Prescribing Patterns for Outpatient Treatment of Constipation, Irritable Bowel Syndrome-Related Constipation, and Opioid-Induced Constipation: A Retrospective Cross-Sectional Study

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ABSTRACT

BACKGROUND: Despite national recommendations for treatment of constipation, prescribing patterns for treatment are inconsistent, and health care utilization has increased.

OBJECTIVE: To identify patterns in pharmacologic and nonpharmacologic treatment of constipation and associations between treatment and other variables across age groups.

METHODS: This was a retrospective cross-sectional study that used the National Ambulatory Medical Care Survey (NAMCS) to compare prescribing from 2000 to 2004 and from 2005 to 2009. Treatment patterns for constipation, irritable bowel syndrome-related constipation (IBS-C), and opioid-induced constipation were considered.

RESULTS: From 2000 to 2009, there were 89.6 million office visits related to constipation: 63.4 million for constipation alone, 28.2 million for IBS-C alone, and 3.7 million for opioid-induced constipation. For constipation, there was an overall decrease in the prescription of combination therapy (17% vs. 11%, $P < 0.05$); an increase in the prescription of medication monotherapy (21% vs. 29%, $P < 0.05$); decreases in the use of lubricants (9% vs. 2%, $P < 0.05$) and saline (7% vs. 1%, $P < 0.001$) among patients aged < 18 years; a decrease in combination therapy (31% vs. 17%, $P < 0.05$); and age group differences in the prescription of specific medications. For IBS-C and opioid-induced constipation, there were no changes in major treatment category or specific medication. Age, gender, race, ethnicity, payer source, physician specialty, and region were all found to be associated with treatment choice.

CONCLUSIONS: Health care utilization for constipation increased, and prescribing patterns shifted significantly from 2000 to 2009 for constipation and IBS-C. Patterns in treatment were significantly influenced by many factors, including age, gender, and race. Changes in treatment categories over time included a decrease in combination therapy for patients aged < 18 years and an increase in medication monotherapy for all ages, which are in contrast to national recommendations.

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What is already known about this subject

- A variety of drugs are used for treating constipation.
- Prior studies suggest that prescriptions for constipation treatments do not align with expert recommendations.

What this study adds

- Prescribing practices for constipation and irritable bowel syndrome-related constipation (IBS-C) are associated with many factors, including age, gender, and race.
- Prescriptions for combination therapy for children and adolescents have decreased over time, while prescriptions for medication monotherapy have increased over time.
- Treatment trends for constipation and IBS-C are not aligned with current treatment recommendations.

Although constipation is not commonly perceived as a high-risk condition by health care providers, it does commonly and significantly impair quality of life, leading to increased health care utilization and costs across all populations.[1,2] While the risk of constipation increases with age, 23% of all children and adolescents suffer from constipation.[2-4] Because of the widespread incidence of constipation and its impact on quality of life, health care expenditures for constipation average $1 billion each year, with additional out-of-pocket expenditures of $800 million annually on laxatives alone.[5,6]

The high cost of constipation management and the impact on quality of life necessitate prompt and appropriate treatment. The treatment goals are to alleviate symptoms (e.g., bloating and abdominal pain) and prevent more severe complications, such as fissures, fecal impaction, hemorrhoids, and loss of stool control.[1,7,8]

Unfortunately, there are limited evidence-based treatment options, and most of the current treatments are based largely on historical practices[1,9]; consequently, there is great variation in the treatments prescribed, varying by factors such as geographical location and physician specialty.[2,10-12] To standardize and optimize treatments, expert recommendations suggest approaches to treating the different types of constipation.[1,7,9-10] For chronic constipation, the recommendations for adults and children are to start with nonpharmacologic lifestyle modifications that include increased exercise, water, and fiber intake. The first step for children also includes the addition of medications, whereas for adults, medications are not added until the second step.[7,9,12] Treatment of irritable bowel syndrome-related

constipation (IBS-C) begins with increasing fiber and then adding medications.[1] Since 2009, an updated set of clinical practice guidelines has been published; however, the general recommendations for treatment have not changed.

Examining the changes in the prescription of treatment for constipation from 1997 to 2006, Trinkley et al. (2010) found that the use of nonpharmacologic monotherapy decreased and the use of medications alone increased.[12] However, this study did not consider IBS-C nor evaluate the treatment of opioid-induced constipation, which are common forms of constipation. To date, no studies have evaluated the prescribing patterns for IBS-C or opioid-induced constipation nor have studies considered the influence of new drugs on prescribing patterns for constipation.

Understanding the prescribing patterns for constipation and IBS-C treatment and how they align with guidelines is of particular importance to managed care pharmacy. Identification of prescribing patterns that deviate from evidence-based recommendations and standards allow for targeted interventions that are meant to improve patient outcomes and reduce health care utilization and costs. To that end, the purpose of this study was to identify the patterns in the medication management of constipation and the associations between treatment and other variables. This study was deemed exempt by the institutional review board for The Ohio State University.

Methods

The National Ambulatory Medical Care Survey

The National Ambulatory Medical Care Survey (NAMCS) provides data on outpatient physician office visits in the United States, such as patient symptoms, diagnoses, medications, and demographics.[13] Since 1973, and annually since 1989, data have been collected by the National Center for Health Statistics and the Centers for Disease Control and Prevention for the purpose of providing objective, reliable information on the provision of medical care. Randomly selected U.S. physicians voluntarily participate and are trained for standardization prior to recording and submitting survey data. Of these physicians, only a randomly selected subset in a given time frame is included in NAMCS to account for confounding variables and for external validity. The subset is defined by a multistage design composed of 3 nested stages: geographical location, physician specialty (of the geographical location), and patient visits (of the physician specialty). Physicians complete data collection for patient visits over a 1-week period. The data are anonymous and publicly available online.

Study Design

This was a retrospective cross-sectional study using NAMCS data from 2000 to 2009 (the most recent data available) on the differences in time periods in pharmacologic and nonpharmacologic treatments for constipation across different age groups.

TABLE 1 Demographics for Constipation-Related Visits, 2000-2009, Percentage of Visits

Visit Type[a]	All	All-Cause Constipation (No IBS-C)	IBS-C Alone	Opioid-Induced Constipation Alone
Visits (n, millions)	89.6	63.4	28.2	3.7
Female	69	65	80	68
Race				
Caucasian	85	83	89	81
African American	10	12	8	12
Asian/Pacific Islander	3	3	3	5
Other	2	2	0	2
Ethnicity				
Non-Hispanic	81	80	84	85
Payment source				
Private insurance	51	46	61	29
Medicaid/Medicare	40	45	30	62
Self-pay	3	3	4	5
Other/unknown	6	6	6	4
Physician specialty				
Gastroenterology[b]	19	14	23	11
General/family practice	26	25	29	46
Internal medicine	20	17	28	18
Pediatrics	15	24	2	—
General surgery	2		1	2
OBGYN	4		3	2
Other specialty	14	20	12	22
Region				
Northeast	16	14		
Midwest	19	18		
South	45	48		
West	20	20		

[a]All values are percentages except first row, which is weighted frequency.
[b]Not available for 2008-2009.
IBS-C = irritable bowel syndrome-related constipation; OBGYN = obstetrics and gynecology.

The NAMCS database contains data on patient-specific office visits, including constipation-related visits.

Data from the NAMCS database were limited to office visits for patients that were associated with an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code related to constipation or with constipation recorded as the "reason for visit" (Appendix A, available in online article). Visits related to constipation included all-cause constipation, IBS-C, and opioid-induced constipation. Since there is no ICD-9-CM code for IBS-C, the nonspecific ICD-9-CM code for IBS was used. It was assumed that a constipation treatment would not be prescribed to someone with diarrhea-predominant IBS (IBS-D). This definition of IBS-D is limited in that some patients with IBS-D may be prescribed fiber; however, this is the best definition available using

| TABLE 2 | Treatment Differences in Time Periods by Major Treatment Category, 2000-2009, Percentage of Constipation and/or IBS Visits (Range) |

Age Range, Years	Weighted Number of Visits (Millions)	Time Period	Medication and Nonpharmacologic Therapy[a]		Medication Only		Nonpharmacologic Therapy Only		No Therapy	
<18	1.2	2000-2004	29	(21-39)[b]	20	(12-32)	20	(13-28)	31	(24-39)
		2005-2009	16	(10-24)[b]	27	(20-36)	19	(14-26)	38	(31-45)
18-44	9.4	2000-2004	11	(7-18)	17	(11-24)	28	(21-36)	45	(37-52)
		2005-2009	9	(5-16)	21	(15-29)	22	(16-30)	47	(38-56)
45-64	10.5	2000-2004	10	(6-17)	6	(4-10)[c]	20	(14-28)	64	(55-72)
		2005-2009	8	(5-12)	20	(14-26)[c]	18	(12-26)	55	(46-62)
≥65	2.8	2000-2004	6	(3-10)	19	(14-26)	24	(18-31)	51	(43-59)
		2005-2009	7	(4-12)	24	(19-31)	21	(16-29)	47	(41-54)
All visits	28.2	2000-2004	13	(10-17)	15	(12-19)[d]	23	(20-27)	48	(44-53)
		2005-2009	10	(8-12)	23	(20-27)[d]	20	(17-24)	47	(43-51)

[a]Represents patients prescribed at least 1 medication.
[b]$P < 0.05$ for 2000-2004 versus 2005-2009.
[c]$P < 0.001$.
[d]$P < 0.01$.
IBS = irritable bowel syndrome.

current coding systems. There is also no ICD-9-CM code for opioid-induced constipation, so it was defined as patients with an ICD-9-CM code for constipation and concurrent opioid use. This definition for opioid-induced constipation was chosen because it is recommended that patients taking opioids for any period of time should be treated either prophylactically or acutely with certain constipation medications, regardless of preexisting constipation.[14] All-cause constipation included patients with opioid-induced constipation, given that the study definition of opioid-induced constipation included an ICD-9-CM code for constipation.

Patients and visits were not linked in the NAMCS database. Data collection in NAMCS occurs over 1 week for each participating provider, so the possibility of capturing data for a given patient more than once is not likely. All constipation medications (over-the-counter and prescription) that were new, administered, or continued at that visit were collected and identified by NAMCS medication codes (Appendix B, available in online article). Data on nonpharmacologic treatments for constipation were also collected, including diet and behavior changes. Diet and behavior changes are predefined options on the NAMCS data collection form. The presence of comorbidities with potential to affect constipation symptoms, or alter treatment, were collected and identified by diagnosis codes. Similarly, concurrent medications (e.g., opioids and anticholinergics) with potential to affect constipation symptoms or alter treatment were collected by NAMCS unique drug codes. Demographic and other variables that may influence constipation management were considered and included age, sex, race, comorbidities, concurrent medications, geographical location, tobacco use, physician specialty, insurance type, pharma-

cologic and nonpharmacologic treatments, and procedures (Appendix C, available in online article).

Outcome Measures

The primary outcome was the proportion of office visits in which each therapy was prescribed for (a) all constipation and IBS-C visits, including opioid-induced; (b) all-cause constipation, including opioid-induced; (c) IBS-C alone; and (d) opioid-induced constipation alone. These proportions were estimated for specific medications, therapeutic classes, and medication and/or nonpharmacologic treatment in general. Estimates were obtained overall, by year, and by diagnosis (the composite of all visits, all-cause constipation, IBS-C alone, and opioid-induced constipation alone). Prescribing activity for each visit was the outcome measure for assessing association of patient and physician characteristics with therapy selection. Data were analyzed, and results were reported as the proportion of prescribed treatments by diagnosis, concurrent medications, comorbidities, treatment type, therapeutic class, new or continuing therapy, physician specialty, and other demographics. Also, an assessment of differences in time periods and predictors of prescribing were reported.

Statistical Analyses

All analyses used NAMCS sampling weights. In order to obtain correct standard error estimates, all patient visits from 2000 to 2009 were used in the analyses. Subgroup analyses were then used to obtain results for the desired target populations of constipation-related visits. Separate analyses were performed for each combination of age group (less than 18, 18-44, 45-64, and ≥65) and type of constipation (all-cause

TABLE 3 Treatment Differences in Time Periods by Medication Type, 2000-2009, Percentage of Constipation and/or IBS Visits with Prescribed Medication (Range)

Age Range, Years	Weighted Number of Visits (Millions)	Time Period	Lubiprostone	Stimulant Laxative	Stool Softener	Prokinetic	Lubricant	Hyperosmolar Agent	Saline Laxative	Sodium Phosphate	Tegaserod	Fiber, Any	Combination Therapy[a]
<18	1.2	2000-2004	—	10 (4-23)	6 (2-15)	2 (1-8)	17 (9-32)[b]	74 (58-85)[c]	6 (2-17)[b]	—	—	3 (1-13)	17 (8-31)
		2005-2009	—	8 (4-17)	3 (1-8)	—	2 (0-7)[b]	90 (82-95)[c]	0 (0-1)[b]	—	—	3 (1-9)	6 (2-14)
18-44	9.4	2000-2004	—	3 (1-11)[c]	21 (9-42)	4 (1-24)	2 (0-8)	34 (19-53)	3 (1-12)	0 (0-2)	22 (9-42)	25 (14-40)	15 (5-38)
		2005-2009	9 (3-21)	15 (7-28)[c]	13 (6-27)	6 (1-23)	4 (1-23)	36 (23-51)	0 (0-2)	—	8 (2-30)	24 (12-41)	19 (10-33)
45-64	10.5	2000-2004	—	13 (4-32)[c]	9 (3-24)	9 (3-24)	—	44 (30-60)	6 (1-19)	—	11 (4-28)	14 (6-30)	4 (1-19)
		2005-2009	6 (2-17)	1 (0-5)[c]	8 (3-16)	3 (1-14)	—	55 (39-69)	1 (0-4)	—	13 (6-26)	15 (7-29)	4 (1-10)
≥65	2.8	2000-2004	—	9 (3-20)	20 (10-37)	2 (1-8)	3 (1-12)	39 (24-56)	10 (4-22)[c]	3 (1-13)	14 (5-30)[c]	23 (13-38)	23 (12-37)
		2005-2009	6 (2-15)	8 (4-16)	21 (12-33)	4 (1-15)	0 (0-2)	46 (34-58)	2 (0-7)[c]	—	2 (1-8)[c]	29 (19-43)	18 (10-29)
All visits	28.2	2000-2004	—	8 (5-14)	13 (8-21)	3 (1-9)	8 (4-13)[b]	52 (42-61)	6 (3-11)[b]	1 (0-3)	10 (6-17)	15 (10-21)	16 (10-24)
		2005-2009	5 (3-9)	8 (5-12)	11 (8-16)	3 (1-8)	2 (0-5)[b]	58 (50-65)	1 (0-2)[b]	—	5 (3-10)	18 (13-25)	12 (8-17)

Note: empty cells indicate zero occurances in the sample
[a]Represents patients prescribed at least 1 medication and nonpharmacologic treatment.
[b]$P < 0.01$.
[c]$P < 0.05$ for 2000-2004 versus 2005-2009.
IBS = irritable bowel syndrome.

constipation, IBS-C, opioid-induced constipation). Descriptive statistics for patient and physician characteristics were calculated as percentages of visits with constipation or IBS-C diagnosis or reason for visit. Prescribing differences in time periods were estimated for major treatment and drug classes. The study period was grouped into two 5-year periods, and differences between time periods were tested by weighted logistic regression models. Periods of 5 years were chosen to ensure sufficient raw (unweighted) data counts. Weighted logistic regression models were also used to test for associations of patient and physician characteristics with treatments. In the case of 2 or more medications prescribed for a single visit, each medication was considered independently. Indicators for the 5-year time period (2000-2004 or 2005-2009) were included as control variables in each model. Independent variables were gender, race, ethnicity, payment source, physician specialty, and geographical region of physician practice. The 4 major treatment categories (medication, nonpharmacologic therapy, both, and neither) were dependent variables in separate models. For each outcome, a model was fit using all visits, and separate models were fit to each of 4 age groups. After modeling associations for

these 4 treatment categories, weighted logistic regression models were fit using the subset of visits from eligible patients who were receiving medication for the treatment of constipation symptoms. The purpose of using these models was to determine factors associated with the choice of specific medications. An alpha level of 0.05 was used as the level of significance for all analyses. All analyses were conducted using STATA statistical software version 10.1 (StataCorp, College Station, TX).

◼ Results

All Constipation and IBS-C Visits

There were 89.6 million visits for constipation and IBS-C between 2000 and 2009 (Table 1). The only major change in overall treatment category or specific medication prescribed was an increase in medication monotherapy over time ($P < 0.01$; Tables 2 and 3).

All-Cause Constipation

As shown in Table 4, 63.4 million visits for constipation that were not IBS-related were identified. Across all visits, there were significant changes in the major treatment category.

TABLE 4 Treatment Differences in Time Periods by Major Treatment Category, 2000-2009, Percentage of All-Cause Constipation Visits (Range)

Age Range, Years	Weighted Number of Visits (Millions)	Time Period	Medication and Nonpharmacologic Therapy[a]		Medication Only		Nonpharmacologic Therapy Only		No Therapy	
< 18	18.0	2000-2004	31	(22-41)[b]	21	(13-28)	19	(13-28)	28	(21-37)
		2005-2009	17	(11-25)[b]	28	(21-37)	19	(13-26)	36	(29-44)
18-44	11.9	2000-2004	15	(8-25)	31	(20-45)	19	(11-30)	36	(26-46)
		2005-2009	12	(6-20)	28	(20-39)	26	(18-36)	34	(25-45)
45-64	13.3	2000-2004	14	(8-25)	8	(4-15)c	16	(8-29)	62	(49-74)
		2005-2009	11	(7-18)	26	(18-35)c	15	(10-23)	48	(38-58)
≥ 65	20.3	2000-2004	5	(3-10)	22	(15-31)	26	(18-34)	48	(39-57)
		2005-2009	7	(4-13)	31	(24-39)	20	(13-28)	42	(35-49)
All visits	63.4	2000-2004	17	(13-21)[b]	21	(16-26)[b]	21	(17-25)	42	(37-48)
		2005-2009	11	(9-15)[b]	29	(24-33)[b]	20	(16-24)	40	(36-45)

[a]Represents patients prescribed at least 1 medication.
[b]P < 0.05 for 2000-2004 versus 2005-2009.
[c]P < 0.01.

Across all Age Groups. Only age and gender were associated with choice of major treatment category across all groups. Adults aged 65 years and older were less likely to receive medication and nonpharmacologic therapy than any other age group (aged < 18 years: odds ratio [OR] = 0.25, 95% confidence interval [CI] = 0.13-0.46, P < 0.001; aged 18-44 years: OR = 0.46, 95% CI = 0.22-0.96, P = 0.04; aged 45-65 years: OR = 0.46, 95% CI = 0.24-0.90, P = 0.02). Males were more likely to receive medications and nonpharmacologic therapy (OR = 1.6, 95% CI = 1.0-2.3, P = 0.03) and less likely to receive nonpharmacologic therapy only (OR = 0.66, 95% CI = 0.48-0.92, P = 0.01).

Across all age groups, the choice of specific medication was associated with age and race. Adults had lower odds of receiving hyperosmolar agents than children (aged 18-44 years: OR = 0.14, 95% CI = 0.06-0.32, P < 0.001; aged 45-64 years: OR = 0.29, 95% CI = 0.13-0.67, P = 0.004; aged ≥ 65 years: OR = 0.19, 95% CI = 0.08-0.46, P < 0.001; Table 5). African-American patients were more likely to receive prokinetics than Caucasian patients (OR = 6.7, 95% CI = 1.4-31.6, P = 0.02).

By Age Group. There were associations between major treatment category and ethnicity, physician specialty, and region by age group. Hispanic patients had higher odds than non-Hispanic patients of receiving only nonpharmacologic treatment in patients aged 18-44 years (OR = 4.4, 95% CI = 1.6-12.3, P = 0.01), but lower odds than non-Hispanic patients of receiving only nonpharmacologic therapy in patients aged 45-64 years (OR = 0.14, 95% CI = 0.03-0.70, P = 0.02). For patients younger than 18 years, pediatricians were more likely to prescribe medication and nonpharmacologic therapy than family medicine practitioners (OR = 6.9, 95% CI = 2.0-24.5, P = 0.003). No therapy was prescribed more often in the South than in the Midwest (OR = 2.3, 95% CI = 1.1-4.5, P = 0.02) or West

(OR = 2.3, 95% CI = 1.2-4.4, P = 0.02). In elderly patients, family medicine practitioners were more likely to prescribe stool softeners than gastroenterologists (OR = 10.2, 95% CI = 2.3-44.6, P = 0.002).

IBS-C Alone

A total of 28.2 million visits for IBS were identified. Across all visits, there were no significant changes in the prescription of major treatment categories or specific agents (Table 6). However, when examining prescribing patterns by patient age, there were significant changes in prescribing within the age groups. The prescription of nonpharmacologic treatments decreased for patients aged 18-44 years (P < 0.05), tegaserod use increased in patients aged 45-64 years (P < 0.05), and combination treatments increased in patients aged 45-64 years (P < 0.05; Tables 6 and 7).

Across all IBS-C visits, there were associations between major treatment category and payment source. Patient visits covered primarily by private insurance were more likely to include medication and nonpharmacologic treatments, compared with those covered primarily by Medicare or Medicaid (OR = 13.2, 95% CI = 1.6-107.9, P = 0.02).

Across All Age Groups. Choice of specific medication was associated with gender across all age groups. Females had higher odds of being prescribed tegaserod (OR = 14, 95% CI = 2-87, P = 0.004) and lower odds of being prescribed fiber (OR = 0.11, 95% CI = 0.02-0.81, P = 0.03) than males.

By Age Group. There were associations between major treatment category and gender, race, pay source, and physician specialty by age group. In patients aged 45-64 years, males had higher odds than females of receiving nonpharmacologic treatment only (OR = 2.7, 95% CI = 1.1-6.7, P = 0.03). In patients aged 18-44 years, family practitioners prescribed

TABLE 5 Treatment Differences in Time Periods by Medication Type, 2000-2009, Percentage of All-Cause Constipation Visits with Prescribed Medication (Range)

Age Range, Years	Weighted Number of Visits (Millions)	Time Period	Lubiprostone	Stimulant Laxative	Stool Softener	Prokinetic	Lubricant	Hyperosmolar Agent	Saline Laxative	Sodium Phosphate	Tegaserod	Fiber, Any	Combination Therapy[a]
< 18	18.0	2000-2004	—	10 (4-23)	6 (2-15)	2 (1-8)	17 (9-32)[b]	74 (58-85)[c]	6 (2-17)[b]	—	—	3 (1-13)	17 (8-31)
		2005-2009	—	8 (4-18)	3 (1-8)	—	2 (0-7)[b]	90 (82-95)[c]	0 (0-1)[b]	—	—	3 (1-9)	6 (2-14)
18-44	11.9	2000-2004	—	3 (1-14)[c]	26 (12-49)	3 (0-16)	3 (1-10)	38 (20-59)	4 (1-14)	0 (0-2)	24 (10-48)	17 (8-33)	18 (6-44)
		2005-2009	5 (1-16)	17 (9-32)[c]	15 (7-31)	5 (1-28)	5 (1-26)	41 (27-57)	0 (0-3)	—	8 (1-35)	21 (9-40)	22 (12-37)
45-64	13.3	2000-2004	—	15 (4-41)[c]	8 (2-26)	6 (1-27)	—	55 (35-73)	8 (2-27)[c]	—	12 (3-35)	3 (1-12)	6 (1-27)
		2005-2009	7 (2-20)	1 (0-6)[c]	9 (4-19)	—	—	59 (42-74)	1 (0-5)[c]	—	11 (4-24)	15 (6-31)	4 (1-12)
≥ 65	20.3	2000-2004	—	10 (4-23)	24 (11-43)	3 (1-10)	4 (1-15)	48 (31-65)	12 (5-26)[c]	4 (1-15)	8 (2-24)	16 (8-30)	27 (15-44)
		2005-2009	6 (2-17)	9 (4-17)	23 (14-35)	1 (0-4)	0 (0-1)	49 (37-62)	2 (0-7)[c]	—	2 (1-8)	24 (15-38)	19 (11-32)
All visits	63.4	2000-2004	—	9 (5-16)	15 (9-23)	3 (1-7)	9 (5-15)[c]	58 (47-68)	7 (4-13)[d]	1 (0-4)	8 (4-16)	9 (6-15)	18 (12-27)
		2005-2009	4 (2-8)	9 (6-13)	12 (9-17)	1 (0-6)	2 (1-5)[c]	62 (54-69)	1 (0-2)[d]	—	4 (2-9)	15 (10-22)	13 (9-18)

Note: empty cells indicate zero occurances in the sample

[a]Represents patients prescribed at least 1 medication and nonpharmacologic treatment..

[b]P<0.01.

[c]P<0.05 for 2000-2004 versus 2005-2009.

[d]P<0.001.

nonpharmacologic monotherapy more frequently than gastroenterologists (OR = 3.9, 95% CI = 1.2-12.2, P = 0.02).

Opioid-Induced Constipation Alone

Visits identified as relating to opioid-induced constipation totaled 3.7 million. Across all visits, there were no significant changes in the prescribing of major treatment categories or specific agents nor were there any associations between treatment and other factors (Appendix D, available in online article).

For each type of constipation, including IBS-C and opioid-induced constipation, there were few visits with concurrent medications (e.g., anticholinergics), comorbidities, or procedures with potential to influence constipation (Appendix E, available in online article).

■ Discussion

Since this study was conducted, updated treatment guidelines have become available, which include recommendations for the use of newly available agents, but the general recommendations have not changed.[16,17] In this study, the prevalence of constipation and possibly IBS-C is increasing when compared with previous findings, which may be related to an increasing

elderly population who are more likely to have constipation than other age groups.[13,18] Given that the first presentation of IBS is typically between the ages of 30 to 50 years, it would be expected that the prevalence increases as the older population increases. This increased health care demand for constipation services reinforces the need for more evidence-based prescribing in order to reach optimal health outcomes and, ultimately, increase the quality of life for these individuals.

The findings of a decrease in prescribing combination therapy for patients aged < 18 years and an increase in prescribing medication monotherapy for patients of all ages with constipation (including IBS-C) is concerning, since this finding contradicts national recommendations for the treatment of constipation.[9,10] According to expert recommendations for the treatment of constipation, all children and adolescents should receive combination therapy, and all adults on 1 or more medications should also be on therapy with nonpharmacologic treatments.[1,9,12] All patients on a medication for constipation should also be prescribed nonpharmacologic therapies.

For visits because of constipation not related to IBS-C, there was also a decrease in prescribing combination therapy for patients aged < 18 years and an increase in medication only

TABLE 6 Treatment Differences in Time Periods by Major Treatment Category, 2000-2009, Percentage of IBS Visits (Range)

Age Range, Years	Weighted Number of Visits (Millions)	Time Period	Medication and Nonpharmacologic Therapy[a]		Medication Only		Nonpharmacologic Therapy Only		No Therapy	
< 18	1.2	2000-2004	—		—		28	(11-55)	72	(45-89)
		2005-2009	10	(2-37)	8	(1-32)	28	(11-54)	54	(29-78)
18-44	9.4	2000-2004	9	(4-18)	4	(1-13)	36	(26-47)[b]	51	(40-62)
		2005-2009	5	(1-18)	10	(4-21)	19	(11-30)[b]	67	(53-79)
45-64	10.5	2000-2004	10	(5-19)[b]	4	(2-10)	23	(15-34)	63	(52-73)
		2005-2009	2	(1-6)[b]	12	(6-21)	22	(11-40)	64	(50-76)
≥ 65	2.8	2000-2004	9	(3-22)	12	(5-27)	18	(10-28)	61	(47-74)
		2005-2009	7	(2-22)	5	(2-10)	26	(15-41)	62	(48-74)
All visits	28.2	2000-2004	9	(6-14)	6	(3-10)	27	(21-33)	58	(52-65)
		2005-2009	5	(2-10)	9	(6-13)	23	(16-31)	64	(55-71)

[a]Represents patients prescribed at least 1 medication.
[b]P < 0.05 for 2000-2004 versus 2005-2009.
IBS = irritable bowel syndrome.

for patients of all ages. In addition, there was a decrease in combination therapy for patients of any age and an increase in medication only in patients aged 45-64 years. Again, these findings for treating constipation are not consistent with the national recommendations for treatment.[9,10] Considering specific choice of treatment, there were decreases in saline and lubricant use across all visits. Compared to previous findings, the current findings of an increase in medication only and a decrease in saline agents across all visits for constipation were consistent.[12] Previously, the use of nonpharmacologic therapies was found to have decreased significantly over time,[12] which is in contrast with the current findings of nonsignificant decreases in nonpharmacologic therapy only (21% vs. 20%). Furthermore, the percentage of visits resulting in a hyperosmolar was much higher in this study compared with a previous study (9%-24% vs. 58%-62%).[13] The difference in hyperosmolar prescribing may be the result of heightened awareness of the safety, efficacy, and tolerability of polyethylene glycol.[9,10]

When comparing the different age groups, there were significant differences in the prescribing patterns for constipation. Although the elderly were not more likely to receive nonpharmacologic or pharmacologic treatment only for constipation, they were less likely to receive combination therapy compared with the other age groups. This could be an attempt to keep the complexity of the treatment regimen simple.

As expected, the percentage of females with constipation was greater than males[9,10]; however, females were less likely to receive combination therapy and more likely to receive nonpharmacologic therapy only. This may be because males are less likely to seek medical attention, and those that present with constipation do so only after their symptoms become severe, warranting initiation with combination therapy, or they already failed nonpharmacologic monotherapy and require adjunctive medication therapy.

Another interesting finding is that African-American patients were more likely to receive prokinetics than Caucasian patients. Although this study did not assess concurrent diabetes, the disproportionately higher prevalence of type 2 diabetes in African-Americans patients,[15] and its potential complication of gastroparesis, may warrant greater use of prokinetics in this group in order to target the motility disorder.

For the prescribing patterns of IBS-C and opioid-induced constipation visits, there were no apparent deviations from the national recommendations.[9,10] Interestingly, howerver, there was a significant increase in the prescription of tegaserod for IBS-C in patients aged 45-64 years, despite its change in status to a restricted drug in 2007, which limited its availability and the ability to prescribe it. Perhaps the increase in prescribing can be attributed to heightened awareness through U.S. Food and Drug Administration (FDA) announcements concerning the efficacy of the drug for patients that are refractory to other treatments. Females were also more likely to receive tegaserod for IBS-C than males, probably because of its product labeling.[18]

While the results of opioid-induced constipation were nonsignificant, the decreased use of stimulants and hyperosmolars are interesting, given that stimulants are recommended, and adjunctive treatment with hyperosmolars is also often recommended in this setting. Stimulants are preferred for opioid-induced constipation treatment and prevention because they specifically target the decreased peristalsis resulting from opioid use. Hyperosmolars are often used because they target the increased water absorption from the small and large colon. A newer drug, lubiprostone, may be an alternative because it facilitates passage of stool secondary to increased intestinal fluid secretions; however, there were no instances of lubiprostone use for opioid-induced constipation in this study. Interestingly, the manufacturer of lubiprostone has applied

TABLE 7 Treatment Differences in Time Periods by Medication Type, 2000-2009, Percentage of IBS Visits with Prescribed Medication (Range)

Age Range, Years	Weighted Number of Visits (Millions)	Time Period	Lubiprostone	Stimulant Laxative	Stool Softener	Prokinetic	Hyperosmolar Agent	Saline Laxative	Tegaserod	Fiber, Any	Combination Therapy[a]
< 18	1.2	2000-2004	—	—	—	—	—	—	—	—	—
		2005-2009	—	37 (4-88)	—	—	100 (NA)	—	—	—	37 (4-88)
18-44	9.4	2000-2004	—	3 (0-17)	16 (2-60)	16 (2-60)	29 (9-63)	—	10 (2-43)	43 (18-71)	16 (2-60)
		2005-2009	25 (6-64)	—	—	10 (2-36)	5 (1-33)	—	31 (9-68)	34 (9-73)	5 (1-33)
45-64	10.5	2000-2004	—	4 (1-27)	7 (1-38)	19 (6-46)	36 (14-66)	—	6 (1-33)[b]	27 (10-57)	—
		2005-2009	—	—	—	14 (3-51)	47 (20-77)	—	27 (9-59)[b]	12 (3-34)	—
≥ 65	2.8	2000-2004	—	—	5 (1-22)	—	—	8 (1-40)	44 (17-75)	43 (17-74)	—
		2005-2009	—	4 (0-27)	—	35 (7-79)	14 (3-46)	—	5 (1-32)	73 (38-92)	—
All visits	28.2	2000-2004	—	2 (1-10)	9 (3-28)	12 (3-36)	23 (11-42)	2 (0-15)	19 (8-37)	37 (22-56)	5 (1-29)
		2005-2009	8 (2-27)	3 (1-14)	—	17 (6-39)	29 (15-50)	—	21 (10-39)	33 (17-55)	4 (1-16)

Note: for this sample, there were zero instances of lubricant for IBS. Empty cells indicate zero occurances in the sample.
[a]Represents patients prescribed at least 1 medication and nonpharmacologic treatment.
[b]P < 0.05 for 2000-2004 versus 2005-2009.
IBS = irritable bowel syndrome; NA = not available.

for an FDA indication for opioid-induced constipation; thus, lubiprostone may become a more common treatment for this indication in the future.

Our results show that there is little consistency in prescribing patterns for the different types of constipation, which points to a lack of evidence-based prescribing. The lack of evidence-based prescribing may compromise optimal symptom improvement. It may also impact payers by increasing the demand for physician visits and, thus, increase health care utilization and costs related to constipation. Streamlining treatments based on the available, albeit limited, evidence may lead to enhanced patient satisfaction and improved outcomes. Health plans may benefit from this streamlined approach not just by improving the patient experience and outcomes, but also by reducing health care utilization and costs associated with constipation.

Limitations

Because of the retrospective study methodology, the data available were limited to the fields available, and accuracy was dependent on each physician who entered data. The results are representative of data from a finite period, preventing assessment of the course of disease and treatment, and it was not possible to determine what treatment options were tried or discussed at past visits. Further, the sample size for opioid-induced constipation and IBS-C visits were small, limiting the findings of significance.

While the NAMCS database includes information on the prescription of over-the-counter medications, patients self-treating with these agents are not captured, limiting the generalizability of the results. This is of particular importance, given that the majority of the agents used to treat constipation are available over the counter. The constipation treatments available at the time of this study that were available by prescription only were anthraquinone- or diphenylmethane-containing products, lactulose, sorbitol, misoprostol, lubiprostone, tegaserod, botulinum toxin, cisapride, and metoclopramide. In addition, changes in availability and regulations of lubiprostone and tegaserod from 2000 to 2009 likely influenced prescribing patterns.

◼ Conclusions

Health care utilization resulting from constipation increased and the prescribing patterns for treatment have shifted significantly from 2000 to 2009 for constipation and IBS-C. The treatment patterns were significantly influenced by age,

gender, race, ethnicity payment source, physician specialty, and region across all ages and within age groups. Overall changes in treatment categories over time included a decrease in combination therapy for patients aged < 18 years and an increase in medication monotherapy across all ages, which are in contrast to the national recommendations. The implications of the identified patterns may include increased health care utilization and lead to additional costs to payers. Accessing constipation-prescribing patterns within their own plan populations may offer payers an opportunity to optimize treatment outcomes and costs.

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APPENDIX A List of ICD-9-CM Codes for the Diagnosis of Constipation

ICD-9-CM Code	Diagnosis
564.0	Constipation
564.09	Other constipation
564.00	Constipation, unspecified
564.02	Outlet dysfunction constipation
564.01	Slow transit constipation
564.1	Irritable bowel syndrome

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

APPENDIX B Medications Used for Constipation and NAMCS Medication Codes

Medications	Type	NAMCS Medication Codes
Anthraquinones-senna	Stimulant laxative	55200, 04615
Anthraquinones-cascara, casanthranol		50935
Phenolphthalein		54405
Diphenylmethane- bisacodyl		50630, 04370
Docusate sodium	Stool softener	51935
Mineral oil	Lubricant	17660, 53720
Polyethylene glycol	Hyperosmolar agent	54590, 94029, 42425, 03437
Lactulose		52995
Sorbitol		28915, 55435
Glycerin suppository		12622, 27429, 22145, 98059
Mg hydroxide	Saline laxative	19375, 24058, 41865
Sodium phosphate	Bowel evacuant	55385
Castor oil	Miscellaneous	25749, 05885
Colchicine		51345
Misoprostol		91011
Lubiprostone		71035
Tegaserod		70642
Botulinum toxin		702166, 70502
Cisapride	Prokinetic	56395
Metoclopramide		53688
Calcium polycarbophil	Fiber	56715, 54587
Psyllium		54965
Methylcellulose		06020, 07345, 19140, 34255, 60325
Stimulant laxative/stool softener	Combination stimulant/stool softener	04176, 04059, 27795, 07268, 09945
Stimulant/fiber	Combination stimulant/fiber	27805, 23415, 05890,
Homeopathic	Combination homeopathic product	04213, 17460, 04147
Miscellaneous combinations	Combination product, other	13330, 25449, 27755, 35020, 05865, 04283, 05830, 05835, 05865, 12588, 19380, 16790, 22260, 20410, 33850, 30625, 33855, 16795, 17245, 27480, 41270, 61175, 40630, 10090, 40635, 60475, 19385, 14950, 30300, 09715
Barium bisacodyl enema	Enema	96074

NAMCS = National Ambulatory Medical Care Survey.

APPENDIX C — Surgeries/Procedures for Treatment or Diagnosis of Constipation and ICD-9-CM Codes

ICD-9-CM Code	Surgery/Procedure Therapy
96.29	Reduction of intussusception of alimentary tract With: fluoroscopy, ionizing radiation enema, ultrasonography guidance, hydrostatic reduction, pneumatic reduction
46.80	Intra-abdominal manipulation of intestine, not otherwise specified Correction of intestinal malrotation Reduction of: intestinal torsion, intestinal volvulus, intussusception
45.8	Total intra-abdominal colectomy Excision of cecum, colon, and sigmoid
46.92	Myotomy of other parts of colon
94.39	Other individual psychotherapy: biofeedback
45.24	Flexible sigmoidoscopy Endoscopy of descending colon
96.39	Other transanal enema
45.23	Colonoscopy
46.8	Dilation and manipulation of intestine

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

APPENDIX D — Treatment Differences in Time Periods by Major Treatment Category, 2000-2009, Percentage of Opioid-Induced Constipation Visits (Range)

Age Range, Years	Weighted Number of Visits (Millions)	Time Period	Medication and Nonpharmacologic Therapy[a]		Medication Only		Nonpharmacologic Therapy Only		No Therapy	
18-44	0.6	2000-2004	—		—		37	(7-83)	63	(18-93)
		2005-2009	—		66	(19-94)	—		34	(6-81)
45-64	1.3	2000-2004	40	(14-74)	12	(2-53)	6	(1-35)	42	(17-72)
		2005-2009	10	(3-30)	37	(13-71)	3	(0-18)	50	(21-79)
≥65	1.8	2000-2004	—		21	(3-69)	11	(1-50)	68	(28-92)
		2005-2009	—		33	(14-60)	24	(8-53)	43	(22-68)
All visits	3.7	2000-2004	14	(5-37)	14	(3-45)	13	(4-34)	58	(36-78)
		2005-2009	3	(1-10)	39	(25-56)	13	(5-30)	45	(28-63)

Note: empty cells indicate zero occurances in the sample.
[a]Represents patients prescribed at least 1 medication.

APPENDIX E — Weighted Percentage of Visits Associated with at Least 1 Concurrent Medication, Comorbidity, Treatment Procedure, and Diagnostic Procedure (Range)

	Any Constipation and/or IBS (Group 1)		Constipation, Excludes IBS Without Constipation (Group 2)		IBS (Group 3)		Opioid-Induced Constipation	
Concurrent medication	5.7	(4.5-7.3)	5.7	(4.2-7.5)	6.1	(4.4-8.6)	100.0	
Comorbidity	13.3	(11.4-15.6)	13.0	(10.8-15.7)	13.4	(10.2-17.4)	14.6	(6.8-28.6)
Procedure, treatment	0.0		0.0		0.0		0.0	
Diagnostic procedure	10.6	(8.1-13.9)	11.7	(8.8-15.4)	8.4	(5.5-12.8)	5.8	(1.8-16.7)

IBS = irritable bowel syndrome.