Health Care Resource Use and Costs Pre- and Post-Treatment Initiation With Linaclotide: Retrospective Analyses of a U.S. Insured Population

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ABSTRACT

Purpose: To evaluate gastrointestinal (GI)-related and irritable bowel syndrome (IBS)/constipation-related health care resource use (HCRU) and costs following linaclotide treatment initiation among U.S. commercially insured (commercial) and Medicare Advantage with Part D (Medicare) patients.

Design: Patients age ≥18 years with ≥1 pharmacy claim for linaclotide between December 2012 and June 2013 were identified using claims data from a U.S. health plan. Index date was the date of the first linaclotide claim. Patients were continuously enrolled in a health plan for 6 months pre- and ≥6 months post-index.

Methodology: GI-related and IBS/constipation-related HCRU and costs were standardized to per patient per month (PPPM), and included physician office, outpatient facility, emergency department (ED), and inpatient visits and pharmacy use.

Results: Overall, 2,254 patients were included (commercial, n=1,822; Medicare, n=432). GI-related PPPM office and outpatient visits decreased post-linaclotide treatment initiation for commercial and Medicare patients (all $P<.001$), while IBS/constipation-related office visits decreased in both populations (both $P<.001$). Although PPPM pharmacy costs increased, PPPM costs decreased for GI-related medical services, including commercial and Medicare office visits and commercial outpatient and ED visits (all $P<.001$). Similarly, mean IBS/constipation-related PPPM costs decreased for commercial and Medicare office visits ($P<.001$) and commercial outpatient ($P=.01$) and ED visits ($P=.004$).

Conclusion: While pharmacy costs increased as expected with the introduction of a new treatment in an over-the-counter/generic treatment dominated market, outpatient GI-related and IBS/constipation-related medical HCRU and costs substantially decreased among commercial and Medicare patients following linaclotide treatment initiation, suggesting a positive impact of linaclotide on patients' health care in this population.

INTRODUCTION

Irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC) are common functional gastrointestinal (GI) disorders, with U.S. prevalence rates between 4.3% and 5.2% for IBS-C (Doshi 2014, Hungin 2005, Saito 2002, Talley 1995) and 12.0% and 19.0% for CIC (Choung 2007, Higgins 2004, Lacy 2016, Lembo 2003). IBS-C is characterized by recurrent abdominal pain associated with bowel symptoms of constipation (Chang 2014a, Lacy 2016). CIC, also referred to as functional constipation or chronic constipation, is characterized by infrequent bowel movements, hard or lumpy stools, straining, and a sensation of incomplete rectal evacuation (Ford 2014). Diagnostic criteria for IBS-C require the presence of abdominal pain and a ≥6-month history of constipation, while in CIC, predominant symptoms include difficult, infrequent, or incomplete defecation. Symptoms are often overlapping between IBS-C and CIC (Ford 2014, Lacy 2016).

The recurrent, bothersome symptoms of IBS-C and CIC may profoundly reduce patients' quality of life (Dibonaventura 2011, Nellesen 2013, Sun 2011), with increased health care-seeking behavior, missed workdays, and disrupted productivity (Heidelbaugh 2015). Additionally, IBS-C and CIC are associated with a substantial economic burden. In a study evaluating health care costs among IBS-C patients in a commercially insured population, incremental annual health care costs associated with IBS-C were $3,856 (2010 U.S. dollars) per patient per year, primarily driven by more frequent use of medical services including inpatient, emergency department (ED), and physician office visits and other outpatient services (Doshi 2014). GI-related and IBS-C-related costs comprised 39.8% and 11.9% of total all-cause costs, respectively (Doshi 2014). In a study of costs associated with CIC, mean annual all-cause health care costs for CIC were estimated at $3,508 (2010 U.S. dollars) per patient per year, the majority of which were attributable to outpatient service use (Cai 2014).

GI-related costs composed 33.7% of the total costs, while constipation-related costs accounted for 10.5% (Cai 2014). An analysis from 2008 using data obtained from a direct health care provider in Olmsted County, Minnesota, found that outpatient medical costs for IBS-C ($6,800) and CIC ($6,284) patients were higher compared to controls ($4,242 and $5,254, respectively) during a two-year period (Herrick 2017). Effective treatments for IBS-C and CIC may potentially reduce health care resource use (HCRU) and associated medical costs, since inadequate symptom control in IBS-C and CIC has been shown to contribute to substantial increases in HCRU and costs (Guerin 2014).

Current medications used to treat IBS-C and CIC include over-the-counter laxatives, bulking agents, and stool softeners, as well as prescription medications including lubiprostone, plecanatide, and linaclotide (Chey 2015, Ford 2014, Jiang 2015). Linaclotide is an orally administered guanylate cyclase-C agonist approved by the FDA for the treatment of adults with IBS-C and CIC (Linzess 2012). Clinical trials of linaclotide showed improvement among patients with IBS-C, including reduced abdominal pain and increased frequency of bowel movements (Ford 2014, Chey 2012). Along with improvement in clinical outcomes, linaclotide use in IBS-C patients is associated with improved quality of life (Atluri 2014), as well as improvements in work productivity and reductions in daily activity impairment (Buono 2014). Similarly, linaclotide-treated CIC patients had statistically significantly improved symptoms and health-related quality of life compared to placebo-treated patients (Chang 2014b). However, the impact of linaclotide treatment on HCRU (including inpatient, outpatient, and ED services) and costs has not been explored. The purpose of this study was to characterize GI-related and IBS/constipation-related HCRU and costs before and after initiation of treatment with linaclotide among a sample of insured patients using data from a large health care claims database.

SOME ABBREVIATIONS USED IN THIS ARTICLE

CIC
Chronic idiopathic constipation
HCRU
Health care resource use
ICD-9-CM
International Classification of Disease, Ninth Revision, Clinical Modification
IBS-C
Irritable bowel syndrome with constipation
ORD
Optum Research Database
PPPM
Per-patient per-month
SD
Standard deviation

METHODS

Data source

Claims data were extracted from the Optum Research Database (ORD). The ORD contains medical and pharmacy claims and enrollment information for approximately 12 million patients annually from a large U.S. health plan with national coverage. The underlying information is geographically diverse and broadly representative of the overall U.S. insured population. Medical claims data include *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes, place of service codes, and health plan- and patient-paid amounts from providers and facilities. Pharmacy claims data consist of National Drug Codes for filled prescriptions, days of supply, quantity of drug supplied, drug strength, and health plan- and patient-paid amounts.

All data used in this study were de-identified and accessed through protocols compliant with the Health Insurance Portability and Accountability Act of 1996; therefore, no waiver of informed consent was required from an institutional review board.

Study design and patient selection

This study was a retrospective U.S. administrative claims database analysis of patients age ≥18 years with ≥1 pharmacy claim for linaclotide during the identification period from Dec. 1, 2012, to June 30, 2013. The date of the first linaclotide claim was defined as the index date. The pre-index period was defined as 6 months prior to the index date; the post-index period began on the index date and extended ≥6 months up until the patient unenrolled from the health plan or January 31, 2014, whichever came first. Patients were required to have continuous enrollment in commercial or Medicare health plans with medical and pharmacy benefits during both the pre-index and post-index periods.

Study measures

Demographic information including age, sex, U.S. census geographic region, and health plan type (commercial or Medicare) and subtype (exclusive provider organization, health maintenance organization, indemnity health plan, point-of-service health plan, or preferred provider organization) were identified on the index date. The Quan-Charlson comorbidity score was calculated based on the presence of diagnosis codes on medical claims during the pre-index period (Bayliss 2012, Quan 2011).

Outcome measures included GI-related and IBS/constipation-related HCRU and costs analyzed for both

the pre- and post-index periods. GI-related HCRU and costs were based on claims for IBS, constipation, and eight GI-related comorbidities prevalent among IBS-C and CIC patients identified using ICD-9-CM diagnosis codes in the primary position, as follows: IBS (564.1x), constipation (564.0x), abdominal pain (789.0x), bloating (787.3x), gastroesophageal reflux disease (530.81), esophagitis (530.1x), dyspepsia (536.8x), gallbladder or biliary disease (574.xx), GI hemorrhage/bleeding (578.xx), or hemorrhoids (455.xx) (Doshi 2014). IBS/constipation-related HCRU and costs were a subset of the GI-related HCRU, and costs focused only on claims with an ICD-9-CM diagnosis code in the primary position for IBS and/or constipation.

HCRU was identified through medical claims for office visits, outpatient facility visits, inpatient facility visits, and ED visits and summarized as per-patient, per-month (PPPM) counts. PPPM counts represented a patient-level measure defined as the outcome captured across the entire post-index period divided by the length of the post-index period multiplied by 30, and as the proportion of patients using each service. PPPM analyses reflect use and costs while considering the maximum sample and patient contributions of variable observation time. Health care costs, adjusted to 2013 U.S. dollars using the Consumer Price Index (BLS 2016), included both health plan- and patient-paid amounts summarized as PPPM costs. Costs were categorized as total costs (sum of medical and pharmacy costs), medical costs (office, outpatient, ED, and inpatient visits), and pharmacy costs. GI-related and IBS/constipation-related medical costs were defined based on the same medical claims criteria used to identify HCRU. GI-related and IBS/constipation-related pharmacy costs were the same and calculated from pharmacy claims for linaclotide and lubiprostone (plecanatide was not available at the time the study was conducted) and additional prescription medications for constipation (stimulant laxatives, osmotic laxatives, bulk-forming agents, lubricant laxatives, stool softeners, and combination products; Appendix A). The overall frequency and cost PPPM of GI-related procedures (Appendix B) pre- and post-index were also calcu-

FIGURE 1
Patient identification flow chart

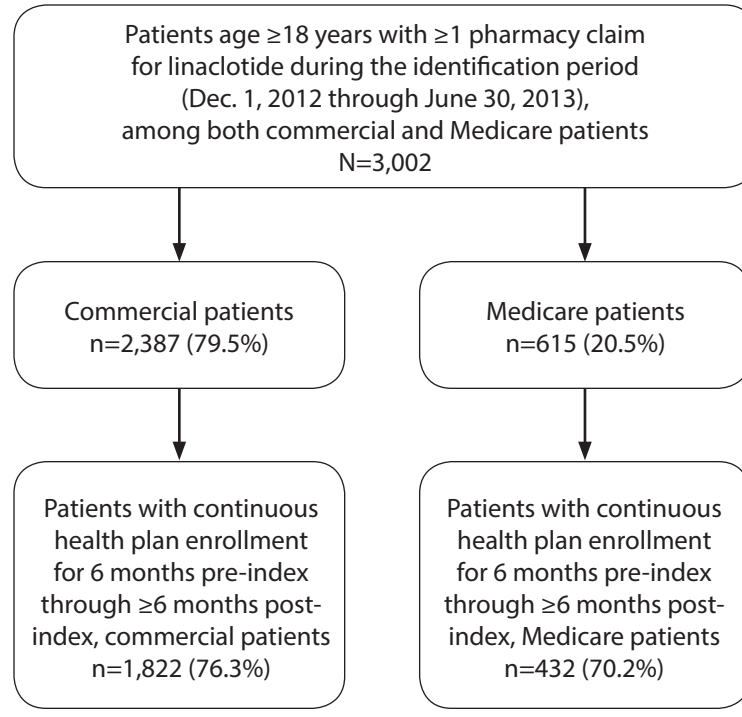

TABLE 1
Demographics and clinical characteristics

	Overall (N=2,254)	Commercial (n=1,822)	Medicare (n=432)
Age, mean (SD)	51.8 (15.2)	48.0 (13.2)	67.8 (12.6)
Female, n (%)	1,859 (82.5)	1,551 (85.1)	308 (71.3)
Quan-Charlson comorbidity score, mean (SD)	0.7 (1.2)	0.5 (1.1)	1.3 (1.6)
Geographic region, n (%)			
Northeast	257 (11.4)	189 (10.4)	68 (15.7)
Midwest	498 (22.1)	386 (21.2)	112 (25.9)
South	1,280 (56.8)	1,047 (57.5)	233 (53.9)
West	219 (9.7)	200 (11.0)	19 (4.4)

SD=standard deviation.

TABLE 2
GI-related and IBS/constipation-related PPPM HCRU counts

	Commercial (n=1,822)			Medicare (n=432)		
Mean (SD) PPPM counts	**Pre-index**	**Post-index**	***P* value**	**Pre-index**	**Post-index**	***P* value**
GI-related HCRU						
Office visits	0.24 (0.26)	0.13 (0.19)	<.001	0.25 (0.32)	0.15 (0.21)	<.001
Outpatient visits	0.16 (0.32)	0.09 (0.21)	<.001	0.15 (0.31)	0.09 (0.19)	<.001
ED visits	0.02 (0.09)	0.01 (0.06)	<.001	0.04 (0.11)	0.03 (0.09)	.20
Inpatient visits	0.01 (0.03)	0 (0.02)	.01	0.02 (0.08)	0.01 (0.05)	.04
IBS/constipation-related HCRU						
Office visits	0.11 (0.16)	0.07 (0.13)	<.001	0.11 (0.17)	0.08 (0.13)	<.001
Outpatient visits	0.04 (0.14)	0.03 (0.11)	<.001	0.04 (0.15)	0.03 (0.11)	.06
ED visits	0.01 (0.03)	0 (0.02)	<.001	0.01 (0.04)	0.01 (0.04)	.93
Inpatient visits	0 (0.01)	0 (0.01)	.87	0 (0.03)	0 (0.02)	.25

ED=emergency department, GI=gastrointestinal, HCRU=health care resource use, IBS=irritable bowel syndrome, PPPM=per patient per month, SD=standard deviation.

TABLE 3
GI-related and IBS/constipation-related PPPM HCRU costs

	Commercial (n=1,822)			Medicare (n=432)		
Mean (SD) PPPM costs, U.S. dollars	**Pre-index**	**Post-index**	***P* value**	**Pre-index**	**Post-index**	***P* value**
GI-related HCRU						
Medical Office visits	36 (66)	19 (52)	<.001	27 (43)	14 (23)	<.001
Outpatient visits	96 (279)	52 (168)	<.001	32 (104)	23 (104)	.18
ED visits	23 (112)	12 (62)	<.001	19 (67)	15 (46)	.21
Inpatient visits	78 (650)	75 (862)	.90	247 (1,184)	213 (1,137)	.64
Pharmacy	17 (50)	99 (83)	<.001	34 (74)	116 (98)	<.001
Total (medical + pharmacy)	254 (789)	261 (904)	.81	365 (1,218)	383 (1,165)	.81
IBS/constipation-related HCRU						
Medical Office visits	14 (30)	9 (40)	<.001	10 (16)	7 (14)	.001
Outpatient visits	20 (95)	13 (75)	.01	7 (32)	7 (75)	.94
ED visits	4 (37)	1 (14)	.004	3 (24)	3 (16)	.54
Inpatient visits	17 (358)	34 (671)	.34	104 (879)	51 (468)	.21
Pharmacy	17 (50)	99 (83)	<.001	34 (74)	116 (98)	<.001
Total (medical + pharmacy)	73 (395)	157 (687)	<.001	160 (889)	183 (490)	.59

ED=emergency department, GI=gastrointestinal, HCRU=health care resource use, IBS=irritable bowel syndrome, PPPM=per patient per month, SD=standard deviation.

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Statistical analysis

Data were analyzed descriptively to compare HCRU and costs in the pre- and post-index periods for commercial and Medicare patients. Counts and percentages are presented for binary and categorical variables; means and standard deviations (SDs) are presented for continuous variables. Differences in HCRU and costs were examined with McNemar's test for binary and categorical variables (exact McNemar's test was used for analysis of GI-related procedures) and paired t-tests for continuous variables. Differences were considered statistically significant at $P<.05$. All analyses were conducted using SAS version 9.2 (SAS, Cary, N.C.).

RESULTS

Patient baseline characteristics

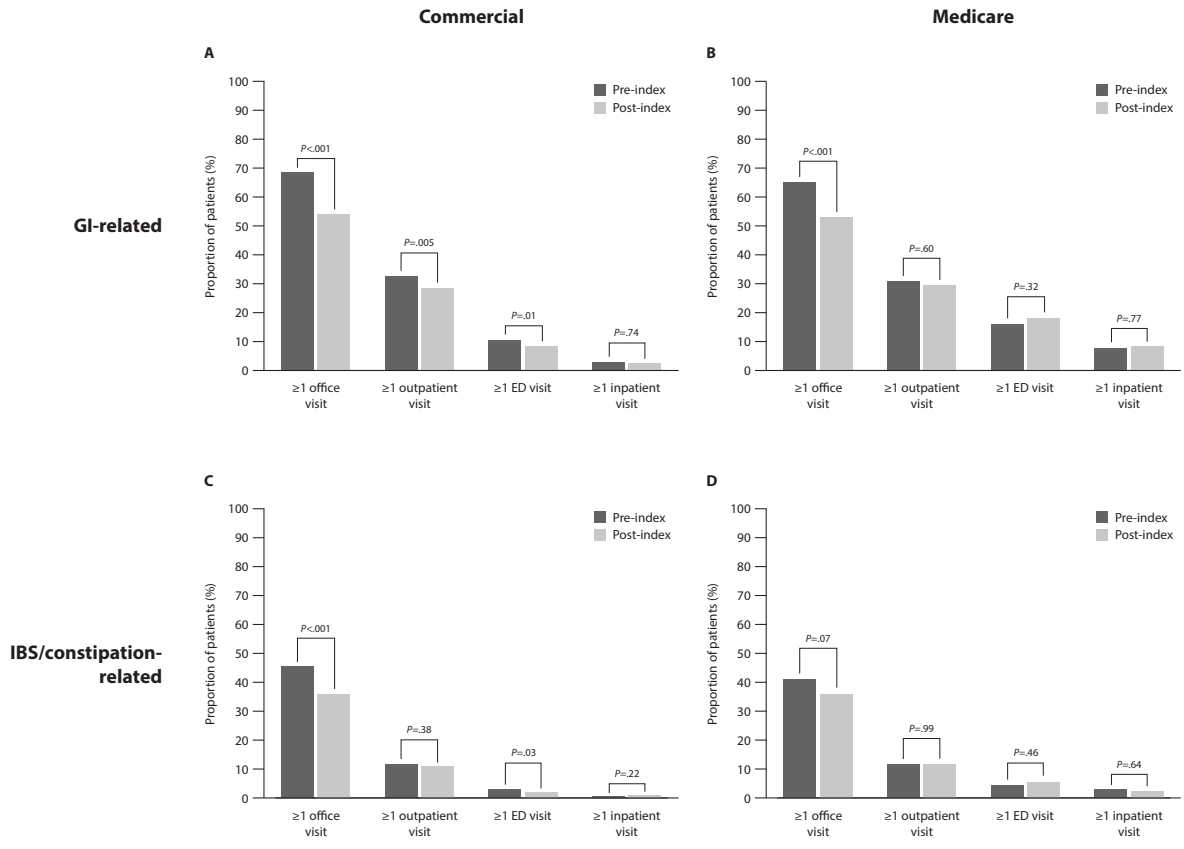
A total of 2,254 patients (1,822 commercial; 432 Medicare) met the inclusion criteria and were included for analysis (Figure 1). Mean age was 51.8 years (commercial, 48.0 years; Medicare, 67.8 years); 82.5% were female (commercial, 85.1%; Medicare, 71.3%). Patients in the Medicare population had a higher Quan-Charlson comorbidity score (mean [SD]: 1.3 [1.6]) compared to those in the commercial population (0.5 [1.1]) [Table 1]. More than three quarters (76.1%) of commercial patients had a point-of-service type of health plan (data not shown).

GI-related HCRU and costs

Following initiation of linaclotide, decreases in GI-related HCRU were observed. In particular, statistically significant reductions were observed among the proportion of commercial patients with at least one GI-related office, outpatient, or ED visit (Figure 2). Furthermore, mean PPPM resource use decreased statistically sig-

FIGURE 2

Proportion of commercial and Medicare patients using GI-related and IBS/constipation-related health care services



ED=emergency department, GI=gastrointestinal, IBS=irritable bowel syndrome.

nificantly among commercial patients for all GI-related categories of service use, including office, outpatient, ED, and inpatient visits (Table 2). GI-related health care costs for office, outpatient, and ED visits decreased after linaclotide treatment initiation among commercial patients, while pharmacy costs increased (Table 3).

Among Medicare patients, reductions in HCRU were also observed for the proportion of patients with at least one GI-related office visit (Figure 2). Mean PPPM resource use decreased statistically significantly among Medicare patients for GI-related office, outpatient, and inpatient visits following the initiation of linaclotide (Table 2). Medicare patients also incurred statistically significantly lower GI-related office visit costs post-linaclotide, while pharmacy costs increased (Table 3).

Among all patients, colonoscopy and esophagogastroduodenoscopy were the most common GI-related procedures pre- and post-linaclotide treatment initiation (Appendix B). The proportion of patients with a claim for a colonoscopy decreased statistically significantly following the initiation of linaclotide (17.0% to 14.2%, P=.01). PPPM costs for GI-related procedures decreased statistically significantly following initiation of linaclotide for colonoscopies ($41 to $19, P<.001) and esophagogastroduodenoscopies ($27 to $16, P<.001) [Appendix B].

IBS/constipation-related HCRU and costs

In analyses specific to IBS/constipation-related HCRU, the proportion of commercial patients with at least one IBS/constipation-related office or ED visit decreased following the initiation of linaclotide (Figure 2). The mean PPPM numbers of IBS/constipation-related office, outpatient, and ED visits decreased statistically significantly among commercial patients, while IBS/constipation-related inpatient visits, which were infrequent, remained unchanged pre- and post-linaclotide treatment initiation (Table 2). Similar to the results observed for GI-related PPPM costs, IBS/constipation-related PPPM costs decreased for office, outpatient, and ED visits among commercial patients, while pharmacy costs increased (Table 3).

For Medicare patients, differences for IBS/constipation-related office, outpatient, ED, and inpatient visits pre- and post-linaclotide treatment initiation were not statistically significantly different (Figure 2). However, mean PPPM IBS/constipation-related office visits decreased significantly (Table 2); office visit PPPM costs also decreased significantly, while pharmacy costs increased (Table 3).

DISCUSSION

This study is the first to provide insight into GI-related and IBS/constipation-related HCRU and costs pre- and post-initiation of linaclotide treatment among patients in a real-world setting. Statistically significant reductions in GI-related and IBS/constipation-related PPPM HCRU and costs were observed for office, outpatient, and ED visits among commercial patients, while GI-related and IBS/constipation-related PPPM HCRU and costs for office visits significantly decreased among Medicare patients following linaclotide treatment initiation. The higher age and increased comorbidities in Medicare patients compared to commercial patients may have contributed to the differences in observed HCRU and costs between these two populations. The statistically significant reductions observed in HCRU and related costs may be meaningful and relevant for most contexts because of the real-world setting of this study.

Pharmacy costs, standardized on a PPPM basis, increased as expected among both commercial and Medicare patients, given the introduction of a new prescription medication to a market dominated by over-the-counter/generic treatments. In this analysis, all patients were required to have a new claim for linaclotide. Patients newly initiating linaclotide therapy may have previously been treated only with over-the-counter or generic medications, thus incurring increased pharmacy costs. However, decreased health care-seeking behavior was observed among patients initiating linaclotide, as evidenced by the observed reductions in medical service use following linaclotide treatment initiation. Specifically, GI-related and IBS/constipation-related PPPM HCRU decreased across multiple visit types for both commercial and Medicare patients, including office and outpatient visits. The GI-related PPPM costs associated with medical HCRU were also significantly lower for office, outpatient, and ED visits among commercial patients and office visits among Medicare patients. These results indicate that increased health care costs primarily driven by pharmacy costs may be associated with the introduction of linaclotide use and were partially offset in some patients by reductions in HCRU.

Similar findings have also been observed with treatment of other chronic diseases, where increased pharmacy costs for prescriptions of novel therapies were offset by reduced HCRU (Ke 2015). Future studies assessing long-term linaclotide treatment use could provide further information on the sustainability of the HCRU and cost reductions observed in this study.

Limitations

As with any retrospective claims database analysis, certain limitations should be taken into consideration. The population included in this analysis consisted of a U.S. commercial and Medicare insured sample; therefore, results may not be generalizable to

uninsured and Medicaid patients. Furthermore, while all patients included in this study had at least one filled prescription for linaclotide, which is FDA-approved only for the treatment of IBS-C and CIC and often requires preauthorization for benefit coverage, the presence of a diagnosis code on a medical claim is not positive proof of disease.

Estimation of HCRU and costs may also be confounded by certain factors. For instance, the reduction in IBS/constipation-related HCRU and costs observed in this study may result from regression to the mean or the length of the follow-up period. Pharmacy use and costs are limited to those medications pre-identified as those for IBS-C and CIC; any other treatments used that may have been related to constipation treatment were not included. Furthermore, the presence of a claim for a filled prescription does not guarantee the medication was taken as prescribed; some patients may receive medication as samples, resulting in an underestimation of pharmacy costs. Indirect costs such as lost work productivity were not available within the ORD, which may contribute to an underestimation of the economic burden associated with IBS-C and CIC and, therefore, the benefit that linaclotide treatment may have on reducing the overall burden associated with these conditions.

Given the recent introduction of linaclotide at the time this study was conducted, this study was completed on a limited timeframe without a comparison cohort. Hence, this study reflects outcomes from limited, early use of linaclotide that may not reflect full use and cost changes as a result of sustained use of linaclotide.

CONCLUSION

In this retrospective database analysis of commercially and Medicare-insured patients treated with linaclotide, pharmacy costs increased for all patients after linaclotide treatment initiation. However, a statistically significant decrease in GI-related and IBS/constipation-related outpatient service use and associated medical costs was observed, suggesting that linaclotide may have been an effective treatment for patients included in this analysis. Despite increased pharmacy costs, effective treatment of IBS-C and CIC patients could decrease HCRU and costs and potentially mitigate the broader economic impact (such as absenteeism and lost productivity) of these conditions.

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Disclosures: This study was sponsored by Allergan plc and Ironwood Pharmaceuticals Inc., which market Linzess (linaclotide), with analysis conducted by Optum. Taylor is an employee of Ironwood Pharmaceuticals Inc. and owns stock/stock options. Abel and Carson are employees of Allergan plc and own stock/stock options. Bancroft, Buzinec, Goolsby Hunter, and Martin are employees of Optum and own stock in UnitedHealth Group, the parent company of Optum; Optum has received funding from Allergan plc and Ironwood Pharmaceuticals, Inc. for completion of the study.

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors. Taylor, Abel, and Carson were involved in the study design, evaluation, and interpretation of data; Bancroft, Buzinec, Goolsby Hunter, and Martin were involved in the study design, analysis, evaluation, and interpretation of data. All authors approved the final submitted manuscript and agree to be accountable for all aspects of the work.

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APPENDIX A

GI-related procedures and GI-related and IBS/constipation-related prescription medications

GI-related procedures
Colonography; GI tract transit and pressure measurement; colostomy; colonoscopy; biopsy of intestine; proctosigmoidoscopy; sigmoidoscopy; anoscopy; colon motility study; colorectal cancer screening; myotomy; upper and lower endoscopy; esophagoscopy; esophagogastroduodenoscopy; endoscopic retrograde cholangiopancreatography
Prescription medication class
Stimulant laxatives; osmotic laxatives; bulk-forming agents; lubricant laxative; stool softeners; combination products

GI=gastrointestinal, IBS=irritable bowel syndrome.

APPENDIX B

Proportion of patients and costs associated with GI-related procedures

Proportion of patients with GI-related procedures, n (%)	**Pre-index (n=2,254)**	**Post-index (n=2,254)**	***P* value**
Colonoscopy	384 (17.0)	319 (14.2)	.01
Esophagogastroduodenoscopy	350 (15.5)	307 (13.6)	.07
Colorectal cancer screening	39 (1.7)	33 (1.5)	.54
Sigmoidoscopy	29 (1.3)	27 (1.2)	.89
Biopsy of intestine	24 (1.1)	24 (1.1)	1.00
Anoscopy	16 (0.7)	23 (1.0)	.32
Upper and lower endoscopy	11 (0.5)	10 (0.4)	.99
Proctosigmoidoscopy	5 (0.2)	10 (0.4)	.30
Endoscopic retrograde cholangiopancreatography	5 (0.2)	4 (0.2)	1.00
GI tract transit and pressure measurement	3 (0.1)	4 (0.2)	1.00
Colonography	3 (0.1)	1 (0.0)	.63
Colon motility study	1 (0.0)	0 (0.0)	1.00
Esophagoscopy	0 (0.0)	1 (0.0)	1.00
Mean (SD) PPPM costs, U.S. dollars	**Pre-index (n=2,254)**	**Post-index (n=2,254)**	***P* value**
Colonoscopy	41 (209)	19 (129)	<.001
Esophagogastroduodenoscopy	27 (105)	16 (64)	<.001
Biopsy of intestine	17 (261)	13 (222)	.45
Upper and lower endoscopy	4 (103)	2 (40)	.27
Sigmoidoscopy	2 (42)	4 (81)	.44
Colorectal cancer screening	1 (15)	1 (7)	.06
Endoscopic retrograde cholangiopancreatography	1 (33)	0 (12)	.16
Proctosigmoidoscopy	0 (1)	2 (79)	.17
Colonography	0 (6)	0 (1)	.45
GI tract transit and pressure measurement	0 (5)	0 (5)	.70
Anoscopy	0 (2)	0 (2)	.42
Esophagoscopy	0 (0)	0 (0)	.32

There were no incidences of colostomy or myotomy.
GI=gastrointestinal, PPPM=per patient per month, SD=standard deviation.