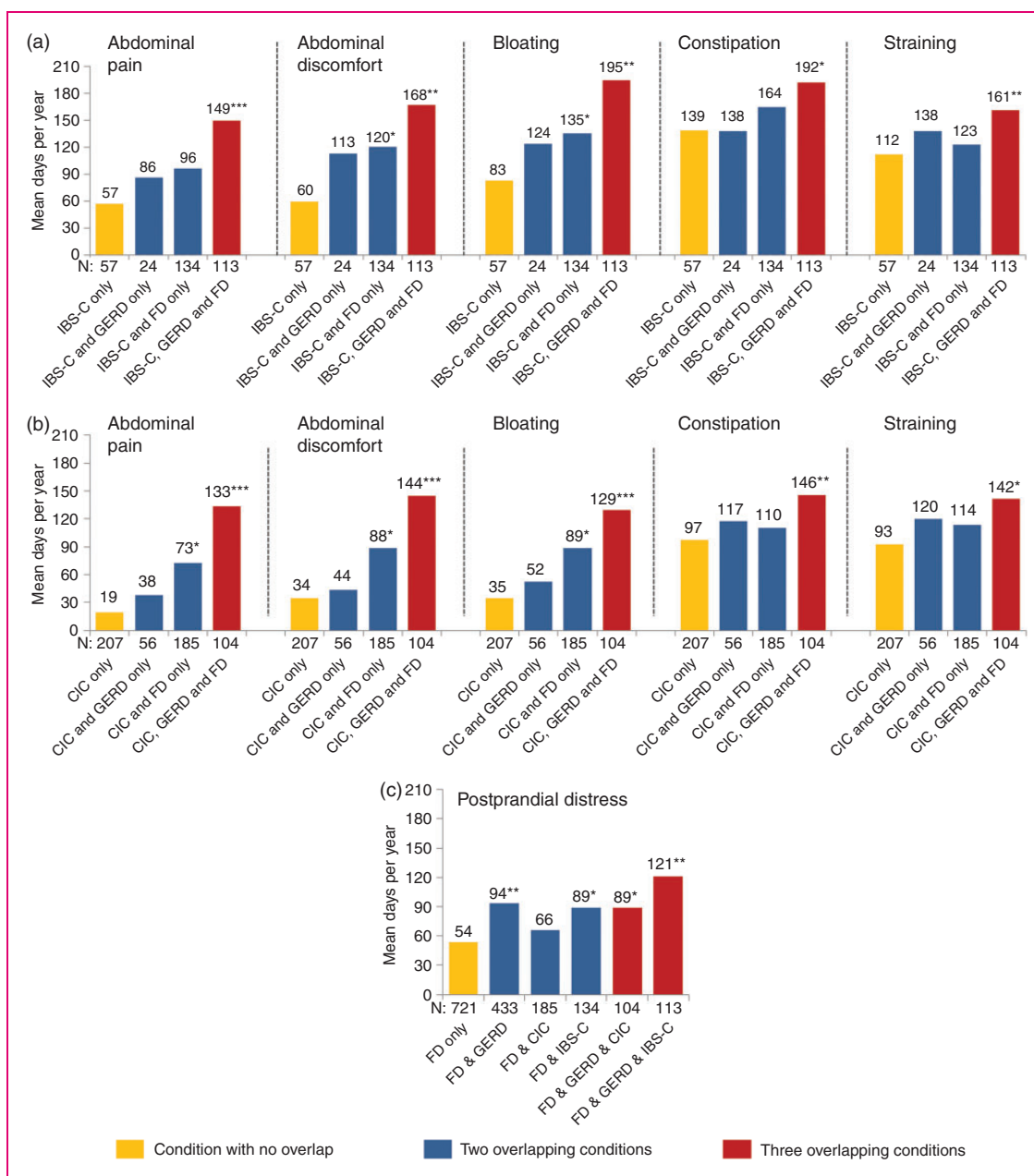


Figure 2. (a) Frequency of symptoms experienced by IBS-C respondents, with and without overlapping condition. *vs. IBS-C only, $p < 0.05$. **vs. IBS-C only and vs. IBS-C-FD overlap, $p < 0.05$. ***vs. IBS-C only, vs. IBS-C-FD overlap, and vs. IBS-C-GERD overlap, $p < 0.05$. (b) Frequency of symptoms experienced by CIC respondents, with and without overlapping conditions. *vs. CIC only, $p < 0.05$. **vs. CIC only and vs. CIC-FD overlap, $p < 0.05$. ***vs. CIC only, vs. CIC-FD overlap, and vs. CIC-GERD, $p < 0.05$. (c) Frequency of postprandial distress experienced by FD respondents, with and without overlapping conditions. *vs. FD only, $p < 0.05$. **vs. FD only and vs. CIC-FD overlap, $p < 0.05$. CIC: chronic idiopathic constipation; IBS-C: constipation-predominant irritable bowel syndrome; FD: functional dyspepsia; GERD: gastroesophageal reflux disease.

Recent guidance from the Food and Drug Administration (FDA) for IBS trials requires adequate measure of benefit be used to capture the critical signs and symptoms of IBS and recommends that primary endpoints measure effects on abnormal defecation and

abdominal pain.¹⁶ Yet, the patient's experience of pain related to IBS may be compounded by pain related to FD, more so if both FD and GERD are present. Similarly, an improvement in constipation in IBS-C may not be associated with improvement in how a

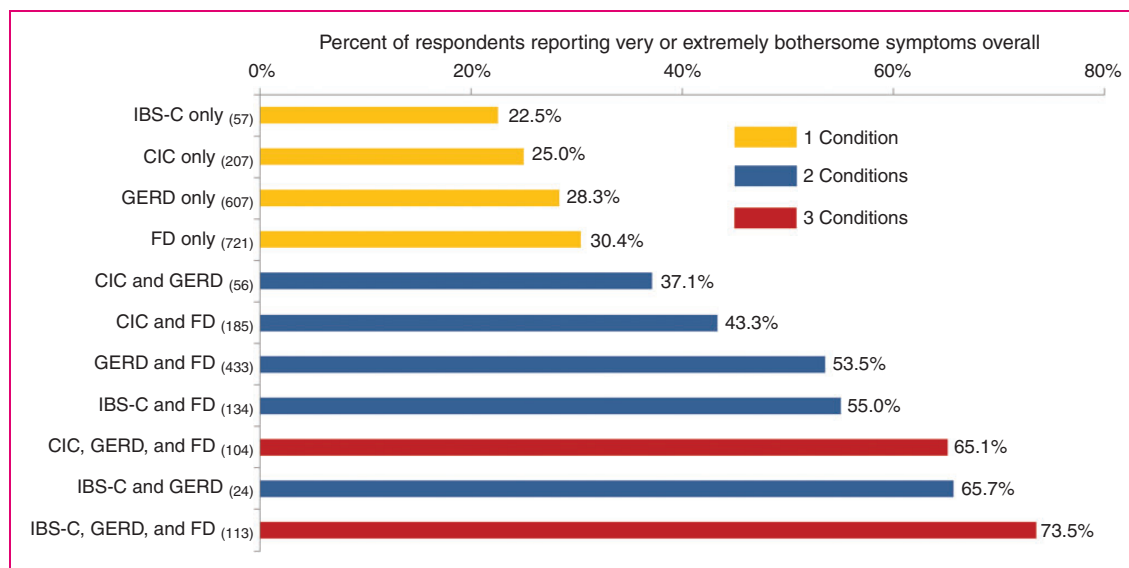


Figure 3. Overall symptom bothersomeness: percentage of respondents reporting very or extremely bothersome symptoms, by condition in rank order. $P < 0.001$, chi square test.

CIC: chronic idiopathic constipation; IBS-C: constipation-predominant irritable bowel syndrome; FD: functional dyspepsia; GERD: gastroesophageal reflux disease.

patient functions or feels if concomitant FD and GERD are present.

A substantial proportion of study respondents had not seen a physician for GI symptoms in the preceding year. Respondents with three overlapping disorders were the most likely to have consulted a physician. With the exception of the IBS-C-GERD overlap group, the respondents with GERD, as a single condition or in combination with the other conditions, had the highest percentages of care seekers. This may be due to greater awareness of GERD and its complications in the general population and deserves further study.

These results contribute to the growing body of knowledge regarding the drivers of consulting behavior among patients with functional GI disorders. In a study based in northern England, only 17% of IBS patients consulted physicians over a 10-year period; factors found to influence IBS consultation were *Helicobacter pylori* infection and dyspepsia-related consultation.¹⁷ In an Australian study, only 56% of dyspeptic patients had ever consulted a physician for their dyspepsia symptoms.¹⁸ Recent studies, including Heidelbaugh and colleagues' evaluation of the study population analyzed here, have reported that CIC patients with abdominal symptoms are more likely to consult physicians than those without.^{4,19} Heidelbaugh et al. also reported that bothersomeness and consulting rates were higher in IBS-C compared with CIC.⁴

There have been a number of studies that have evaluated the overlap between individual syndromes.

A recent meta-analysis of gastroesophageal reflux-type symptoms (GERS) in individuals with IBS concluded that the prevalence of GERS is approximately four times higher in individuals with IBS than in individuals without IBS, though prevalence assessments vary considerably with definitions of the disorders.²⁰ A meta-analysis of studies published on the overlap of IBS and dyspepsia also found that the prevalence of overlap varied with the diagnostic definitions used for the disorder, but concluded that individuals with dyspepsia have an eight-fold increase in prevalence of IBS as compared with the general population.¹⁰ However, there have been no prior studies that have evaluated multiple overlapping disorders in a single population and analyzed the symptom experience across these overlapping disorders.

A strength of our study is that it is based on a large cohort of patients identified in the community and thus provides an assessment of functional disorders and GERD in a general US population. Furthermore, we used Rome III criteria to establish symptom-based diagnoses and adjusted the data to provide a representative sample of the US population.

This study is limited by its focus on four conditions. Most notably, only one of the IBS subtypes is included. The focus of the study was shaped by the study sponsors' interest in CIC and IBS-C. While providing insights into the symptom burden of overlapping conditions, further research would be necessary to address the impact of overlap with the other IBS subtypes and other functional GI disorders.

Table 3. Symptoms experienced as very or extremely bothersome (percentage of respondents)

Colors depict force ranking of frequencies relative to the median for each symptom lowest median highest

	SINGLE CONDITIONS				TWO CONDITIONS					THREE CONDITIONS	
	GERD ONLY	FD ONLY	CIC ONLY	IBS-C ONLY	FD & GERD	CIC & GERD	CIC & FD	IBS-C & GERD	IBS-C & FD	CIC & FD & GERD	IBS-C & FD & GERD
N (total = 2641)	607	721	207	57	433	56	185	24	134	104	113
Gas pain*	28.9%	35.7%	23.6%	46.3%	52.4%	27.2%	50.7%	44.5%	54.1%	64.4%	77.1%
Abdominal pain*	21.9%	37.0%	17.7%	40.1%	45.3%	16.6%	50.2%	37.4%	58.1%	57.9%	65.8%
Abdominal discomfort*	18.8%	36.9%	20.1%	38.3%	44.3%	24.6%	51.9%	41.1%	60.7%	52.4%	67.8%
Stomach Cramping*	19.2%	34.3%	16.4%	36.3%	43.2%	16.7%	49.2%	40.6%	53.6%	55.2%	57.2%
Bloating*	15.5%	32.1%	16.1%	36.4%	40.6%	26.9%	43.5%	37.1%	53.4%	47.9%	72.8%
Constipation*	18.6%	26.3%	48.6%	53.8%	34.3%	53.6%	56.0%	54.9%	73.8%	64.4%	82.0%
Straining during BM*	21.0%	24.5%	40.9%	47.0%	35.9%	53.8%	51.2%	69.9%	62.2%	56.3%	74.7%
Hard/lumpy stool*	11.9%	14.7%	33.2%	31.9%	24.9%	49.8%	35.3%	55.7%	47.9%	44.3%	58.3%
Pellet-like stools*	6.5%	9.5%	18.4%	29.2%	15.4%	24.3%	20.7%	44.8%	28.6%	29.3%	42.0%
Inability to have BM*	10.6%	17.4%	30.4%	46.0%	24.1%	37.3%	51.6%	45.2%	55.1%	45.7%	62.5%
Rectal pain during BM*	10.7%	16.5%	22.2%	32.2%	28.2%	41.0%	40.0%	34.1%	41.5%	40.2%	56.0%
Incomplete evacuation*	14.6%	20.6%	33.1%	36.6%	30.0%	29.0%	43.4%	48.5%	48.6%	47.5%	58.0%
Diarrhea*	23.7%	39.1%	17.2%	19.7%	47.2%	15.3%	31.3%	20.2%	25.2%	35.9%	33.5%
BM Urgency*	20.3%	31.8%	12.4%	13.2%	39.4%	15.0%	29.1%	35.7%	31.4%	41.9%	46.3%
Heartburn/Acid Reflux*	61.1%	22.5%	16.3%	15.4%	68.8%	58.4%	20.2%	48.8%	16.6%	73.3%	76.1%
Postprandial distress*	5.9%	16.0%	2.3%	4.4%	27.0%	9.1%	23.8%	10.2%	22.8%	20.9%	37.0%

*P<0.001, chi-square test

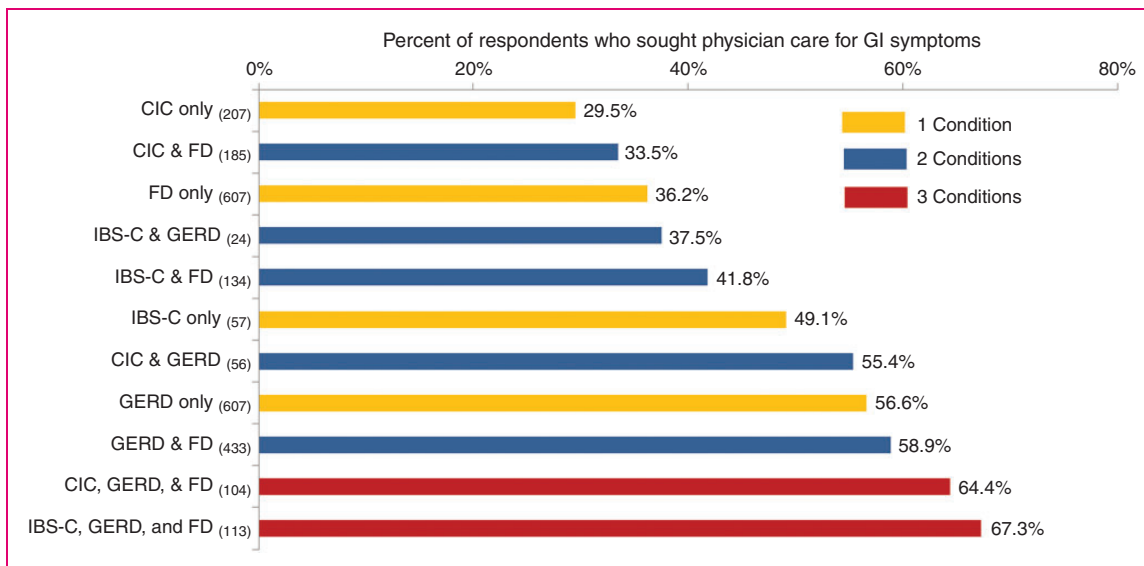


Figure 4. Percentage of respondents who sought physician care for GI symptoms in past 12 months, in rank order by condition. GI: gastrointestinal; CIC: chronic idiopathic constipation; IBS-C: constipation-predominant irritable bowel syndrome; FD: functional dyspepsia; GERD: gastroesophageal reflux disease.

The study is also limited by being a post-hoc analysis of a cross-sectional survey, with functional GI classifications based on patient recall of symptoms. As such, the study was not able to account for migrations between subtypes of IBS, or to assess the potentially episodic nature of alterations in bowel habits seen in IBS patients.²¹ Also, there were no opportunities for physicians to rule out structural disease or otherwise confirm diagnoses. Symptom severity and quality of life were not assessed. Though participants were asked about medication use, the recall periods for medication use and symptom experience did not allow for correlating the two (observed diarrhea rates, for example, may be associated with treatments for the overlapping disorders).^{22–25}

Additional areas for study include understanding the behavior of non-consulters and examining underlying factors that may contribute to overlapping disorders. For example, somatization and anxiety may be common underlying factors that sensitize the patient to various symptoms. Nam et al. recently found that IBS was associated with non-erosive reflux disease and not with erosive esophagitis and that somatization and anxiety were risk factors.²⁶ Somatization and anxiety also deserve further study in overlap populations; these may also provide insights into consulting behavior. If this were the case, an important aspect of identifying patients with overlapping disorders would be to concurrently treat the anxiety and somatization disorder.

In conclusion, functional GI disorders frequently overlap with each other and with GERD. Patients with overlapping disorders experience more frequent and more bothersome symptoms. Symptoms have a greater impact on work and school activities in patients with overlapping disorders. Patients with overlapping disorders are also more likely to consult physicians. Clinical guidelines and regulatory guidance may need to account for patients with overlapping disorders as they form a substantial proportion of the patients seeking health care.

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Conflicts of interest

N. Vakil has served as an advisor or consultant for Astra Zeneca, Ironwood Pharmaceuticals, Respiratory Technology Solutions and Bayer. M.A. Stelwagon and E.P. Shea are full-time employees of and own stock/stock options in Ironwood Pharmaceuticals Inc. S.A. Miller has served as a market research consultant to Actavis and Ironwood Pharmaceuticals.

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