

# FUNCTIONAL GASTROINTESTINAL DISORDER COMORBIDITIES: Comparisons of Prevalence and Costs in the 6 Months Before and After Diagnoses of Constipation (C) and Irritable Bowel Syndrome and Constipation (IBS+C)

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## Introduction

- Patients with constipation (C) and irritable bowel syndrome (IBS) can present with a wide range of gastrointestinal conditions.
- Prior research has documented the association of both C and IBS with coexisting gastrointestinal medical conditions (comorbidities) as well as other functional gastrointestinal disorders [FGIDs], including functional dyspepsia, gastroesophageal reflux disease [GERD], non-motility gastrointestinal disorders, and somatic conditions.<sup>1-7</sup>
- How often these FGID comorbidities occur and their temporal relationship to C and IBS is not extensively researched.
- Methodologically, differentiating the occurrence of FGID comorbidities before and after diagnoses of C and IBS may provide stronger evidence of association and relatedness.
- A California Medicaid (Medi-cal) study quantified the percent of constipation subjects with specific FGID comorbidities (including hemorrhoids, fecal impaction, intestinal obstruction) but did not use any comparator groups<sup>8</sup>
- Few studies have compared comorbidities occurring with constipation and IBS, and the studies that did compare them explored IBS instead of IBS+C.<sup>9</sup>
- Comorbidities inevitably contribute to the overall cost of care for constipation and IBS+C.
- Similarities in the total cost of care for constipation and IBS+C suggest that the healthcare system manages these conditions similarly<sup>10</sup>

## AIM

- To evaluate the prevalence and costs of FGID comorbidities in a large sample of patients in the 6 months before and after diagnoses (DXs) of C and IBS+C (co-occurring DXs of IBS and C) and to compare with controls (persons without C and without IBS).

## Methods

- A retrospective analysis was performed on healthcare claims data (1/1/2001 to 6/30/2006) extracted from the Human Capital Management Services (HCMS) Research Reference Database consisting of approximately 510,000 employees representative of the US Employed Civilian Labor Force (2004).
- Anonymity of person-level data was maintained according to the Health Insurance Portability and Accountability Act guidelines.
- Healthcare for the entire employee cohort was provided through managed care plans contracted by respective employers.
- International Classification of Diseases-9 (ICD-9) codes were used to identify employees with primary, secondary, or tertiary diagnoses of constipation in claims records:
  - 564.0 (Constipation)
  - 564.00 (Unspecified)
  - 564.01 (Slow Transit)
  - 564.09 (Other)
- Persons with IBS+C were required to have an ICD-9 for constipation plus an ICD-9 for IBS (564.1) in claims records.
- Employee cohorts were identified for comparison purposes:
  - Constipation (C) cohort: Employees with a record of constipation-related diagnosis (Constipation ICD-9 codes listed above) and no ICD-9 for IBS.
  - Irritable Bowel Syndrome with constipation (IBS+C) cohort: Employees with record of constipation-related diagnosis (Constipation ICD-9 codes listed above) plus an ICD-9 for IBS.
  - Control (CTRL) cohort: Employees without constipation and without IBS.
- For each employee in the IBS+C cohort, 5 C employees and 180 Controls were matched using logistic regression and propensity scores for age, tenure (years with current employer), sex, marital status, race, exempt/nonexempt status (exempt employees are not paid on an hourly basis and are not paid for

overtime work), full-time/part-time status, salary, Charlson Comorbidity Index score,<sup>11</sup> region (defined by first digit of employee's postal zip code), and existence of a direct medical claim.

- Index dates were established for each cohort as follows:
  - C cohort: the date of first diagnosis of constipation during 2001 or later as noted by ICD-9 code in the claims record;
  - IBS+C cohort: the date of first diagnosis of IBS during 2001 or later as noted by ICD-9 code in the claims record;
  - Control Cohort: the average index date of the cohorts with disease (C and IBS+C)
- Employees were required to be continuously employed and eligible for health benefits for at least six months before and six months after their index date.
- The prevalence of the following FGID comorbidity ICD-9s were compared between cohorts as well as before and after index dates:
  - Impaction of Intestine (560.3x)
  - Anal Fissure (565.0x)
  - Hemorrhoids (455.xx)
  - Intestinal Obstruction (560.xx)
  - Ulcer of Anus and Rectum (569.41)

## Statistical Analysis

- All costs were adjusted to 2006 dollars.
- Prevalence comparisons used z-scores of log odds ratios (Woolf method).
- Cost comparisons used Satterthwaite t tests.
- Comparisons were performed:
  - Within (before vs. after) each cohort (C, IBS+C, and Control) and
  - Between (C vs. IBS+C vs. Control) cohorts.
- Differences were explored for significance:
  - Between cohorts (C vs. IBS+C vs. Controls), for the:
    - 6 months before the index date,
    - 6 months after the index date,
  - Within cohorts (for C, IBS+C, and Controls):
    - 6 months before index date vs. 6 months after index date
- Differences were considered significant at P≤0.05.

## Results

- Data were available for 309 IBS+C persons, 1,545 matched C persons and 55,620 matched controls, for which there were no statistically significant differences in characteristics (**Table 1**).
- Between Group Prevalence (**Table 2**)
  - The prevalence of all comorbidities (intestinal impaction, anal fissure, hemorrhoids, intestinal obstruction, and ulcer of anus and rectum) was significantly greater in the C cohort versus controls in the period after diagnosis.
  - The prevalence of all comorbidities was significantly greater in the IBS+C cohort versus controls in the period after diagnosis.
  - Prevalence of comorbidities after diagnosis was similar in C and IBS+C cohorts except for intestinal impaction and hemorrhoids, which were significantly greater for IBS+C.
- Between Group Costs (**Table 3**)
  - Costs for hemorrhoids were significantly increased in both C and IBS+C cohorts versus controls after diagnosis.
  - Costs were similar between the C and IBS+C cohorts both before and after diagnosis.

- Within Group (after-before) Prevalence (**Figure 1**)
  - Prevalence was numerically increased for all comorbidities after diagnosis versus before diagnosis in both C and IBS+C cohorts except ulcer of the anus and rectum within the IBS+C cohort.
  - Hemorrhoids and Anal Fissures were significantly increased after diagnosis versus before diagnosis within C and IBS+C cohorts.
- Within Group (after-before) Cost
  - The Costs of Hemorrhoids were significantly increased.
- Constipation \$30.5 (P=0.0014)
- IBS+C \$54.3 (P=0.0359)

## Limitations

- Both Constipation and IBS+C may be underreported in healthcare databases due to ICD-9 coding in healthcare claims data.
- The methodological requirement of a medical visit in all cohorts may have produced a clinically non-significant increase in comorbidity prevalence and costs for the controls.

**TABLE 1.** Descriptive Statistics for Matched Cohorts of Employees with Constipation vs. Employees with IBS-C and Controls (neither Constipation or IBS+C)

Variable	Employees					
	with Constipation		with IBS+C		W/O C or IBS (Controls)	
	N	Mean or %	N	Mean or %	N	Mean or %
Mean age at index date, years [S.E.]	1,545	41.00 [0.27]	309	40.20 [0.59]	55,620	40.91 [0.04]
Mean tenure at index date, years [S.E.]	1,545	8.71 [0.20]	309	8.45 [0.44]	55,620	8.75 [0.03]
Women, %	1,545	73.8%	309	77.3%	55,620	73.8%
Married, %	1,411	50.4%	285	48.8%	50,861	50.5%
Race	1,187		239		42,757	
White, %		59.9%		62.8%		60.5%
Black, %		13.7%		12.1%		13.2%
Hispanic, %		14.8%		13.4%		14.8%
Exempt employees, %	1,545	30.4%	309	33.0%	55,620	30.6%
Full Time employment, %	1,545	94.1%	309	94.8%	55,620	94.1%
Mean annual salary [S.E.], \$US	1,545	\$48,900 [\$720]	309	\$49,676 [\$1513]	55,620	\$49,194 [\$232]

S.E. Standard Error  
All variables similar (P>0.05)

**TABLE 2.** Between Groups Prevalence Comparisons

Prevalence of Specific Condition (ICD9)	Controls (N=55,620)	Constipation (N=1,545)	IBS+C (N=309)	Constipation vs. Controls (P-Value)	IBS+C vs. Controls (P-Value)	Constipation vs. IBS+C (P-Value)
<b>During 6 Months Before Diagnosis</b>						
Impaction of Intestine (560.3x)	0.01%	0.19%	0.65%	<0.0001	<0.0001	0.1866
Anal Fissure (565.0x)	0.10%	0.52%	0.32%	<0.0001	0.2399	0.6569
Hemorrhoids (455.xx)	0.79%	4.14%	8.09%	<0.0001	<0.0001	0.0036
Intestinal Obstruction (560.xx)	0.10%	0.78%	2.59%	<0.0001	<0.0001	0.0080
Ulcer of Anus and Rectum (569.41)	0.01%	0.00%	0.65%	N/A	<0.0001	N/A
<b>During 6 Months After Diagnosis</b>						
Impaction of Intestine (560.3x)	0.03%	0.26%	1.62%	<0.0001	<0.0001	0.0061
Anal Fissure (565.0x)	0.15%	1.17%	1.62%	<0.0001	<0.0001	0.5132
Hemorrhoids (455.xx)	1.10%	12.49%	17.80%	<0.0001	<0.0001	0.0128
Intestinal Obstruction (560.xx)	0.12%	1.49%	2.91%	<0.0001	<0.0001	0.0851
Ulcer of Anus and Rectum (569.41)	0.01%	0.19%	0.00%	<0.0001	N/A	N/A

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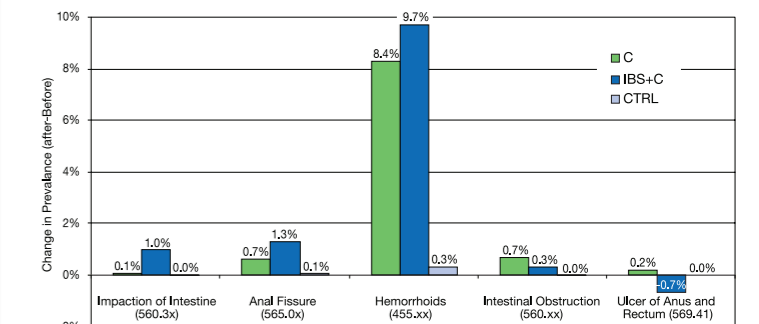
## Summary and Conclusions

- The prevalence of certain GI comorbidities was similar in both the C and IBS+C cohorts before diagnosis and after diagnosis.
  - Prevalence of hemorrhoids and anal fissures increased significantly after diagnoses of C and IBS+C.
  - There was an increased, though nonsignificant, trend in the prevalence of other GI comorbidities after diagnoses of C and IBS+C.
- The costs of certain GI comorbidities were similar between the C and IBS+C cohorts both before diagnosis and after diagnosis.
  - Costs for hemorrhoids increased significantly after diagnoses of C and IBS+C.
  - There was an increased, though nonsignificant, trend in the costs of other GI comorbidities.
- The C and IBS+C cohorts may have been comprised of both mild and severe patients, reducing magnitude of results.
- These results suggest that effective management of both Constipation and IBS+C may avert FGID comorbidities and reduce costs from an employer perspective.

**TABLE 3.** Between Groups Cost Comparisons

Cost of Specific Condition (ICD9)	Controls (N=55,620)	Constipation (N=1,545)	IBS+C (N=309)	Constipation vs. Controls (P-Value)	IBS+C vs. Controls (P-Value)	Constipation vs. IBS+C (P-Value)
<b>During 6 Months Before Diagnosis</b>						
Impaction of Intestine (560.3x)	\$0.0	\$0.3	\$0.7	0.3199	0.3191	0.6096
Anal Fissure (565.0x)	\$0.5	\$2.5	\$14.5	0.2462	0.3353	0.4124
Hemorrhoids (455.xx)	\$3.6	\$15.9	\$28.4	0.0090	0.0066	0.2203
Intestinal Obstruction (560.xx)	\$1.6	\$15.5	\$69.8	0.3517	0.0635	0.1701
Ulcer of Anus and Rectum (569.41)	\$0.0	\$0.0	\$0.0	0.1397	0.1397	N/A
<b>During 6 Months After Diagnosis</b>						
Impaction of Intestine (560.3x)	\$0.1	\$0.5	\$1.6	0.2839	0.2841	0.4493
Anal Fissure (565.0x)	\$0.7	\$9.0	\$8.3	0.0398	0.2620	0.9257
Hemorrhoids (455.xx)	\$5.4	\$46.4	\$82.7	<0.0001	0.0015	0.1581
Intestinal Obstruction (560.xx)	\$3.3	\$21.6	\$23.2	0.1156	0.2152	0.9364
Ulcer of Anus and Rectum (569.41)	\$0.1	\$1.4	\$0.0	0.1199	0.1549	0.0833

**FIGURE 1.** Within Group Changes in Prevalence (After-Before)



### Significant (P<0.05) Within Group Prevalence Changes (After-Before):

- Constipation: Anal Fissure (P=0.0412), Hemorrhoids (P<0.0001)
- IBS+C: Anal Fissure (P=0.0453), Hemorrhoids (P=0.0003)
- Controls: Anal Fissure (P=0.0149), Hemorrhoids (P<0.0001)

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NOTES

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**ABSTRACT**

**Background:** Patients with C and IBS can present with a wide range of functional gastrointestinal disorder (FGID) comorbidities. However, it is unknown how often these comorbidities occur or their temporal relationship to C and IBS. Few studies have differentiated the occurrence of FGID comorbidities before and after diagnoses of C and IBS.

**Objective:** To evaluate the prevalence and costs of FGID comorbidities in a large sample of patients in the 6 months before and after diagnoses (DXs) of C and IBS+C (co-occurring DXs of IBS and C).

**Methods:** A retrospective analysis was performed in an employer database of greater than 500,000 employees. Patient cohorts with C (ICD9s 564.0, 564.00, 564.01, and 564.09), IBS+C (ICD9 564.1x and co-occurring C) and a Control group (neither C nor IBS+C) were identified. For each IBS+C patient identified, 5 C patients and 180 Control patients were matched using logistic regression and propensity scores for age, job tenure, gender, marital status, race, exempt- and full-time employment status, salary, region, Charlson Comorbidity Index Score, and the existence of medical claims. Prevalence and costs for FGID co-morbidities were calculated for the 6 months before and after C and IBS+C DXs by FGID ICD9 code (see table). Comorbidity comparisons were performed within (before vs after) and between (C vs IBS-C vs control) groups. Prevalence comparisons used z-scores of log odds ratios (Woolf method) and costs were compared by Satterthwaite t-tests.

**Results:** Data were available for 309 IBS-C patients, 1545 C patients, and 55,620 matched Controls. All cohorts averaged 41 years of age and 74% were female. The prevalence and costs of FGID comorbidities within and between C, IBS-C, and Control groups generally increased. Many findings were significant (see table).

**Conclusion:** The prevalence and costs of FGID comorbidities increase after diagnoses of C and IBS+C. Prevalence and costs of comorbidities were similar between C and IBS+C cohorts.

Diagnosis (ICD9)	Time (relative to DX)	Prevalence (% of cohort)		6-Month Costs	
		C	IBS+C	C	IBS+C
Hemorrhoids (455.xx)	Before	4.14 <sup>†</sup>	8.09 <sup>†</sup>	\$15.9 <sup>†</sup>	\$28.4 <sup>†</sup>
	After	12.49 <sup>†‡§</sup>	17.80 <sup>†§</sup>	\$46.4 <sup>†§</sup>	\$82.7 <sup>†</sup>
Intestinal Obstruction (560.xx)	Before	0.78 <sup>†</sup>	2.59 <sup>†</sup>	\$15.5	\$69.8
	After	1.49 <sup>†</sup>	2.91 <sup>†</sup>	\$21.6	\$23.2
Anal Fissure (565.0x)	Before	0.52 <sup>†</sup>	0.32	\$2.5	\$14.5
	After	1.17 <sup>†*</sup>	1.62 <sup>†*</sup>	\$9.0 <sup>§</sup>	\$8.3
Impaction of Intestine (560.3x)	Before	0.19 <sup>†</sup>	0.65 <sup>†</sup>	\$0.3	\$0.7
	After	0.26 <sup>†*</sup>	1.62 <sup>†</sup>	\$0.5	\$1.6
Ulcer of Anus and Rectum (569.41)	Before	0.00	0.65 <sup>†</sup>	\$0.0	\$0.0
	After	0.19 <sup>†</sup>	0.00	\$1.4	\$0.0

Between-group comparisons: <sup>†</sup> P<0.01 (vs Control) <sup>‡</sup> P<0.01 (IBS-C vs C); Within-group comparisons (Pre- vs Post-DX): <sup>§</sup> P<0.01; <sup>\*</sup> P<0.05