

## SUPPLEMENTAL MATERIAL

### Risk for Post-Colonoscopy Irritable Bowel Syndrome in Patients with and without Antibiotic Exposure: A Retrospective Cohort Study

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## Supplemental methods

### Data source additional details

We chose 2005 as the study start year because it was one year after Optum first captured complete inpatient data. We used data from May 1, 2000 – December 31, 2004 to assess exclusion criteria. Medical diagnoses were identified using ICD codes in any encounter. ICD-9 was used prior to October 1, 2015, and ICD-10 was used thereafter. General equivalence mappings from the United States Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project were used to convert ICD-9 codes to ICD-10. Procedure and tests were identified by ICD, Current Procedural Terminology (CPT), and Healthcare Common Procedure Coding System (HCPCS) codes. Medication use was identified by National Drug Codes and classified into pharmacologic classes using American Hospital Formulary Service codes.

### Screening colonoscopy cohort exclusion criteria

Individuals with ICD medical claims for IBS any time before the index colonoscopy were excluded. Individuals with claims for abdominal pain, change in bowel habits, constipation, or diarrhea any time prior to the end of the exposure assessment window were also excluded as these may be symptoms of undiagnosed IBS. To exclude other causes of pre-existing abdominal pain, individuals with *Helicobacter pylori* infection, *Helicobacter pylori* testing (fecal antigen, serum antigen, breath test, or culture), diverticulitis, small intestinal bacterial overgrowth, or small intestinal bacterial overgrowth breath testing any time before colonoscopy were also excluded. To exclude pre-existing diarrhea, individuals with infectious diarrhea testing by stool culture, enteric pathogens polymerase chain reaction, stool ova and parasites, or *Clostridioides difficile* testing any time prior to colonoscopy were excluded (codes in **Supplemental table 5**). Additionally, individuals with prescriptions for IBS medications such as

alosetron, dicyclomine, diphenoxylate-atropine, eluxadoline, hyoscyamine, linaclotide, loperamide, lubiprostone, plecanatide, rifaximin, tricyclic antidepressants, or selective serotonin-reuptake inhibitors prior to colonoscopy were excluded (codes in **Supplemental table 2**). As antibiotics received during hospitalization are not recorded in Optum, individuals who were hospitalized 90 days or less before index colonoscopy were excluded to avoid potential exposure misclassification. All individuals in the cohort must have had at least 14 days of continuous follow-up after colonoscopy to allow for sufficient time for antibiotic exposure ascertainment.

**Supplemental table 1. Administrative codes to identify primary IBS outcome**

<b>Code</b>	<b>Condition</b>	<b>Code type</b>
5970	Celiac disease	ICD-9
K900	Celiac disease	ICD-10
5771	Chronic pancreatitis	ICD-9
K861	Chronic pancreatitis	ICD-10
1530	Colorectal cancer	ICD-9
1531	Colorectal cancer	ICD-9
1532	Colorectal cancer	ICD-9
1533	Colorectal cancer	ICD-9
1534	Colorectal cancer	ICD-9
1536	Colorectal cancer	ICD-9
1537	Colorectal cancer	ICD-9
1538	Colorectal cancer	ICD-9
1539	Colorectal cancer	ICD-9
C180	Colorectal cancer	ICD-10
C182	Colorectal cancer	ICD-10
C183	Colorectal cancer	ICD-10
C184	Colorectal cancer	ICD-10
C185	Colorectal cancer	ICD-10
C186	Colorectal cancer	ICD-10
C187	Colorectal cancer	ICD-10
C188	Colorectal cancer	ICD-10
C189	Colorectal cancer	ICD-10
Z85038	Colorectal cancer	ICD-10
1540	Colorectal cancer	ICD-9
1541	Colorectal cancer	ICD-9
1548	Colorectal cancer	ICD-9
C19	Colorectal cancer	ICD-10
C20	Colorectal cancer	ICD-10
Z85048	Colorectal cancer	ICD-10
5500	Crohn's disease	ICD-9
5551	Crohn's disease	ICD-9
5552	Crohn's disease	ICD-9
5559	Crohn's disease	ICD-9

K5000	Crohn's disease	ICD-10
K50011	Crohn's disease	ICD-10
K50012	Crohn's disease	ICD-10
K50013	Crohn's disease	ICD-10
K50014	Crohn's disease	ICD-10
K50018	Crohn's disease	ICD-10
K50019	Crohn's disease	ICD-10
K5010	Crohn's disease	ICD-10
K50111	Crohn's disease	ICD-10
K50112	Crohn's disease	ICD-10
K50113	Crohn's disease	ICD-10
K50114	Crohn's disease	ICD-10
K50118	Crohn's disease	ICD-10
K50119	Crohn's disease	ICD-10
K5080	Crohn's disease	ICD-10
K50811	Crohn's disease	ICD-10
K50812	Crohn's disease	ICD-10
K50813	Crohn's disease	ICD-10
K50814	Crohn's disease	ICD-10
K50818	Crohn's disease	ICD-10
K50819	Crohn's disease	ICD-10
K5090	Crohn's disease	ICD-10
K50911	Crohn's disease	ICD-10
K50912	Crohn's disease	ICD-10
K50913	Crohn's disease	ICD-10
K50914	Crohn's disease	ICD-10
K50918	Crohn's disease	ICD-10
K50919	Crohn's disease	ICD-10
56360000	Five amino-salicylates	AHFS
5641	Irritable bowel syndrome	ICD-9
K580	Irritable bowel syndrome	ICD-10
K581	Irritable bowel syndrome	ICD-10
K582	Irritable bowel syndrome	ICD-10
K588	Irritable bowel syndrome	ICD-10
K589	Irritable bowel syndrome	ICD-10
5712	Liver cirrhosis	ICD-9

5715	Liver cirrhosis	ICD-9
5716	Liver cirrhosis	ICD-9
K7030	Liver cirrhosis	ICD-10
K740	Liver cirrhosis	ICD-10
K7460	Liver cirrhosis	ICD-10
K7469	Liver cirrhosis	ICD-10
K743	Liver cirrhosis	ICD-10
K744	Liver cirrhosis	ICD-10
K745	Liver cirrhosis	ICD-10
5791	Malabsorption	ICD-9
5792	Malabsorption	ICD-9
5793	Malabsorption	ICD-9
5794	Malabsorption	ICD-9
5798	Malabsorption	ICD-9
5799	Malabsorption	ICD-9
K901	Malabsorption	ICD-10
K902	Malabsorption	ICD-10
K912	Malabsorption	ICD-10
K903	Malabsorption	ICD-10
K9041	Malabsorption	ICD-10
K9049	Malabsorption	ICD-10
K9089	Malabsorption	ICD-10
K909	Malabsorption	ICD-10
5589	Microscopic colitis	ICD-9
K52831	Microscopic colitis	ICD-10
K52832	Microscopic colitis	ICD-10
K52838	Microscopic colitis	ICD-10
K52839	Microscopic colitis	ICD-10
K5289	Microscopic colitis	ICD-10
K529	Microscopic colitis	ICD-10
1830	Ovarian cancer	ICD-9
C569	Ovarian cancer	ICD-10
1986	Ovarian cancer	ICD-9
C7960	Ovarian cancer	ICD-10
1570	Pancreatic cancer	ICD-9
1571	Pancreatic cancer	ICD-9

1572	Pancreatic cancer	ICD-9
1573	Pancreatic cancer	ICD-9
1574	Pancreatic cancer	ICD-9
1578	Pancreatic cancer	ICD-9
1579	Pancreatic cancer	ICD-9
C250	Pancreatic cancer	ICD-10
C251	Pancreatic cancer	ICD-10
C252	Pancreatic cancer	ICD-10
C253	Pancreatic cancer	ICD-10
C254	Pancreatic cancer	ICD-10
C257	Pancreatic cancer	ICD-10
C258	Pancreatic cancer	ICD-10
C259	Pancreatic cancer	ICD-10
5560	Ulcerative colitis	ICD-9
5561	Ulcerative colitis	ICD-9
5562	Ulcerative colitis	ICD-9
5563	Ulcerative colitis	ICD-9
5564	Ulcerative colitis	ICD-9
5565	Ulcerative colitis	ICD-9
5566	Ulcerative colitis	ICD-9
5568	Ulcerative colitis	ICD-9
5569	Ulcerative colitis	ICD-9
K5100	Ulcerative colitis	ICD-10
K51011	Ulcerative colitis	ICD-10
K51012	Ulcerative colitis	ICD-10
K51013	Ulcerative colitis	ICD-10
K51014	Ulcerative colitis	ICD-10
K51018	Ulcerative colitis	ICD-10
K51019	Ulcerative colitis	ICD-10
K5120	Ulcerative colitis	ICD-10
K51211	Ulcerative colitis	ICD-10
K51212	Ulcerative colitis	ICD-10
K51213	Ulcerative colitis	ICD-10
K51214	Ulcerative colitis	ICD-10
K51218	Ulcerative colitis	ICD-10
K51219	Ulcerative colitis	ICD-10

K5130	Ulcerative colitis	ICD-10
K51311	Ulcerative colitis	ICD-10
K51312	Ulcerative colitis	ICD-10
K51313	Ulcerative colitis	ICD-10
K51314	Ulcerative colitis	ICD-10
K51318	Ulcerative colitis	ICD-10
K51319	Ulcerative colitis	ICD-10
K5140	Ulcerative colitis	ICD-10
K51411	Ulcerative colitis	ICD-10
K51412	Ulcerative colitis	ICD-10
K51413	Ulcerative colitis	ICD-10
K51414	Ulcerative colitis	ICD-10
K51418	Ulcerative colitis	ICD-10
K51419	Ulcerative colitis	ICD-10
K5150	Ulcerative colitis	ICD-10
K51511	Ulcerative colitis	ICD-10
K51512	Ulcerative colitis	ICD-10
K51513	Ulcerative colitis	ICD-10
K51514	Ulcerative colitis	ICD-10
K51518	Ulcerative colitis	ICD-10
K51519	Ulcerative colitis	ICD-10
K5180	Ulcerative colitis	ICD-10
K51811	Ulcerative colitis	ICD-10
K51812	Ulcerative colitis	ICD-10
K51813	Ulcerative colitis	ICD-10
K51814	Ulcerative colitis	ICD-10
K51818	Ulcerative colitis	ICD-10
K51819	Ulcerative colitis	ICD-10
K5190	Ulcerative colitis	ICD-10
K51911	Ulcerative colitis	ICD-10
K51912	Ulcerative colitis	ICD-10
K51913	Ulcerative colitis	ICD-10
K51914	Ulcerative colitis	ICD-10
K51918	Ulcerative colitis	ICD-10
K51919	Ulcerative colitis	ICD-10



**Supplemental table 2. American Hospital Formulary Service (AHFS) codes to identify IBS prescriptions**

<b>AHFS code</b>	<b>AHFS class</b>	<b>Examples</b>
56080000	Antidiarrhea agents	Diphenoxylate-atropine, loperamide
12080800	Antimuscarinics/antispasmodics	Dicyclomine, hyoscyamine
56120000	Cathartics and laxatives	Lubiprostone
56360000	Anti-inflammatory agents	Alosetron
56920000	Miscellaneous GI drugs	Eluxadoline, linaclotide
8122830	Rifamycins	Rifaxamin
28160420	Selective-serotonin reuptake inhibitors*	
28160428	Tricyclic antidepressants*	

Note: \* Used for exclusion criteria only. These were not considered for the composite outcome of IBS, IBS medications, or IBS symptoms.

**Supplemental table 3. Bowel preparation types**

<b>Category</b>	<b>Example brand names</b>
Polyethylene glycol containing	Miralax, GoLytely, NuLytely, Colyte, Gavilyte, Trilyte, Moviprep, Halflytely
Magnesium citrate	Citroma
Sodium phosphate	Osmoprep
Sodium sulfate	Suprep, Prepopik
Polyethylene glycol and sodium sulfate	Suclear

**Supplemental table 4. Average number of claims (95% CI) for IBS and IBS symptoms after meeting outcome criteria**

		IBS	Abdominal pain	Change in bowel habits	Constipation	Diarrhea	Days from outcome to last IBS/IBS symptom claim
IBS	No antibiotics (n = 151)	1.8 (1.2 - 2.3)	1.8 (1.3 - 2.3)	0.1 (0.0 - 0.2)	0.5 (0.2 - 0.7)	0.4 (0.2 - 0.7)	930.2 (734.5 - 1125.9)
	Antibiotics (n = 166)	1.3 (0.9 - 1.7)	1.9 (1.3 - 2.6)	0.1 (0.0 - 0.2)	0.2 (0.1 - 0.4)	0.5 (0.2 - 0.7)	903.1 (706.7 - 1099.5)
Composite outcome	No antibiotics (n = 754)	0.5 (0.3 - 0.6)	2.7 (2.4 - 3.0)	0.1 (0.1 - 0.1)	0.5 (0.4 - 0.6)	0.9 (0.7 - 1.1)	822.5 (737.1 - 907.9)
	Antibiotics (n = 834)	0.4 (0.3 - 0.5)	3.0 (2.2 - 3.9)	0.2 (0.1 - 0.2)	0.5 (0.3 - 0.6)	1.0 (0.8 - 1.2)	963.7 (874.9 - 1052.5)

**Supplemental table 5. Administrative codes to identify exclusion diagnoses and procedures**

<b>Code</b>	<b>Condition</b>	<b>Code type</b>
78900	Abdominal pain	ICD-9
78901	Abdominal pain	ICD-9
78902	Abdominal pain	ICD-9
78903	Abdominal pain	ICD-9
78904	Abdominal pain	ICD-9
78905	Abdominal pain	ICD-9
78906	Abdominal pain	ICD-9
78907	Abdominal pain	ICD-9
78909	Abdominal pain	ICD-9
R1010	Abdominal pain	ICD-10
R1011	Abdominal pain	ICD-10
R1012	Abdominal pain	ICD-10
R1013	Abdominal pain	ICD-10
R1030	Abdominal pain	ICD-10
R1031	Abdominal pain	ICD-10
R1032	Abdominal pain	ICD-10
R1033	Abdominal pain	ICD-10
R1084	Abdominal pain	ICD-10
R109	Abdominal pain	ICD-10
87493	C difficile testing	CPT
87230	C difficile testing	CPT
87324	C difficile testing	CPT
78799	Change in bowel habits	ICD-9
R194	Change in bowel habits	ICD-10
56400	Constipation	ICD-9
56401	Constipation	ICD-9
56402	Constipation	ICD-9
56409	Constipation	ICD-9
K5900	Constipation	ICD-10
K5901	Constipation	ICD-10
K5902	Constipation	ICD-10
K5903	Constipation	ICD-10
K5904	Constipation	ICD-10
K5909	Constipation	ICD-10
5645	Diarrhea	ICD-9
0092	Diarrhea	ICD-9
0093	Diarrhea	ICD-9

78791	Diarrhea	ICD-9
K591	Diarrhea	ICD-10
A09	Diarrhea	ICD-10
R197	Diarrhea	ICD-10
56211	Diverticulitis	ICD-9
56213	Diverticulitis	ICD-9
K5720	Diverticulitis	ICD-10
K5721	Diverticulitis	ICD-10
K5730	Diverticulitis	ICD-10
K5731	Diverticulitis	ICD-10
K5732	Diverticulitis	ICD-10
K5733	Diverticulitis	ICD-10
K5740	Diverticulitis	ICD-10
K5741	Diverticulitis	ICD-10
K5750	Diverticulitis	ICD-10
K5751	Diverticulitis	ICD-10
K5752	Diverticulitis	ICD-10
K5753	Diverticulitis	ICD-10
K5780	Diverticulitis	ICD-10
K5781	Diverticulitis	ICD-10
K5790	Diverticulitis	ICD-10
K5791	Diverticulitis	ICD-10
K5792	Diverticulitis	ICD-10
K5793	Diverticulitis	ICD-10
4186	H pylori	ICD-9
B9681	H pylori	ICD-10
83013	H pylori breath test	CPT
83014	H pylori breath test	CPT
87081	H pylori culture	CPT
87205	H pylori culture	CPT
86677	H pylori serum antigen	CPT
87338	H pylori stool antigen	CPT
91065	Hydrogen breath test	CPT
5641	Irritable bowel syndrome	ICD-9
K580	Irritable bowel syndrome	ICD-10
K581	Irritable bowel syndrome	ICD-10
K582	Irritable bowel syndrome	ICD-10
K588	Irritable bowel syndrome	ICD-10
K589	Irritable bowel syndrome	ICD-10
849	Small intestinal bacterial overgrowth	ICD-9

A048	Small intestinal bacterial overgrowth	ICD-10
A049	Small intestinal bacterial overgrowth	ICD-10
87045	Stool culture	CPT
87046	Stool culture	CPT
87427	Stool culture	CPT
87177	Stool ova and parasite	CPT
87209	Stool ova and parasite	CPT
87015	Stool ova and parasite	CPT
87206	Stool ova and parasite	CPT
87329	Stool ova and parasite	CPT
87169	Stool ova and parasite	CPT

Supplemental figure 1. Study design diagram

