Impact of Alvimopan (Entereg) on Hospital Costs After Bowel Resection

Results From a Large Inpatient Database

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ABSTRACT

Purpose: Delayed gastrointestinal (GI) recovery after bowel resection is associated with longer hospital stays and increased health care costs. Alvimopan (Entereg), a peripherally acting mu-opioid receptor antagonist, accelerates GI recovery after bowel-resection surgery. We undertook a study to evaluate the economic impact of alvimopan in clinical practice.

Methods: We conducted a retrospective matched cohort study using data from a large national hospital database and identified adults who had undergone small-bowel or large-bowel resection with primary anastomosis. The patients were discharged between January 1, 2009, and June 30, 2009. The surgery was performed at a hospital where alvimopan was used at least once during the study period. We matched each alvimopan patient ("user") with two controls ("non-users"). The primary outcome of total hospital costs (including the cost of alvimopan) and secondary outcomes of cost components and length of stay were compared between groups.

Results: The final study cohort included 480 alvimopan patients and 960 matched controls. The mean total hospital cost was $12,865 for alvimopan patients, compared with $13,905 for controls, for a difference of $1,040 ($P = 0.033$). There was a nonsignificant trend toward lower ileus-related costs between groups ($83 for alvimopan vs. $114 for controls, $P = 0.086$). Pharmacy and diagnostic radiology costs did not differ significantly. The mean length of stay was 5.6 days for alvimopan patients and 6.5 days for controls ($P < 0.001$).

Conclusion: Patients receiving alvimopan capsules had significantly lower total hospital costs compared with controls. Along with other initiatives to improve quality and reduce costs of surgical care, alvimopan might be a good choice for use in the perioperative management of patients who undergo segmental bowel resection with primary anastomosis.

Key words: alvimopan, bowel resection, hospital cost, postoperative ileus, length of stay

INTRODUCTION

Many health policy discussions today are focused on how to improve surgical outcomes and reduce costs.[1,2] Delayed gastrointestinal (GI) recovery after bowel resection increases the risk of in-hospital morbidity, and it is the most common cause of prolonged length of stay (LOS).[3,4] Delayed hospital discharge resulting from slow GI recovery (defined as a first bowel movement after surgery and toleration of solid food) represents a suboptimal clinical outcome and may increase health care costs.[5–7] A variety of approaches, including the use of minimally invasive procedures and clinical pathways, [8–10] can help to accelerate GI recovery and decrease LOS. For example, laparoscopic surgery reduces LOS, compared with an open surgical approach, but its ability to produce cost savings is inconsistent.[11–14] Moreover, in several studies, implementation of accelerated perioperative care protocols decreased hospital LOS, costs, or both.[15–19]

Although many factors can affect GI recovery after surgery, opioids, which are commonly used to treat perioperative and postoperative pain after bowel resection, play an important role in the return of GI function.[8] In 2008, the FDA approved alvimopan (Entereg, Adolor/GlaxoSmithKline), a peripherally acting mu-opioid receptor antagonist. Alvimopan is designed to mitigate the deleterious effects of opioids on the GI tract and to accelerate upper and lower GI recovery after large-bowel or small-bowel resection with primary anastomosis.[20]

In double-blind, placebo-controlled, randomized clinical trials enrolling patients undergoing bowel resection, those receiving 12 mg of alvimopan once preoperatively and twice daily postoperatively for up to seven in-hospital days experienced faster GI recovery by 11 to 26 hours and a reduced time to discharge by 13 to 21 hours, compared with patients receiving placebo.[21–26]

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Accepted for publication November 23, 2010.

Disclosure. Dr. Poston and Dr. Cook are employees of GlaxoSmithKline. Dr. Broder and Dr. Chang are employees at Partnership Health Analytic Research, LLC, which was paid a consulting fee by Adolor Corp. As a Data Analyst Consultant, Dr. Gibbons received an honorarium from Adolor Corp. As an Investigator, Dr. MacLaren received grant support from Hospira and a consulting fee from Cadence and Javelin. As a consultant, Dr. VandePol received a consulting fee from Adolor Corp. Dr. Techner is an employee of Adolor Corp. and receives stock options.

In a *post hoc* economic analysis of these trial data, alvimopan-treated patients spent one less day in the hospital, and mean total hospital costs were $897 less than those for placebo-treated patients.[3] Of note, a multimodal, standardized, accelerated-care pathway was used to facilitate GI recovery in both alvimopan and placebo patients.

Although randomized controlled trials are considered the gold standard for assessing efficacy, they do not always measure effectiveness accurately and they often fail to measure costs outside the rigors and constraints of such studies. Observational studies using data from large and diverse patient populations can provide valuable information on the effectiveness of medical and surgical interventions.[27,28] To more clearly understand the use of alvimopan in non-research confined clinical settings, we undertook a study to compare, in clinical practice, total direct hospital cost for bowel resection in alvimopan-treated patients (users) compared with matched controls (non-users). Secondary outcomes of interest included between-group comparisons of various subgroup components of hospital costs (e.g., for postoperative ileus ([POI]) and LOS.

METHODS

Study Design

We conducted a matched cohort study of patients who underwent laparoscopic or open bowel resection to compare costs and LOS between patients receiving alvimopan and controls. Alvimopan is available only in hospitals registered in the Entereg Access Support and Education (E.A.S.E.) program. To increase the comparability of the perioperative care delivered to patients in the study, we restricted the analysis to patients who had surgery at hospitals enrolled in the program. Hospitals with at least one patient who had received alvimopan were presumed to be registered with E.A.S.E. for purposes of this study.

Data Source

We used the Premier Perspective Comparative Database, which includes data for 45 million discharges from more than 600 hospitals. Patient data were de-identified in accordance with the Health Insurance Portability and Accountability Act (HIPAA). Our study was therefore exempt from review by an institutional review board in order to protect patient privacy. Data encompassed hospital discharges from January 1, 2009, through June 30, 2009.

Study Population

The study included patients 18 years of age or older who were discharged after laparoscopic or open bowel resection and who were identified according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes for the primary procedure. Patients were classified as having undergone laparoscopic colon and rectal surgeries by a laparoscopic-specific ICD-9-CM procedure code (e.g., 17.3X), or, in the absence of a specific open or laparoscopic ICD-9-CM code, by the laparoscopic instruments used, or by the presence of a conversion code.

Patients were excluded from the study if they had undergone an ostomy during the index admission (i.e., had no functioning anastomosis), if they had taken more than 15 doses of alvimopan during the index admission (i.e., an amount inconsistent with the product label), or if their surgery had been performed at a non–E.A.S.E-registered hospital. If a patient was admitted more than once during the study time period, only the first admission was included.

Patients were grouped into alvimopan users and non-users based on the presence or absence of pharmacy charges for alvimopan.

Outcomes

The primary study outcome was total direct hospital costs, and the primary comparison was between the unadjusted mean cost (the arithmetic mean) for alvimopan patients and matched controls. The Premier database captures the total hospital cost of each admission (including supplies, labor, and equipment depreciation) and verifies, reconciles, and validates the recorded data; however, it does not confirm the accuracy of the data abstraction.

Secondary outcomes included LOS, pharmacy, POI-related costs, and radiology. POI-related costs were defined as the supply and labor costs of postoperative nasogastric tube (NGT) insertion, parenteral nutrition, and antiemetic drugs or GI stimulants such as metoclopramide (Reglan, Baxter).

Baseline Variables and Outcomes

Using the Premier database, we collected all variables from hospital discharge forms. Demographic variables included age, sex, Medicaid or charity care (as a proxy for low income status), marital status, race, and ethnicity. Clinical conditions, identified by ICD-9-CM codes, included specific diagnoses (GI cancer, inflammatory bowel disease or diverticular disease), selected major cardiac risk factors (e.g., diabetes, hypertension), and the total number of chronic conditions.[29]

We captured overall risk of morbidity and mortality rates using All Patient Refined Diagnosis Related Groups (APR–DRGs) software. The APR–DRG Computer Program (Version 12.0, 3M, Wallingford, Conn., 1995) uses DRGs to classify patients' entire hospital stay into risk categories for reimbursement.

Index bowel-resection surgeries were grouped by ICD-9-CM codes into the following categories: (1) laparoscopic colon and rectal procedures; (2) open colon and rectal procedures; (3) laparoscopic small-bowel procedures; (4) open small-bowel procedures; and (5) ostomy take-downs (closures), bypasses, and other procedures. Because ICD-9-CM procedure codes do not specify whether small-bowel resections were performed via an open or a laparoscopic technique, billing codes for laparoscopic surgery equipment were used to classify these surgeries as either open or laparoscopic small-bowel resections.

We recorded the calendar quarter of surgical admission, the admission type (urgent/emergent or elective), the presence of trauma on admission, the day of surgery (e.g., day 1 if surgery was performed on the day of admission), and specific hospital characteristics (e.g., teaching vs. nonteaching).

Surgeon case volume for bowel resection was dichotomized at the 75th percentile (more than 11 procedures in six months). Patients were characterized by whether their surgery was performed by a surgeon with a high or a low case volume of these procedures.

Statistical Analysis

To account for inherent differences in baseline characteristics between cohorts, we used a two-level matching process that employed both propensity scores and exact matching.[30,31] Alvimopan patients were matched with controls in a 1-to-2 ratio. Propensity scores were estimated with a logistic regression model that incorporated most baseline measures (e.g., age, sex, race, procedure-related diagnosis, comorbidities, cardiovascular disease risk factors) as independent variables and alvimopan use as the dependent variable. The independent variables used for the matching process did not include collected APR–DRG indexes (risk of mortality and disease severity), because some of the events used to determine these indexes occur after surgery; therefore, these were not considered to be baseline variables.

Two-way interactions were considered. We used forward selection to include significant interaction terms in the final model.

For each alvimopan-treated patient, all controls who had an exact match for hospital region (to account for regional differences in care or cost) and category of index procedure (e.g., laparoscopic colon/rectal or open colon/rectal) and who were within one quarter of a standard deviation (SD) of the logit of the propensity score were selected as potential matches. Mahalanobis distances between those potential matches and the alvimopan patients were calculated based on the teaching hospital, the hospital's location, and the surgeon's case volume of bowel resections. The two controls with the smallest Mahalanobis distances were chosen as final matches; alvimopan-treated patients without two matches were excluded.

Descriptive statistics, including percentages, medians, means, and SDs, were calculated for all baseline variables. We made univariate comparisons of the baseline measures between alvimopan patients and controls with *chi*-square tests for categorical variables and *t* tests for continuous variables.

We compared the means of total hospital costs, components of cost, and LOS directly between matched cohorts using *t* tests. Cost outcomes are not always normally distributed; however, we studied hospital costs in patients with hospitalizations. The study included a large number of observations, so we used untransformed hospital cost for the primary analysis.[32–34]

Using a sensitivity analysis to account for skewness, we repeated the outcome comparisons, assuming an underlying gamma (rather than a normal) distribution. Other sensitivity analyses included both a regression model to account for differences between groups that remained after the matching procedure and stratification of the sample by the surgeon's case volume and surgical approach.

We performed all data extraction and statistical analyses using SAS Version 9.1 (SAS Institute, Cary, N.C.). All statistical tests were two-sided with a 0.05 significance level.

RESULTS

Study Population

We identified 25,422 patient admissions for small-bowel or large-bowel resection during the study period (Figure 1). We excluded 3,729 admitted patients with a diverting ostomy, 284 patients younger than 18 years of age, and 114 hospital stays for patients with more than one admission. Of the 21,295 remaining patients, 678 had received alvimopan and 20,617 patients had not.

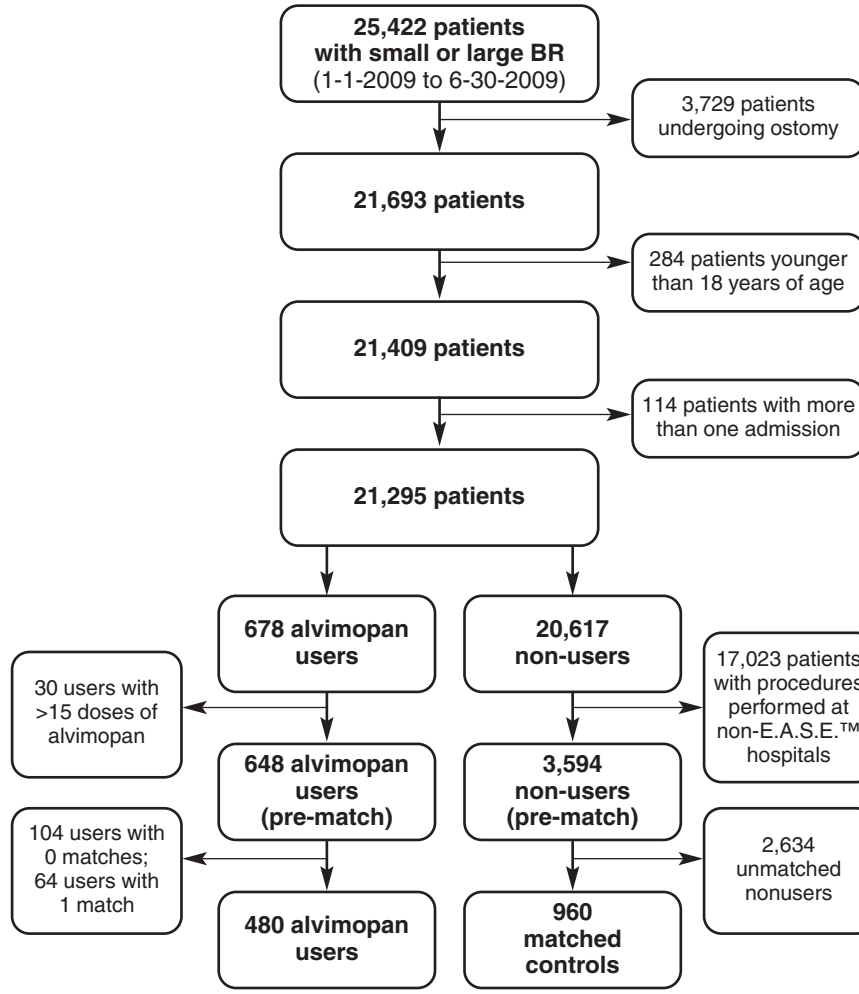

Figure 1 Selection of alvimopan patients (users) and controls (non-users) for matched cohort study. *Note:* If a patient had more than one hospital admission in the study time period, only the first admission was included in the study; 114 hospital stays were excluded.
BR = bowel resection; E.A.S.E. = Entereg Access Support and Education.

Table 1 Characteristics of Patients, Physicians, Hospitals, and Procedures Before Matching

Variable	Total (N = 4,242)	Alvimopan Patients (n = 648; 15.3%)	Controls (n = 3,594; 84.7%)	*P* Value
Patient Characteristic				
Age (years) (Mean, SD)	62.8 (15.2)	63.6 (13.8)	62.6 (15.5)	0.101
		No. (%)		
Age group (years)				0.025
18–44	527 (12.4)	59 (9.1)	468 (13.0)	
45–64	1,655 (39.0)	271 (41.8)	1,384 (38.5)	
65–74	978 (23.1)	159 (24.5)	819 (22.8)	
75+	1,082 (25.5)	159 (24.5)	923 (25.7)	
Female	2,273 (53.6)	325 (50.2)	1,948 (54.2)	0.057
Race/ethnicity				0.009
White	2,866 (67.6)	462 (71.3)	2,404 (66.9)	
Black	439 (10.3)	46 (7.1)	393 (10.9)	
Other	937 (22.1)	140 (21.6)	797 (22.2)	
No. of chronic conditions (Mean, SD)	3.4 (1.8)	3.2 (1.7)	3.4 (1.8)	0.004
Admission and Procedure Characteristics				
Index procedure type[a]				<0.001
Laparoscopic colon and rectal	1,559 (36.8)	322 (49.7)	1,237 (34.4)	
Open colon and rectal	1,495 (35.2)	242 (37.3)	1,253 (34.9)	
Laparoscopic small-bowel	101 (2.4)	0	101 (2.8)	
Open small-bowel	644 (15.2)	30 (4.6)	614 (17.1)	
Ostomy take-downs, bypasses, other	443 (10.4)	54 (8.3)	389 (10.8)	
Operative time (min) (Mean, SD)	199.4 (104.2)	189.2 (78.6)	201.3 (108.1)	<0.001
Red blood cell transfusion	202 (4.8)	22 (3.4)	180 (5.0)	0.076
Diagnosis[b]				
Cancer of intestine	1,297 (30.6)	266 (41.0)	1,031 (28.7)	<0.001
Inflammatory bowel disease	183 (4.3)	24 (3.7)	159 (4.4)	0.406
Diverticular disease	1,139 (26.9)	178 (27.5)	961 (26.7)	0.700
Hospital and Physician Characteristics				
Hospital region				<0.001
Midwest	987 (23.3)	202 (31.2)	785 (21.8)	
Northeast	806 (19.0)	111 (17.1)	695 (19.3)	
South	2,257 (53.2)	320 (49.4)	1,937 (53.9)	
West	192 (4.5)	15 (2.3)	177 (4.9)	
Location				<0.001
Rural	683 (16.1)	202 (31.2)	481(13.4)	
Urban	3,559 (83.9)	446 (68.8)	3,113 (86.6)	
Teaching hospital	2,317 (54.6)	371 (57.3)	1,946 (54.1)	0.144
Physician specialty				<0.001
General surgeon	3,213 (75.7)	477 (73.6)	2,736 (76.1)	
Colorectal surgeon	636 (15.0)	128 (19.8)	508 (14.1)	
Other	284 (6.7)	31 (4.8)	253 (7.0)	
Unknown	109 (2.6)	12 (1.9)	97 (2.7)	
Bowel resection case volume[c]				<0.001
Low case volume (1–11)	1,685 (39.7)	104 (16.0)	1,581 (44.0)	
High case volume (12+)	2,557 (60.3)	544 (84.0)	2,013 (56.0)	

min = minutes; SD = standard deviation.

[a] Procedures coded as laparoscopy, having charges for laparoscopic instruments, or having a code for conversion to open, were classified as laparoscopic, as follows: laparoscopic colon and rectal (ICD-9-CM 17.3x, 46.94, 48.63, 48.69, and 48.74); open colon and rectal (ICD-9-CM 45.7x, 46.94, 48.63, 48.69, and 48.74); laparoscopic small bowel (ICD-9-CM 45.61, 45.62, and 46.93); open small-bowel (ICD-9-CM 45.61, 45.62, and 46.93); and ostomy take-downs, bypasses, other procedures (ICD-9-CM 45.90-45.94, 46.02, 46.04, and 46.5x).

[b] Cancer of intestine (ICD-9-CM 152.x, 153.x, 154.0, 154.1, 154.8, and 159.x); inflammatory bowel disease: (ICD-9-CM 555.x and 556.x); and diverticular disease (ICD-9-CM 555.x, 556.x, and 562.1x).

[c] Low/high cutoff was based on the 75th percentile of the surgeon's case volume for procedures in the first two quarters of 2009.

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We excluded 30 patients who had received more than 15 doses of alvimopan and 17,023 controls who had undergone surgery at hospitals where alvimopan use had not been recorded; these were presumed to be non-E.A.S.E. hospitals. The pre-matched groups, therefore, included 648 alvimopan patients and 3,594 controls.

Pre-match Patient Characteristics

Before matching, the groups differed significantly with regard to patient, procedure, hospital, and physician characteristics (Table 1, page 212). Differences in the distribution of procedures were statistically significant ($P < 0.001$); more laparoscopic colon and rectal procedures were performed among alvimopan patients than controls. No laparoscopic small-bowel resections were performed in the alvimopan group.

Mean operative times were 189.2 minutes for alvimopan patients and 201.3 minutes for controls ($P < 0.001$); 84% of alvimopan patients had been admitted voluntarily, compared with 61.1% of controls ($P < 0.001$). More alvimopan patients (88.7%) had surgery on the first hospital day compared with controls (68.8%) ($P < 0.001$).

Matched Cohort Characteristics

Two matches were identified for 480 alvimopan patients (74%), one match for 64 patients (10%), and no matches for 104 patients. The final cohort, therefore, included 480 alvimopan patients and 960 matched controls. After matching, there were no statistically significant differences between the alvimopan patients and the matched controls (Table 2).

The mean age of both groups was 63 years, and 52% of the patients were women. The types of surgery were matched exactly; 46% were laparoscopic colon and rectal procedures, 38% were open colon and rectal procedures, and 6% were open small-bowel procedures. The rest of the operations consisted of ostomy take-downs, bypasses, and other procedures. Mean operative time was slightly over three hours for both groups. The mean number of alvimopan doses was 7.7 in the treated cohort.

Cancer was the most common underlying diagnosis, followed by diverticular disease, then inflammatory bowel disease. The mean number of chronic conditions was similar for the alvimopan and matched control cohorts (3.2 vs. 3.1, respectively; $P = 0.643$).

General surgeons performed 68% of operations in both groups; 21% of alvimopan patients and 25% of controls had surgeons with low case volumes ($P = 0.114$).

Costs and Length of Stay

After matching, mean total hospital costs (including alvimopan costs) were $12,865 for alvimopan patients and $13,905 for controls, for a difference of $1,040 ($P = 0$ .033) (Table 3). There was a nonsignificant trend toward lower POI-related costs (including postoperative NGT insertion, parenteral nutrition, and antiemetic agents or GI stimulants) between the groups—$83 for alvimopan patients and $114 for controls ($P = 0.086$).

Pharmacy and radiology costs did not differ significantly between the groups. Mean LOS was 5.6 days for alvimopan patients and 6.5 days for controls ($P < 0.001$).

Sensitivity Analyses

Two sensitivity analyses addressed differences in surgeon case volume.

The first analysis used a multivariate regression model to control for residual differences between groups. Between-group differences in costs and LOS were unchanged ($P = 0.034$ for total costs, $P < 0.001$ for LOS, and $P \geq 0.05$ for other analyses). The second analysis stratified matched patients into high-case-volume and low-case-volume cohorts. Differences in costs and LOS between alvimopan patients and controls remained for both groups. In our sensitivity analysis, which used a gamma rather than a normal distribution, the *P* value for the total cost difference remained significant ($P < 0.007$); however, it was not significant for the other cost comparisons.

In a *post hoc* subanalysis that stratified patients as having laparoscopic or open colon and rectal procedures, statistically significant differences favored alvimopan for both cost savings ($13,230 vs. $15,714, respectively; $P = 0.004$) and LOS (6.2 days vs. 7.6 days, respectively; $P < 0.001$) in patients who had the open surgical approach and for LOS (4.9 days vs. 5.5 days, respectively; $P = 0.025$) in patients who had laparoscopic surgery.

Costs for laparoscopic colon and rectal procedures did not differ significantly between alvimopan patients and controls ($12,575 vs. $12,646, respectively; $P = 0.888$).

DISCUSSION

Total hospital costs were $1,040 less for alvimopan patients than for a matched control group who did not receive the treatment, even after accounting for the cost of the medication. Mean hospital stay was nearly a full day shorter for alvimopan patients than for matched controls.

The extent of cost savings and LOS reduction was similar to that reported in clinical trials. In a study of pooled randomized trial data for alvimopan, the mean LOS was estimated to be one day shorter for the alvimopan group, compared with the placebo group, and the mean hospital cost (including the cost of alvimopan) was $879 to $977 less with alvimopan use.[3]

Our findings are supported by previous work demonstrating that delayed GI recovery increases costs and LOS. A chart review of colectomy patients at a large teaching hospital showed that LOS was longer and costs were higher in patients with delayed GI recovery or POI than in patients without these complications.[5] Similarly, a retrospective study that also used the Premier database found increased LOS and costs for colectomy patients with coded POI compared with colectomy patients without coded POI.[6] Clinical trials have demonstrated the ability of alvimopan to accelerate GI recovery. Alvimopan, therefore, can be expected to mitigate the increased LOS and costs associated with delayed GI recovery.

Delayed GI recovery or POI after abdominal surgery costs the American health care system approximately $1.46 billion annually.[7] Improving quality of care and reducing costs are consistent with the goals of the American College of Surgeons.[35] Most interventions that improve outcomes—whether they be drugs, devices, or health programs—increase the cost of care[36] and require complex cost–benefit assessments. However, alvimopan may improve patient outcomes[4,20] while reducing costs.[3]

Other approaches after bowel-resection surgery include

Table 2 Characteristics of Patients, Physicians, Hospitals, and Procedures After Matching

Variable	Alvimopan Patients (n = 480; 33.3%)	Matched Controls (n = 960; 66.7%)	*P* Value
Patient Characteristic			
Age (years) (Mean, SD)	63.1 (14.0)	62.5 (14.0)	0.434
	No. (%)		
Age group			0.898
18–44	47 (9.8)	104 (10.8)	
45–64	206 (42.9)	414 (43.1)	
65–74	113 (23.5)	227 (23.6)	
75+	114 (23.8)	215 (22.4)	
Female	248 (51.7)	495 (51.6)	0.970
Race/ethnicity			0.797
White	330 (68.8)	676 (70.4)	
Black	40 (8.3)	78 (8.1)	
Other	110 (22.9)	206 (21.5)	
No. of chronic conditions (Mean, SD)	3.2 (1.7)	3.1 (1.7)	0.643
Pre-existing conditions increasing risk for chronic heart disease, %			
Hypertension	51.5	50.7	0.794
Lipid disorders	29.2	26.9	0.359
Diabetes	19	18.5	0.848
Coronary atherosclerosis	10.2	10.6	0.808
Obesity	10	10.6	0.714
Other form of chronic heart disease	5.6	6.5	0.536
Myocardial infarctions in previous 6 months	0.4	0.3	0.751
Admission and Procedure Characteristics			
No. of alvimopan doses (Mean, SD)	7.7 (3.8)	0	—
Index procedure type[a]			N/A[d]
Laparoscopic colon and rectal	222 (46.3)	444 (46.3)	
Open colon and rectal	183 (38.1)	366 (38.1)	
Open small-bowel	30 (6.3)	60 (6.3)	
Ostomy take-downs, bypasses, other	45 (9.4)	90 (9.4)	
Operative time (min) (Mean, SD)	193.0 (81.4)	192.0 (91.6)	0.838
Red blood cell transfusion	17 (3.5)	29 (3.0)	0.596
Diagnosis[b]			
Cancer of intestine	183 (38.1)	344 (35.8)	0.395
Inflammatory bowel disease	19 (4.0)	39 (4.1)	0.925
Diverticular disease	133 (27.7)	264 (27.5)	0.934
Hospital and Physician Characteristics			
Hospital region			N/A[d]
Midwest	116 (24.2)	232 (24.2)	
Northeast	83 (17.3)	166 (17.3)	
South	269 (56.0)	538 (56.0)	
West	12 (2.5)	24 (2.5)	
Location			0.959
Rural	76 (15.8)	153 (15.9)	
Urban	404 (84.2)	807 (84.1)	
Teaching hospital	297 (61.9)	594 (61.9)	0.999
Physician specialty			0.719
General surgeon	328 (68.3)	652 (67.9)	
Colorectal surgeon	123 (25.6)	236 (24.6)	
Other	17 (3.5)	46 (4.8)	
Unknown	12 (2.5)	26 (2.7)	
Bowel resection case volume[c]			0.114
Low case volume (1–11)	101 (21.0)	238 (24.8)	
High case volume (12+)	379 (79.0)	722 (75.2)	

min = minutes; N/A = not applicable; SD = standard deviation.

[a] Procedures coded as laparoscopy, having charges for laparoscopic instruments, or having a code for conversion to open, were classified as laparoscopic, as follows: laparoscopic colon and rectal (ICD-9-CM 17.3x, 46.94, 48.63, 48.69, and 48.74); open colon and rectal (ICD-9-CM 45.7x, 46.94, 48.63, 48.69, and 48.74); laparoscopic small bowel (ICD-9-CM 45.61, 45.62, and 46.93); open small-bowel (ICD-9-CM 45.61, 45.62, and 46.93); and ostomy take-downs, bypasses, other procedures (ICD-9-CM 45.90-45.94, 46.02, 46.04, and 46.5x).

[b] Cancer of intestine (ICD-9-CM 152.x, 153.x, 154.0, 154.1, 154.8, and 159.x); inflammatory bowel disease: (ICD-9-CM 555.x and 556.x); and diverticular disease (ICD-9-CM 555.x, 556.x, and 562.1x).

[c] Low/high cutoff was based on the 75th percentile of the surgeon's case volume for procedures in the first two quarters of 2009.

[d] Matched exactly.

Table 3 Cost and Utilization in Alvimopan Patients and Matched Controls

Variable		Alvimopan Patients (n = 480; 33.3%)	Matched Controls (n = 960; 66.7%)	*P* Value
Total hospital cost ($)	Mean (SD)	12,865 (7,826)	13,905 (10,305)	0.033
	95% CI	12,163–13,567	13,252–14,558	
Diagnostic radiology ($)	Mean (SD)	181 (445)	210 (492)	0.252
	95% CI	141–220	179–241	
Total pharmacy ($)	Mean (SD)	1,431 (1,892)	1,331 (2,024)	0.369
	95% CI	1,261–1,601	1,203–1,460	
POI-related[a] ($)	Mean (SD)	83 (286)	114 (400)	0.086
	95% CI	57–109	89–140	
Length of stay (days)	Mean (SD)	5.6 (4.1)	6.5 (4.6)	<0.001
	95% CI	5.2–6.0	6.2–6.8	

CI = confidence interval; POI = postoperative ileus; SD = standard deviation.

[a] Including supply and labor costs of postoperative nasogastric tubes insertion, parenteral nutrition, and antiemetic agent or gastrointestinal stimulants (e.g., metoclopramide).

multimodal fast-track or enhanced recovery protocols that combine various preoperative, intraoperative, and postoperative interventions with the goal of accelerating GI recovery and shortening LOS after surgery.[8,10,15–19,37] These protocols may reduce LOS by hours or days, depending on the procedure.[37] For example, in a case–control study of patients who underwent ileal pouch–anal anastomosis, a fast-track protocol reduced mean hospital costs by $980 and LOS by 0.9 days.[17] In another study, a fast-track protocol for colon resection resulted in a mean decrease in both hospital costs and LOS.[38] In clinical trials, alvimopan in conjunction with an accelerated multimodal care pathway has also resulted in a shorter LOS compared with the pathway alone.

Laparoscopic bowel surgery, compared with open surgery, reduces LOS, but its impact on costs remains uncertain. Results from a large inpatient retrospective database study revealed a shorter LOS (by 1.2 days) but a higher (by $398) total hospital cost associated with laparoscopic surgery compared with open colectomy.[12] By contrast, a case–control study showed a decreased LOS and lower costs (by $446) for laparoscopic surgery compared with open colectomy.[13]

Larger studies with more detailed data collection would be useful to determine the effectiveness of various methods for reducing costs and LOS after bowel surgery and to investigate clinical outcomes associated with bowel resection and their impact on LOS and costs.

STUDY LIMITATIONS

Our study had several limitations; it was retrospective, and unmeasured differences between groups might have biased the results. As with other administrative claims database studies, coding errors and incomplete reporting might have affected the accuracy of the data. There is no ICD-9-CM code for POI, nor is there a universally accepted clinical definition; this fact may lead to underreporting of ileus and an underestimation of its cost.[5]

Another potential limitation is that we enrolled only patients whose surgery was performed in hospitals that were part of the E.A.S.E. program and in the Premier database. This selection process could have affected our ability to generalize the results.

In the *post hoc* subanalysis of laparoscopic and open colon and rectal procedures, some patients who were classified as having undergone laparoscopic procedures based on laparoscopic instrument charges could have been misclassified, depending on the reliability of this method of classification. For example, patients undergoing an open procedure could have been included in the laparoscopic subgroup. Further studies of patients undergoing laparoscopic and open colon and rectal procedures are recommended.

Because this was an administrative claims database study, we could not investigate clinical variables that were not captured in this type of database, such as opioid doses, a history of POI or multiple GI surgeries, and the use of an accelerated care pathway. Nonetheless, because of the rigorous matching procedures that we used, it is reasonable to assume that these variables would be similar between cohorts.

The study nonetheless had significant value. Because we analyzed data from actual practice, our work adds to the body of literature surrounding use of alvimopan outside of the rigorous confines of a clinical trial setting as well as outside of the multimodal standardized accelerated care pathway used in both alvimopan and placebo arms of the clinical trials.

The variety of centers in this study and their wide geographic distribution increase the likelihood that our results can be replicated. We also used rigorous matching techniques to eliminate differences between the treatment and control groups. Total costs were reported by individual hospitals for benchmarking purposes and thus were likely to be accurate. Finally, the results were robust to a variety of sensitivity analyses.

CONCLUSION

Our study confirmed the reduction in LOS in non-research controlled clinical settings that had been previously observed in clinical trials of alvimopan (Entereg) as well as a reduction in total hospital costs. Along with other initiatives to improve both the quality and cost of surgical care, alvimopan represents a viable option for use in the perioperative management of patients undergoing segmental bowel resection with primary anastomosis.

Acknowledgments. The authors would like to thank Gregory C. Giguere, MS, at GlaxoSmithKline for his statistical review and Amy W. Rachfal, PhD, at Adolor Corp. for her editorial assistance.

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