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GENERAL GI

Prevalence and Financial Burden of Digestive Diseases in a Commercially Insured Population

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BACKGROUND & AIMS: **Digestive diseases represent a diverse group of clinical conditions that impact the population. Their heterogeneity in classification, presentation, acuity, chronicity, and need for drug therapy presents a challenge when comparing and contrasting the burden associated with these conditions. Prior studies use an outdated classification system and aggregate costs at the population level or focus on specific diseases, limiting the ability to characterize the overall landscape. Our aim was to provide the most up-to-date assessment of cost, utilization, and prevalence associated with digestive diseases.**

METHODS: **We examined digestive disease claims and payment data for a commercially insured adult population between 2016 and 2018 to provide a comprehensive summary of costs, utilization, and prevalence across 38 conditions. Outcome variables included point prevalence and relative prevalence, annualized all-cause medical and drug costs, digestive disease-specific average medical cost, digestive disease-specific cost per fill, and utilization by clinical setting and by clinical condition.**

RESULTS: **A total of 7,297,435 individuals with a digestive disease diagnosis were included in the study. The point prevalence of having a digestive disease in the total population was 24%. Annualized total costs by clinical category ranged from $10,038 (eosinophilic esophagitis) to $107,007 (hepatitis C), with medical costs accounting for most of the expenditures in a majority of conditions. Annualized total costs for common conditions included $39,653 for alcoholic liver disease, $42,554 for acute pancreatitis, $62,735 for Crohn's disease, $13,948 for functional gastrointestinal disorders, $53,214 for nonalcoholic cirrhosis, and $36,441 for ulcerative colitis. Average cost of inpatient stays ranged from $12,218 (noninfectious gastroenteritis/colitis) to $78,259 (nonalcoholic steatohepatitis). Outpatient visits ranged from $784 (gastrointestinal infection) to $4629 (gallbladder and biliary tract disease). Average drug cost per fill ranged from $83 (gastroesophageal reflux disease) to $1458 (hepatitis C). A total of 27,429,046 clinical encounters occurred across all conditions during the study period, with 90% taking place as outpatient visits. Abdominal pain was the single largest contributor to outpatient visits and emergency department to home encounters. Inpatient stays were considerably more heterogeneous, with no condition accounting for more than 12% (gallbladder and biliary tract disease) of the total.**

CONCLUSIONS: **The results demonstrate digestive diseases are common, heterogeneous in cost and utilization, and collectively exact a significant financial burden on the U.S. adult population.**

Keywords: Healthcare Cost; Healthcare Utilization; Prevalence; Financial Burden.

Estimates of cost and utilization relating to disease provide stakeholders in medicine with a comprehensive perspective of the burden associated with any condition. In addition, these data can have a wide-ranging impact on policy, research, clinical management, reimbursement, and insurance coverage. Digestive diseases have been characterized both at the macro level

Abbreviations used in this paper: **ED, emergency department; GI, gastrointestinal; ICD, International Classification of Diseases.**

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and on an individual and disease basis. However, there are challenges associated with each of these approaches. The larger, national studies[1–8] commonly include data from multiple databases, each with different disease/symptom categories, data definitions, clinical settings, and time periods, resulting in a fragmented depiction of costs. These studies typically provide aggregated costs instead of costs on an individual or clinical episode basis. Smaller, disease-focused studies[9–22] are challenged by limited sample size, varied inclusion criteria, and explicit exclusion of other comorbid gastrointestinal (GI) conditions. As a result, the ability to compare and contrast GI disease with other conditions on a relative basis is not straightforward. In addition, most prior studies evaluating costs used International Classification of Disease (ICD), 9th version, Clinical Modification codes instead of ICD-10-CM. The latter is more representative of the current state of billing in clinical care and cost.

To address these limitations, we examined digestive disease claims and payment data for a commercially insured population between 2016 and 2018 to provide a comprehensive and up-to-date summary of costs and utilization across major GI conditions, clinical settings, and drug categories. This analysis included the point prevalence and relative prevalence of gastroenterology and hepatology diagnoses, as defined by individuals with specific ICD-10 diagnosis codes.

What You Need to Know

Background

Prior efforts to characterize the broad landscape of financial burden associated with digestive conditions have been limited by use of outdated disease classification systems, varying cost methodologies, and use of disparate data sources. Our study provides an updated and comprehensive evaluation of cost and utilization across 38 major digestive conditions in a commercially insured population.

Findings

Nearly 7.3 million individuals in the study had a digestive disease diagnosis, accounting for approximately one-fourth of the total population. The vast majority of care for digestive conditions care occurred in the ambulatory setting, whereas costs were largest in the inpatient setting. All-cause total annualized cost ranged from $10,038 to $107,007.

Implications for patient care

This study confirms that digestive diseases are common, heterogeneous in cost and utilization, and collectively exact a significant financial burden on the U.S. adult population. The findings support additional resources for the diagnosis, treatment, and prevention of digestive diseases.

Methods

Data Source and Study Population

Deidentified patient claims and commercial payment data were obtained from the IBM MarketScan Research Databases (Armonk, NY). These databases contain medical utilization, clinical diagnoses, and allowed payment amounts on nearly 50 million beneficiaries across the United States who are enrolled in employer-sponsored health insurance plans.

The study sample included all members aged 18 years or older by January 2016 with at least one claim between 2016 and 2018 having a principal ICD-10 diagnosis code indicating GI or hepatology associated condition. Continuous enrollment was not required, although the duration of coverage had to be greater than 0. Only in-network claims greater than 0 were included; 0 dollar claims and those with negative values are typically due to a billing error or balance adjustment. Out-of-network and capitated claims were excluded because of the considerable variation in allowed amounts. Additional inclusion criteria relating to specific revenue codes, service categories, and places of service are included in Supplement 1. A retrospective cohort study design, using descriptive statistics, provided monthly utilization data and episodic cost data (allowed amounts) for commercially insured GI patients. There was no comparison group.

Clinical Condition and Symptom Categories

All applicable digestive disease ICD-10 codes were grouped into 38 condition categories. These groupings were based in part on the most recent comprehensive GI burden assessment,[1] where the underlying codes were abstracted and reorganized into a broader ICD-10 based classification (Supplement 2). Frequency distributions at the condition level, using the primary diagnosis field, showed the number of unique individuals with each condition; individuals could have more than one condition over the study period.

Point Prevalence

The point prevalence of GI disease was determined by dividing the total number of unique individuals with a particular condition during the study period by the total number of unique individuals in the MarketScan database. Because subjects were not required to have continuous enrollment, point prevalence was computed annually at December 2016, 2017, and 2018. The total GI population during this specified time period is lower than the total GI population used to calculate costs because the latter is inclusive of all individuals enrolled during any month in the study period.

Annualized All-Cause Medical Cost

All-cause cost, which is inclusive of all costs including that of non-GI conditions, was determined by first identifying individuals with a primary GI diagnosis code attributable to one of the major condition categories. Second, all claims costs were summed at the individual member level from the time of diagnosis through the end of the study period or until a new primary GI diagnosis (in a different condition category) occurred. At this point, these costs and future costs were attributed to the new condition category, using the same logic. Attribution of costs was limited to a 365-day duration if the GI diagnosis did not recur within the 365-day period. If more than one GI condition was present on a single date of service, the costs were split and attributed equally among the clinical categories. If an individual did not have a single GI diagnosis on any day during the study period, the individual was excluded to minimize ambiguous attribution. Annualized all-cause cost was calculated by dividing the summation of individual all-cause costs for a condition by the number of days the individuals were assigned to the category; this daily mean cost was multiplied by 365 days.

Gastrointestinal-Specific Medical Cost and Utilization

GI-specific cost and utilization data were computed separately for inpatient and outpatient setting categories as defined by the Centers for Medicare and Medicaid Services. Episodic cost and utilization data for outpatient settings included all costs (allowed amounts) incurred on the date of service at an outpatient facility for an individual with a GI diagnosis. Encounters with multiple principal ICD-10 GI diagnoses on the same day were excluded. As a result, episodic, GI-specific costs were derived using only data for when a single diagnosis was present to minimize confounding of comorbid conditions. As a result, this may underestimate the true costs of GI conditions. Inpatient costs and utilization included all hospital and provider costs incurred during the entire length of stay for individuals with a GI diagnosis. Inpatient costs and utilization were stratified by direct admissions versus emergency department (ED) admissions. For analyses presented using undifferentiated inpatient data, a weighted average was used to combine the direct and ED admission values. ED costs and utilization were computed for individuals who were not admitted to the facility and included facility and provider costs for the visit.

Annualized All-Cause Drug Cost

All-cause drug costs were calculated using the same attribution methodology as all-cause medical cost with all drug costs summed and attributed to the identified condition category. Similarly, costs were split when multiple categories were present concurrently and attributed to a new category when a subsequent new GI diagnosis occurred. All-cause drug cost was derived first by dividing the total drug cost for each category by the total number of days of all unique individuals with the category, which yielded a mean daily drug cost. The mean daily cost was multiplied by 365 to obtain annualized all-cause drug cost. Drugs administered in the hospital, ED, or clinic setting were billed via the hospital claim or under the physician claim. As a result, these costs were attributed to the "medical" category of costs per convention. This attribution should be considered when evaluating conditions where infusions or injections are common (eg, inflammatory bowel disease).

Gastrointestinal-Specific Drug Costs

The MarketScan Databases assign all prescribed drugs to a therapeutic class. All drugs in the GI class were included in the calculation of GI-specific drug costs. In addition, medications in other therapeutic classes that are commonly prescribed for GI conditions were included if accompanied by a primary GI diagnosis or symptom within 7 days before the dispensing date (Supplement 3). All other medications were excluded. Drug costs were computed by attributing the dispensed medication cost to the category using the member's principal diagnosis. Medication costs associated with individuals who had multiple categories during the study period were attributed to all categories. Cost per fill was determined by dividing total GI-specific drug costs for a category by the total number of fills attributable to GI medications for that category.

Results

Study Population and Prevalence

There were 33,516,039 total individuals in the database during the 3-year study period, of which there were 7,297,435 individuals who were included for the GI-specific cost and utilization analyses. Demographic characteristics of the GI study and background population are detailed in Figure 1.

The population point estimates used to calculate disease prevalence included 28,428,058 unique individuals enrolled in December 2016, 2017, or 2018, of which 6,830,133 unique individuals had a principal GI diagnosis during those same time periods. As a result, the corresponding point prevalence of any GI condition in the total population during the study period was 24%. Further breakdown by category and relative prevalence by GI condition among those with any GI diagnosis are shown in Figure 2. Abdominal pain was the most common condition, with 40% of all individuals having this diagnosis.

Demographics of Study Population

Commercially Insured Population, 2016 - 2018

Demographic	Indviduals with GI diagnosis	Percent of all GI individuals	Individuals with any Diagnosis	Percent of all individuals
Total	7,297,435	100%	33,516,039	100%
Age – Mean	44	N/A	41	N/A
Age – Median	46	N/A	41	N/A
Age – 18-34	2,090,096	29%	13,366,807	40%
Age – 35-44	1,348,747	18%	7,355,748	22%
Age – 45-54	1,737,768	24%	7,653,691	23%
Age – 55-64	2,031,136	28%	7,112,160	21%
65+ (at end of the study)	89,688	1%	453,851	1%
Female	4,358,586	60%	17,482,389	52%
Male	2,938,849	40%	16,033,650	48%
Industry				
Oil & Gas Extraction, Mining	74,498	1%	297,896	1%
Manufacturing, Durable Goods	1,055,602	14%	4,118,620	12%
Manufacturing, Nondurable Goods	412,872	6%	1,812,564	5%
Transportation, Communications, Utilities	734,429	10%	2,929,564	9%
Retail Trade	285,644	4%	1,493,486	4%
Finance, Insurance, Real Estate	654,836	9%	2,816,505	8%
Services	1,200,600	16%	5,683,710	17%
Agriculture, Forestry, Fishing	3,740	0%	17,612	0%
Construction	15,335	0%	84,147	0%
Wholesale	38,077	1%	202,562	1%
Missing	2,821,802	39%	14,128,184	42%
Region				
Northeast	1,317,869	18%	5,555,275	17%
North Central	1,378,492	19%	6,674,795	20%
South	3,485,941	48%	15,551,091	46%
West	1,095,934	15%	5,828,135	17%
Unknown	19,199	0%	123,065	0%

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Figure 1. Demographics of study population.

Prevalence by Clinical Condition

Commercially Insured Population, 2016 - 2018

Condition	Percent of Individuals with GI diagnosis	Percent of Individuals with Any Diagnosis
Abdominal Pain	43.515%	10.511%
GERD	15.106%	3.689%
GI and Hepatic Neoplasms	10.723%	2.626%
Nausea and Vomiting	8.501%	2.046%
Diarrhea	6.958%	1.692%
Anorectal Disorders	6.873%	1.679%
Noninfectious gastroenteritis/colitis	6.515%	1.578%
Other Liver Disease	6.395%	1.560%
Other	5.758%	1.408%
GI Bleeding	5.540%	1.347%
Gastroduodenal Disorders	5.114%	1.250%
Hernias	4.681%	1.143%
GI Infection	4.623%	1.123%
Functional GI Disorders	4.396%	1.070%
Gallbladder and biliary tract disease	4.334%	1.055%
Constipation	4.266%	1.037%
Dysphagia	3.362%	0.823%
Diverticular Disease	3.341%	0.818%
NAFLD	2.597%	0.639%
Bloating and Gas	2.153%	0.529%
Peptic Ulcer Disease	1.647%	0.401%
Other Esophageal Disorders	1.613%	0.395%
Ulcerative Colitis	1.153%	0.276%
Crohn's Disease	1.108%	0.261%
Appendiceal Disorders	1.030%	0.252%
Barrett's Esophagus	0.791%	0.194%
Acute Pancreatitis	0.673%	0.161%
Hepatitis C	0.548%	0.130%
Intestinal Obstruction	0.538%	0.130%
Non-Alcoholic Cirrhosis	0.389%	0.090%
Eosinophilic esophagitis	0.317%	0.078%
NASH	0.277%	0.068%
Other Pancreatic Disorders	0.210%	0.051%
Alcoholic Liver Disease	0.179%	0.042%
Pancreatic Cysts	0.164%	0.040%
Chronic Pancreatitis	0.161%	0.038%
Hepatitis B	0.151%	0.037%
Achalasia	0.053%	0.013%

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Figure 2. Prevalence by clinical condition.

Medical and Drug Costs

The annualized all-cause medical and drug costs as well as totals by condition are represented in Figure 3. The costliest annualized medical spending was associated with intestinal obstruction ($40,255), whereas hepatitis C accounted for the highest annualized drug spend ($93,432) and total annualized spend ($107,007). The average GI-specific spends by clinical setting (inpatient, outpatient, ED to home) and average drug cost per fill by condition are shown in Figure 4. Average inpatient costs across all conditions were higher than any of the other cost settings, with hepatologic conditions accounting for the top 3 inpatient costs (nonalcoholic steatohepatitis [NASH], $78,259; nonalcoholic cirrhosis, $43,733; and hepatitis C, $37,012). Highest outpatient costs were associated with gallbladder and biliary tract disease ($4629), hernias ($3710), and appendiceal disorders ($3452), which also accounted for the highest ED to home cost ($2174). Cost per fill was highest in hepatitis C ($1458), followed by Crohn's disease ($829) and ulcerative colitis ($674).

Utilization

Among individuals with a GI condition, there were 27,429,046 total visits (inpatient, outpatient, and ED to home) during the study period. Utilization as measured by the number of visits in each setting is demonstrated in Figure 5 by condition and in Figure 6 by clinical setting. With exception of intestinal obstruction, acute pancreatitis, and appendiceal disorders, all other conditions had a clear majority of utilization taking place in the outpatient setting. ED to home had the highest utilization for appendiceal

Annualized All-Cause Cost by Clinical Condition

Commercially Insured Population, 2016 - 2018

$2,234 $107,007

Condition	Annualized Medical	Annualized Drug	Annualized Total
Abdominal Pain	$10,149	$3,937	$14,086
Achalasia	$18,268	$6,474	$24,743
Acute Pancreatitis	$35,362	$7,191	$42,554
Alcoholic Liver Disease	$27,262	$12,391	$39,653
Anorectal Disorders	$7,648	$4,893	$12,541
Appendiceal Disorders	$23,171	$2,234	$25,405
Barrett's Esophagus	$8,654	$5,149	$13,803
Bloating and Gas	$8,312	$5,076	$13,388
Chronic Pancreatitis	$19,816	$15,408	$35,224
Constipation	$9,802	$6,166	$15,969
Crohn's Disease	$22,481	$40,255	$62,735
Diarrhea	$8,135	$5,812	$13,948
Diverticular Disease	$13,828	$4,185	$18,013
Dysphagia	$13,662	$5,907	$19,569
Eosinophilic esophagitis	$5,851	$4,188	$10,038
Functional GI Disorders	$7,695	$6,238	$13,933
Gallbladder and biliary tract disease	$21,406	$4,547	$25,953
Gastroduoenal Disorders	$10,590	$4,022	$14,612
GERD	$7,555	$4,777	$12,332
GI and Hepatic Neoplasms	$16,234	$6,173	$22,407
GI Bleeding	$12,171	$5,791	$17,962
GI Infection	$8,119	$3,665	$11,784
Hepatitis B	$8,666	$15,213	$23,880
Hepatitis C	$13,575	$93,432	$107,007
Hernias	$16,239	$4,231	$20,470
Intestinal Obstruction	$45,533	$7,681	$53,214
NAFLD	$9,263	$6,139	$15,402
NASH	$12,027	$10,071	$22,098
Nausea and Vomiting	$12,234	$4,480	$16,714
Non-Alcoholic Cirrhosis	$25,080	$28,479	$53,559
Noninfectious gastroenteritis/colitis	$7,474	$4,991	$12,466
Other	$13,622	$6,608	$20,230
Other Esophageal Disorders	$10,270	$4,307	$14,577
Other Liver Disease	$15,340	$9,393	$24,733
Other Pancreatic Disorders	$27,183	$21,863	$49,046
Pancreatic Cysts	$19,580	$8,372	$27,952
Peptic Ulcer Disease	$9,258	$3,805	$13,063
Ulcerative Colitis	$14,355	$22,086	$36,441

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Figure 3. Annualized all-cause cost by clinical condition.

Average Cost by Clinical Setting

Commercially Insured Population, 2016 - 2018

$82 $80,000

Condition	Inpatient	Outpatient	ED to Home	Cost per Fill
Abdominal Pain	$12,469	$1,264	$1,453	$100
Achalasia	$25,109	$1,242	$1,335	$111
Acute Pancreatitis	$17,147	$1,669	$1,587	$91
Alcoholic Liver Disease	$26,571	$1,211	$1,485	$132
Anorectal Disorders	$17,925	$1,376	$1,161	$165
Appendiceal Disorders	$18,004	$3,452	$2,174	$102
Barrett's Esophagus	$18,791	$1,200	$1,370	$97
Bloating and Gas	$15,086	$1,091	$1,171	$125
Chronic Pancreatitis	$23,238	$1,962	$1,413	$93
Constipation	$13,829	$1,122	$1,196	$142
Crohn's Disease	$22,984	$1,481	$1,533	$829
Diarrhea	$13,697	$1,334	$1,260	$172
Diverticular Disease	$19,523	$915	$1,579	$90
Dysphagia	$18,015	$1,276	$1,131	$92
Eosinophilic esophagitis	$13,407	$1,265	$1,285	$87
Functional GI Disorders	$18,644	$1,206	$1,315	$157
GERD	$18,049	$1,181	$1,230	$83
GI Bleeding	$18,867	$1,272	$1,319	$218
GI Infection	$16,113	$784	$1,323	$125
GI and Hepatic Neoplasms	$36,256	$1,042	$1,395	$112
Gallbladder and biliary tract disease	$20,534	$4,629	$1,658	$101
Gastroduoenal Disorders	$18,753	$1,130	$1,386	$96
Hepatitis B	$16,648	$516	$1,232	$269
Hepatitis C	$37,012	$840	$1,171	$1,458
Hernias	$25,536	$3,710	$1,368	$105
Intestinal Obstruction	$19,542	$1,228	$1,842	$250
NAFLD	$15,454	$1,302	$1,339	$114
NASH	$78,259	$994	$1,303	$107
Nausea and Vomiting	$13,320	$1,058	$1,345	$86
Non-Alcoholic Cirrhosis	$43,733	$1,079	$1,349	$358
Noninfectious gastroenteritis/colitis	$12,218	$1,277	$1,401	$216
Other	$28,979	$1,361	$1,335	$191
Other Esophageal Disorders	$20,743	$1,231	$1,341	$104
Other Liver Disease	$29,245	$1,165	$1,439	$156
Other Pancreatic Disorders	$28,820	$1,745	$1,496	$103
Pancreatic Cysts	$35,172	$2,043	$1,645	$117
Peptic Ulcer Disease	$22,966	$1,076	$1,365	$82
Ulcerative Colitis	$23,507	$1,352	$1,592	$674

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Figure 4. Average cost by clinical condition.

disorders (25%), followed by nausea and vomiting (20%) and noninfectious gastroenteritis/colitis (16%).

There was significant heterogeneity in the distribution of conditions comprising the inpatient setting (Figure 6), with no condition accounting for more than 12% of the total. In contrast, the outpatient and ED to home categories were dominated by abdominal pain (26% and 48%, respectively). Drug utilization was approximated by calculating average number of fills per person by clinical condition and is detailed in Supplemental Figure 1.

Discussion

These findings suggest that nearly one-fourth of individuals in a commercially insured population have a GI diagnosis. Because the study population excluded individuals on the basis of claims-related considerations (eg, total pay <0, all out-of-network claims, etc) to achieve more accurate cost estimates and because prevalence was based on point estimates, it is conceivable that true prevalence was higher. In addition, the relatively low percentage of older adults in the study population likely underestimated the prevalence of chronic GI conditions. However, the significant female predominance of the study population may have counterbalanced some of these effects because some common conditions are known to have a greater female prevalence (eg, irritable bowel syndrome, gallbladder disease). At the individual condition level, prevalence was lower than many recent estimates, such as the 40% worldwide estimate of functional GI disorders[23] or 31% for gastroesophageal reflux disease.[24] However, these differences may be due to the different methodologies used (eg, survey vs

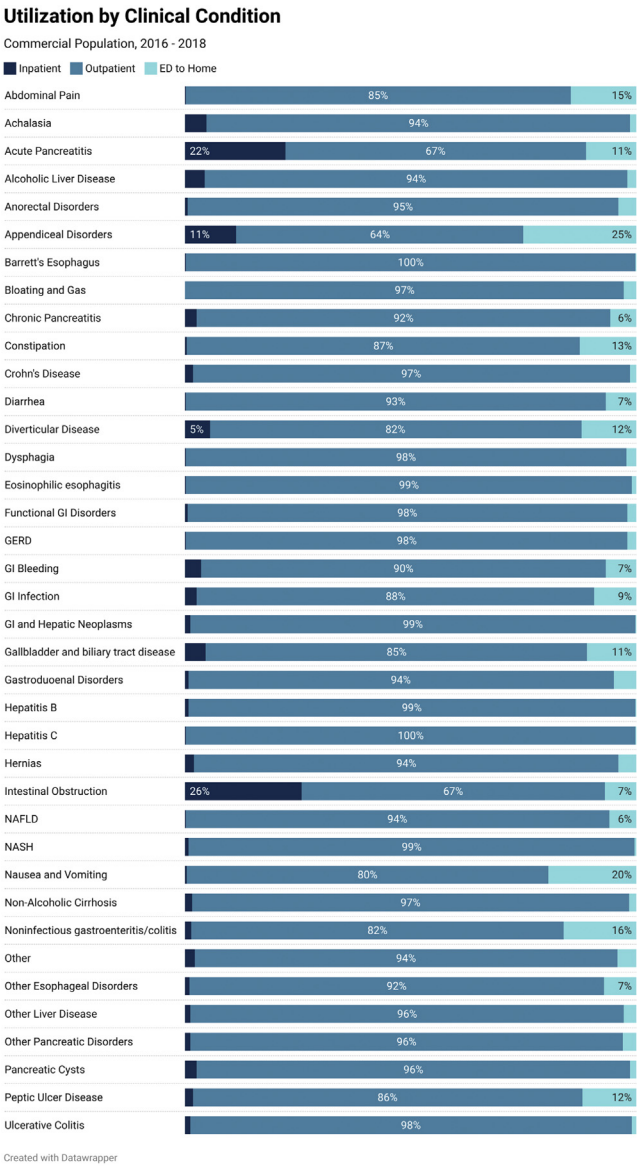

Figure 5. Utilization by clinical condition.

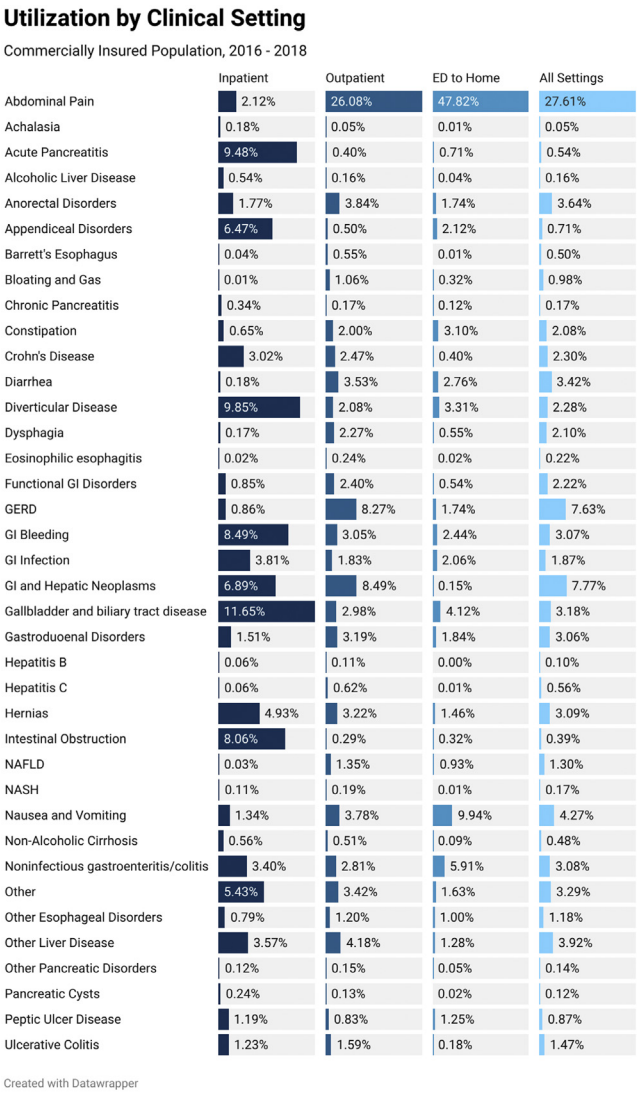

Figure 6. Utilization by clinical setting.

claims), approach to disease classification, and demographic differences such as percent population older than age 65 and socioeconomic variables.

The vast majority of GI encounters during the study period were either outpatient or ED to home, which highlighted the predominance of GI care in the ambulatory setting. Across any condition, inpatient utilization accounted for 10% or more of encounters in only 3 conditions: acute pancreatitis, appendiceal disorders, and intestinal obstruction, the latter of which accounted for the largest single percentage, 26%. In contrast, there were 9 conditions that accounted for 10% or more of ED to home encounters, with appendiceal disorders representing the largest single condition at 25%.

Total annualized all-cause costs for GI conditions ranged broadly, with considerable heterogeneity in medical versus drug costs as well as their relative contributions to the total cost. Intestinal obstruction was the condition with the highest medical spend ($45,533), which was modestly higher than a prior estimate ($29,549–$35,789) that did not include all-cause cost.[25] Hepatitis C had the highest annualized drug cost ($93,432), which was also consistent with previously reported ranges in the United States for a single course of newer direct acting antiviral agents ($17,965–$111,659).[26]

Average costs by setting were dominated in magnitude by inpatient stays across all conditions. NASH had the highest average episodic, inpatient cost ($78,259), which was considerably higher than its corresponding annualized all-cause cost ($22,098), which is more in line with previous all-cause estimates ($21,828–$39,658).[27] This difference supports the corresponding data in Figure 1 that inpatient visits account for only small minority of encounters on average for this condition.

In addition, for many conditions, the average outpatient cost was higher than the average ED to home cost. This may be explained by the majority of endoscopic procedures being performed in ambulatory surgical centers, which are classified as outpatient. This was most

clearly supported by the gallbladder and biliary tract disease condition category ($4629 outpatient vs $1658 ED to home), where non-urgent endoscopic retrograde cholangiopancreatography would likely have a role in driving this cost difference. Because not all GI conditions are chronic, cost per fill data were selected as the metric for episodic drug costs because it can be interpreted more easily across all conditions. The finding of hepatitis C accounting for the highest cost per fill amount is consistent with this condition also having the highest annualized drug spend (Figure 3).

The top 2 conditions driving outpatient utilization (abdominal pain and gastroesophageal reflux disease; Figure 6) were consistent with prior findings in the most recent large-scale analysis.[1] Similarly, the top 3 conditions resulting in ED to home visits (abdominal pain, nausea and vomiting, and noninfectious gastroenteritis/colitis) were also the same. However, there were differences when comparing inpatient utilization; gallbladder and biliary tract disease was the highest condition in this study, followed by acute pancreatitis and gastrointestinal bleeding, whereas Peery et al[1] identified gastrointestinal bleeding as highest, followed by pancreatitis, and cholelithiasis and cholecystitis.

Although assessing the cost of non-GI conditions was out of the scope of this analysis, it is possible to provide some context using outside reference points. For example, the average all-cause cost for other conditions included $16,752 for diabetes,[28] $28,590 for coronary artery disease with angina,[29] $76,969 for stage 4-5 chronic kidney disease,[30] $52,951 for severe systemic lupus erythematosus,[31] $64,555 for sickle cell disease with 2 or more vaso-occlusive crises per year,[32] $18,829 for newly diagnosed multiple sclerosis,[33] and $16,654 for treatment-resistant major depressive disorder.[34] Taken holistically with differences in methodologies aside, the economic burden of digestive conditions in many cases exceeds that of other common and costly diseases.

Limitations

There are several limitations associated with the analyses that impact interpretability of the results. First, the condition groupings reflect a broad range of diseases with variable disease trajectories and acuities. As a result, the summary cost and utilization data may not be representative of all the conditions within a category, and the averages will be biased toward more prevalent conditions. However, these groupings were necessary to provide an aggregate view of the GI landscape and to provide a basis for comparison between categories. Prior studies made inter-condition comparisons more challenging because data were frequently from different sources and time periods, and cost/utilization methodologies varied accordingly. Second, all-cause costs reflected the total healthcare spending associated with a condition category and were inclusive of non-GI conditions claims. As a result, these costs should not be interpreted as solely attributable to GI conditions. To minimize confounding associated with other GI diagnoses in the all-cause analysis, costs were split when concurrent diagnoses were present, and summing of costs stopped when a new GI diagnosis occurred. In this way, costs were not double-counted and were mutually exclusive. In addition, to provide a better sense for GI attribution, the average episodic costs by clinical setting were calculated using data from when only a single GI condition was present and did not include costs from non-GI conditions.

Summary

This analysis provides the most up-to-date assessment of cost, utilization, and prevalence associated with digestive diseases. Because of the single data source used and the standard methodology applied to all clinical categories, the analysis facilitates pragmatic comparison among a wide range of digestive conditions. The results demonstrated that GI conditions are common, heterogeneous in cost and utilization, and collectively exact a significant financial burden on the U.S. adult population.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2021.06.047.

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Conflicts of interest
This author discloses the following: Dr Mathews is an officer at Vivante Health with stock options. The remaining authors disclose no conflicts.

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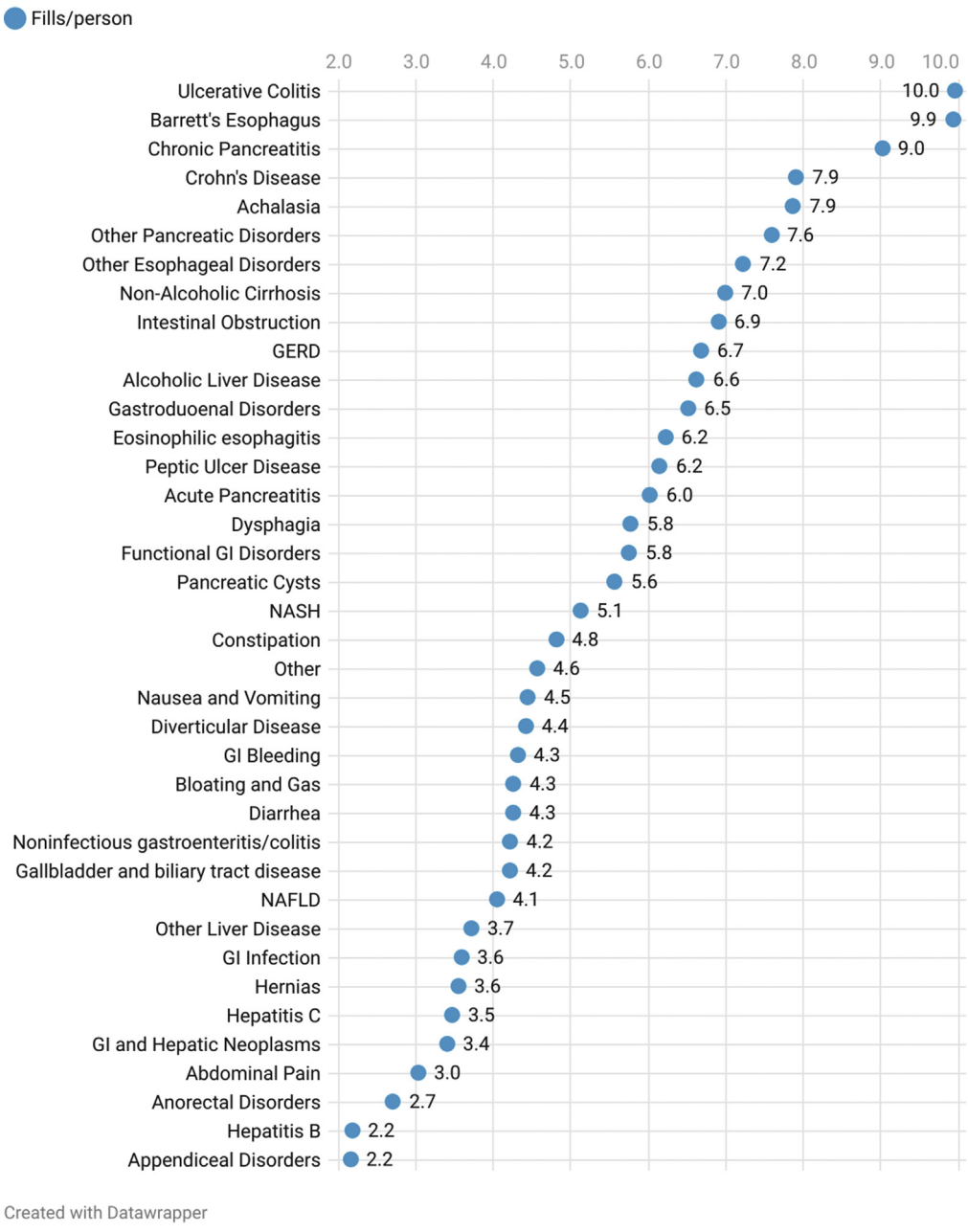

Supplemental Figure 1. Utilization of drug fills by condition.

Supplement 1. Inclusion Criteria

- Subjects with a primary diagnosis in Supplement 2
- Duration of coverage >0
- Capitated = no
- In network = yes
- Total pay >0 (for the claim)
- Also one of the following conditions
  - Revenue code of 450, 451, 452, 456, or 459
    - These are for ED
  - Service categories 12210–12399; 21115–21299; 22315–22588; 30410–30888; 31410–80199 or missing
    - These are all the OP facility codes, so there were excludes when computing IP costs
  - Place of service = 23 and service category > 12399
    - 23 = ED facility; codes >12399 are for professional services (lower codes are facility)

ED, emergency department; IP, inpatient; OP, outpatient.

Supplement 2. ICD-10 Category Groupings

Condition	ICD-10 code(s)
Abdominal pain	R100, R1010, R1011, R1012, R1013, R102, R1030, R1031, R1032, R1033, R10811, R10812, R10813, R10814, R10815, R10816, R10817, R10819, R10821, R10822, R10823, R10824, R10825, R10826, R10827, R10829, R1083, R1084, R109, R1930, R1931, R1932, R1933, R1934, R1935, R1936, R1937
Achalasia	K220
Acute pancreatitis	K850, K8500, K8501, K8502, K851, K8510, K8511, K8512, K852, K8520, K8521, K8522, K853, K8530, K8531, K8532, K858, K8580, K8581, K8582, K859, K8590, K8591, K8592
Alcoholic liver disease	K700, K7010, K7030, K709
Anorectal disorders	K594, K600, K601, K602, K603, K604, K605, K610, K611, K612, K613, K6131, K6139, K614, K615, K620, K621, K622, K623, K624, K626, K627, K6281, K6282, K6289, K629, K640, K641, K642, K643, K644, K645, K648, K649, O872
Appendiceal disorders	K352, K3520, K3521, K353, K3530, K3531, K3532, K3533, K3580, K3589, K35890, K35891, K36, K37, K380, K381, K382, K383, K388, K389
Barrett's esophagus	K2270, K22710, K22711, K22719
Bloating and gas	R140, R141, R142, R143
Chronic pancreatitis	K860, K861
Constipation	K5641, K5900, K5902, K5903, K5904, K5909
Crohn's disease	K5000, K50012, K50013, K50014, K50018, K50019, K5010, K50112, K50113, K50114, K50118, K50119, K5080, K50812, K50813, K50814, K50818, K50819, K5090, K50912, K50913, K50914, K50918, K50919, K51413, K51414
Diarrhea	R197
Diverticular disease	K5700, K5710, K5712, K5720, K5730, K5732, K5740, K5750, K5752, K5780, K5790, K5792
Dysphagia	R130, R1310, R1311, R1312, R1313, R1314, R1319
Eosinophilic esophagitis	K200
Functional GI disorders	K598, K599, K591, K30, K3184, K580, K581, K582, K588, K589, K5901
Gallbladder and biliary tract disease	K9186, K8000, K8001, K8010, K8011, K8012, K8013, K8018, K8019, K8020, K8021, K8030, K8031, K8032, K8033, K8034, K8035, K8036, K8037, K8040, K8041, K8042, K8043, K8044, K8045, K8046, K8047, K8050, K8051, K8060, K8061, K8062, K8063, K8064, K8065, K8066, K8067, K8070, K8071, K8080, K8081, K810, K811, K812, K819, K820, K821, K822, K823, K824, K828, K829, K82A1, K82A2, K830, K8301, K8309, K831, K832, K833, K834, K835, K838, K839, K87
Gastroduodenal disorders	K2920, K2930, K2940, K2950, K2960, K2970, K2980, K2981, K2990, K310, K311, K312, K313, K314, K315, K316, K317, K31819, K3183, K3189, K319, K5281, T182XXA, T183XXA
GERD	K210, K219, R12
GI and hepatic neoplasms	C155, C159, C160, C162, C163, C168, C169, C180, C181, C182, C183, C186, C187, C188, C189, C19, C20, C210, C220, C221, C228, C240, C250, C251, C254, C257, C259, C7A019, C7A026, C7A092, C7B02, D010, D013, D120, D121, D122, D123, D124, D125, D126, D127, D128, D129, D130, D131, D132, D1339, D134, D135, D136, D139, D371, D372, D373, D374, D375, D378, D3A026, K635
GI bleed	K9421, K91870, K91871, I8511, K2211, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K2901, K2921, K2931, K2941, K2951, K2961, K2971, K2991, K31811, K3182, K51411, K51511, K5521, K5701, K5711, K5713, K5721, K5731, K5733, K5741, K5751, K5753, K5781, K5791, K5793, K50011, K50111, K50811, K50911, K51011, K51211, K51811, K51911, K51311, K5701, K5711, K5713, K5721, K5731, K5733, K5741, K5751, K5753, K5781, K5791, K5793, K625, K6381, K91840, K91841, K920, K921, K922, K9401, K9411, P543
GI infection	A000, A001, A009, A011, A012, A013, A014, A020, A028, A029, A030, A031, A032, A033, A038, A039, A040, A041, A042, A043, A044, A045, A046, A0471, A0472, A048, A049, A050, A051, A052, A053, A058, A059, A060, A061, A062, A064, A065, A0689, A069, A070, A071, A072, A073, A074, A078, A079, A080, A0811, A0819, A082, A0831, A0832, A0839, A084, A088, A09, A213, A360, A369, B9681, K630, K650, K651, K652, K653, K658, K659, K9402, K9412, K9422, K9501, K9581, L02211

Supplement 2. Continued

Condition	ICD-10 code(s)
Hepatitis B	B160, B161, B162, B169, B170, B1910, B1911
Hepatitis C	B1710, B1711, B182, B1920, B1921
Hernias	K4000, K4001, K4010, K4011, K4020, K4021, K4030, K4031, K4040, K4041, K4090, K4091, K4100, K4101, K4110, K4111, K4120, K4121, K4130, K4131, K4140, K4141, K4190, K4191, K420, K421, K429, K430, K431, K432, K434, K435, K436, K437, K439, K440, K441, K449, K450, K451, K458, K460, K461, K469
Intestinal obstruction	K433, K561, K562, K563, K5649, K565, K5650, K5651, K5652, K5660, K56600, K56601, K56609, K5669, K56690, K56691, K56699, K913, K9130, K9131, K9132
NAFLD	K760
NASH	K7581
Nausea and vomiting	G43A0, G43A1, K910, R110, R1110, R1111, R1112, R1113, R1114, R112
Nonalcoholic cirrhosis	K7460, K7469
Noninfectious gastroenteritis/colitis	K520, K521, K522, K5221, K5222, K5229, K523, K5281, K5282, K52831, K52832, K52838, K52839, K5289, K529, K5150, K51512, K51518, K51519, K51513, K51514, K5530, K5533
Other	R198, R194, R195, R196, O99613, K9589, K9509, K9423, K9429, K9419, K9420, K9413, K9281, K9289, K929, K9400, I880, K550, K55011, K55012, K55019, K55021, K55022, K55029, K55031, K55032, K55039, K55041, K55042, K55049, K55051, K55052, K55059, K55061, K55062, K55069, K551, K5520, K558, K559, K560, K567, K592, K593, K5939, K631, K632, K633, K634, K6389, K639, K654, K660, K661, K668, K669, K67, K900, K901, K902, K904, K9041, K9049, K9081, K9089, K909, K911, K912, K915, K9161, K9162, K9171, K9172, K9181, K91850, K91858, K91872, K91873, K9403, K9409, K9410, K9189, R150, R151, R152, R1911, R1912, R1915, R192, R159, T184XXA, T185XXA, T188XXA, T188XXD, T189XXA, R161
Other esophageal disorders	B3781, K208, K209, K2210, K222, K223, K224, K225, K228, K229, K23, T18100A, T18108A, T18110A, T18118A, T18120A, T18128A, T18190A, T18198A
Other liver disease	B150, B159, B172, B178, B180, B181, B188, B189, B190, B199, B2681, K716, K7200, K7201, K7210, K7211, K7290, K7291, K730, K731, K732, K738, K739, K740, K741, K742, K743, K744, K745, I8500, I8510, I864, K750, K751, K752, K753, K754, K761, K762, 763, K764, K765, K766, K767, K7681, K7689, K769, K77, K9182, K9183, O26611, O26612, O26613, O26619, O2662, R162, R17, R180, R160, R188, R932, K7589, K759, R740, R945
Other pancreatic disorders	K868, K8681, K8689, K869, K903
Pancreatic cysts	K862, K863
Peptic ulcer disease	K251, K253, K255, K257, K259, K261, K263, K265, K267, K269, K271, K273, K275, K277, K279, K281, K283, K285, K287, K289, K2900
Ulcerative colitis	K5100, K51012, K51013, K51014, K51018, K51019, K5120, K51212, K51213, K51214, K51218, K51219, K5130, K5180, K51812, K51813, K51814, K51818, K51819, K5190, K51912, K51913, K51914, K51918, K51919, K51312, K51313, K51314, K51318, K51319, K5140, K51412, K51418, K51419, K5931

GERD, gastroesophageal reflux disease; GI, gastrointestinal; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

Supplement 3. Drugs Included From Non-GI Therapeutic Class

Drug name	Non-GI therapeutic class
Methylprednisolone	Adrenals & Comb, NEC
Methylprednisolone Acetate	Adrenals & Comb, NEC
Methylprednisolone Sodium Succinate	Adrenals & Comb, NEC
Mometasone Furoate	Adrenals & Comb, NEC
Prednisolone	Adrenals & Comb, NEC
Prednisolone Sodium Phosphate	Adrenals & Comb, NEC
Prednisone	Adrenals & Comb, NEC
Lactulose	Ammonia Detoxicants, NEC
Albendazole	Anthelmintics, NEC
Ivermectin	Anthelmintics, NEC
Mebendazole	Anthelmintics, NEC
Praziquantel	Anthelmintics, NEC
Pyrantel Pamoate	Anthelmintics, NEC
Erythromycin	Antibiot, Erythromycn&Macrolid
Erythromycin Ethylsuccinate	Antibiot, Erythromycn&Macrolid
Erythromycin Stearate	Antibiot, Erythromycn&Macrolid
Fidaxomicin	Antibiot, Erythromycn&Macrolid
Vancomycin HCl;Solution, Multi Ingredient	Antibiotics, Misc
Vancomycin Hydrochloride	Antibiotics, Misc
Erythromycin	Antiinf S/MM,Antibiotic & Comb
Ciprofloxacin Hydrochloride	Antiinfect, Antibiotics EENT
Ciprofloxacin Hydrochloride/Dexamethasone	Antiinfect, Antibiotics EENT
Ciprofloxacin Hydrochloride/Fluocinolone Acetonide	Antiinfect, Antibiotics EENT
Ciprofloxacin Hydrochloride/Hydrocortisone	Antiinfect, Antibiotics EENT
Erythromycin	Antiinfect, Antibiotics EENT
Prednisolone Sodium Phosphate/Sulfacetamide Sodium	Antiinfect, Antiinflam EENT
Trifluridine	Antiinfect, Antivirals EENT
Budesonide	Antiinflam Agents EENT, NEC
Dexamethasone	Antiinflam Agents EENT, NEC
Dexamethasone Sodium Phosphate	Antiinflam Agents EENT, NEC
Prednisolone Acetate	Antiinflam Agents EENT, NEC
Prednisolone Sodium Phosphate	Antiinflam Agents EENT, NEC
Daclatasvir	Antivirals, NEC
Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir	Antivirals, NEC
Dasabuvir;Ombitasvir/Paritaprevir/Ritonavir	Antivirals, NEC
Elbasvir/Grazoprevir	Antivirals, NEC
Glecaprevir/Pibrentasvir	Antivirals, NEC
Ledipasvir/Sofosbuvir	Antivirals, NEC
Ombitasvir/Paritaprevir/Ritonavir	Antivirals, NEC
Ribavirin	Antivirals, NEC

Supplement 3. Continued

Drug name	Non-GI therapeutic class
Ribavirin;Ribavirin	Antivirals, NEC
Simeprevir	Antivirals, NEC
Sofosbuvir	Antivirals, NEC
Sofosbuvir/Velpatasvir	Antivirals, NEC
Sofosbuvir/Velpatasvir/Voxilaprevir	Antivirals, NEC
Natalizumab	Biological Response Modifiers
Mercaptopurine	Chemotherapy
Methotrexate	Chemotherapy
Adalimumab	Immunosuppressants, NEC
Adalimumab;Adalimumab	Immunosuppressants, NEC
Azathioprine	Immunosuppressants, NEC
Certolizumab Pegol	Immunosuppressants, NEC
Cyclosporine	Immunosuppressants, NEC
Cyclosporine, Modified	Immunosuppressants, NEC
Golimumab	Immunosuppressants, NEC
Infliximab	Immunosuppressants, NEC
Infliximab-abda	Immunosuppressants, NEC
Infliximab-dyyb	Immunosuppressants, NEC
Tacrolimus	Immunosuppressants, NEC
Tofacitinib Citrate	Immunosuppressants, NEC
Ustekinumab	Immunosuppressants, NEC
Vedolizumab	Immunosuppressants, NEC
Peginterferon Alfa-2A	Interferons, Antineoplastic
Peginterferon Alfa-2B	Interferons, Antineoplastic
Cholestyramine	Pharmaceutical Aids/Adjuv, NEC
Cholestyramine Resin	Pharmaceutical Aids/Adjuv, NEC
Hydrocortisone	Pharmaceutical Aids/Adjuv, NEC
Hydrocortisone Acetate	Pharmaceutical Aids/Adjuv, NEC
Hydrocortisone Acetate, Micronized	Pharmaceutical Aids/Adjuv, NEC
Hydrocortisone, Micronized	Pharmaceutical Aids/Adjuv, NEC
Methotrexate	Pharmaceutical Aids/Adjuv, NEC
Methylprednisolone	Pharmaceutical Aids/Adjuv, NEC
Methylprednisolone Acetate, Micronized	Pharmaceutical Aids/Adjuv, NEC
Metoclopramide Hydrochloride	Pharmaceutical Aids/Adjuv, NEC
Metronidazole	Pharmaceutical Aids/Adjuv, NEC
Metronidazole Benzoate	Pharmaceutical Aids/Adjuv, NEC
Ondansetron Hydrochloride	Pharmaceutical Aids/Adjuv, NEC
Peppermint Oil	Pharmaceutical Aids/Adjuv, NEC
Prednisolone	Pharmaceutical Aids/Adjuv, NEC
Prednisolone Acetate	Pharmaceutical Aids/Adjuv, NEC
Prednisolone Sodium Phosphate	Pharmaceutical Aids/Adjuv, NEC

Supplement 3. Continued

Drug name	Non-GI therapeutic class
Prednisone	Pharmaceutical Aids/Adjuv, NEC
Prednisone, Micronized	Pharmaceutical Aids/Adjuv, NEC
Rifaximin	Pharmaceutical Aids/Adjuv, NEC
Simethicone	Pharmaceutical Aids/Adjuv, NEC
Sulfasalazine	Pharmaceutical Aids/Adjuv, NEC
Tacrolimus	Pharmaceutical Aids/Adjuv, NEC
Ciprofloxacin	Quinolones, NEC
Ciprofloxacin Hydrochloride	Quinolones, NEC
Ciprofloxacin/Ciprofloxacin Hydrochloride	Quinolones, NEC
Tacrolimus	S/MM Miscellaneous, NEC
Sulfasalazine	Sulfonamides & Comb, NEC
Metronidazole	
Prednisolone	
Prednisolone Sodium Phosphate	
Varicella Virus Vaccine, Live	