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.[1-7]
- 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[8]
- Few studies have compared comorbidities occurring with constipation and IBS, and the studies that did compare them explored IBS instead of IBS+C.9
- 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 suggests that the healthcare system manages these conditions similarly[10]

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-occuring 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,[11] 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 ICD9s 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, and
  - 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, 1,545 matched C persons and 55,620 matched controls, for which there were no 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 IBC+C cohorts except for intestinal impaction and hemorrhoids, which were significantly greater for IBS+C.
- Between Group Costs **(Table 3)**
  - Costs were increased for all comorbidities except ulcer of anus and rectum in both C and IBS-C cohorts versus controls after diagnosis.
  - 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 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.

Summary and Conclusions

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

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

	Employees					
	with Constipation		with IBS+C		W/O C or IBS (Controls)	
Variable	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)
During 6 Months Before Diagnosis						
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
During 6 Months After Diagnosis						
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

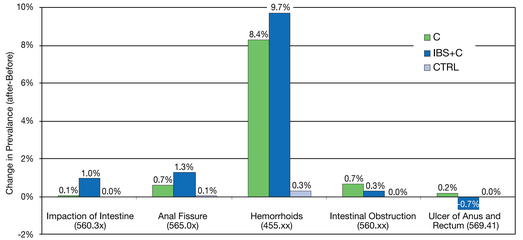
P-values in bold are statistically significant.

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)
During 6 Months Before Diagnosis						
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
During 6 Months After Diagnosis						
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

P-values in bold are statistically significant.

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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