

**DOES THE DOSING FREQUENCY OF PROTON PUMP INHIBITORS (PPIs) AFFECT  
SUBSEQUENT RESOURCE UTILIZATION AND COSTS AMONG PATIENTS  
DIAGNOSED WITH GASTROESOPHAGEAL REFLUX DISEASE (GERD)?**

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"European-style" presentation)

## ABSTRACT

**OBJECTIVE:** To assess utilization and costs of healthcare services for patients diagnosed with gastroesophageal reflux disease (GERD) that were dispensed once (QD) vs. twice (BID) daily PPIs.

**METHODS:** Employing Thomson's MarketScan Database, GERD patients 18+ years of age with 1+ PPI dispensed, but had no erosive esophagitis or Barrett's esophagus diagnosed during 2003-2004 were selected. The date of the first observed PPI was considered as the index date. Frequency of PPI dosing (QD vs. BID) was assessed from pharmacy claims. Differences in total and GERD-related costs by cohort for the 12-month period following the index date were assessed using multivariate regression, adjusting for demographic and clinical characteristics (age, gender, region, Charlson comorbidity score [CCS], pre-index diagnosis of esophageal stricture or hemorrhage [ESH], and pre-index use of PPIs).

**RESULTS:** A total of 219,365 GERD patients on QD PPI therapy and 23,011 patients on BID PPI therapy were identified. The cohorts were similar in age, but the QD cohort had a larger proportion of males (41% vs 37%,  $p<0.01$ ). Mean CCS was higher in the BID cohort (1.2 vs 1.0,  $p<0.01$ ). A higher proportion of BID patients had pre-index ESH diagnosed (4% vs 3%,  $p<0.01$ ) and PPI's dispensed (58% vs 47%,  $p<0.01$ ). In the 12-month follow-up period, the mean number of office visits was higher among BID patients (14.5 vs 12.4,  $p<0.01$ ). Unadjusted total healthcare payments were about \$2,900 higher for BID patients (\$11,102 vs \$8,169,  $p<0.01$ ), 55% of which were payments for medical services. GERD-related costs were about \$750 higher for BID patients (\$1,941 vs \$1,187,  $p<0.01$ ). On an adjusted basis, total and GERD-related payments were approximately \$1,500 and \$450 higher among the BID cohort.

**CONCLUSION:** These findings indicate that patients diagnosed with GERD who receive BID PPI therapy incur more total and GERD-related healthcare resource utilization and plan payments relative to those on QD therapy.

## **BACKGROUND**

- In the US, GERD-associated symptoms affect approximately 60% of adults annually and up to 10% daily. The estimated lifetime prevalence of GERD is 25-35%.<sup>1-5</sup>
- In one analysis of managed care data, the average person with GERD had \$1500-\$2000 more in annual total healthcare expenditures than those without GERD.<sup>6</sup>
- There are limited data on the impact of once daily versus twice daily PPI dosing regimens on patterns of healthcare resource utilization and associated direct costs.

## **STUDY OBJECTIVES**

Among GERD patients, for those prescribed once daily versus twice daily PPIs, this study:

- Profiled demographic and clinical characteristics
- Assessed patterns of total and GERD-related healthcare resource utilization
- Quantified associated direct total and GERD-related healthcare costs

## **METHODS**

### **Data Source**

- A retrospective cohort design employing administrative claims data from Thomson Medstat's MarketScan Commercial Claims & Encounters and Medicare Supplement and COB databases (July 1, 2001-December 31, 2005) were used to address the research objectives
- Data from patient level enrollment files, pharmacy files, and medical services files were used for the study

### **Patient Selection & Cohort Identification**

- Health enrollment requirement: continuous enrollment for at least 12 months prior to the index date through 12 months following the index date (i.e. study period).
- Patients 18+ years of age were required to have one or more medical visits with an associated diagnosis of GERD (ICD-9-CM code 530.10, 530.11, 530.12, 530.19, or 530.81) during the calendar years of 2003 and 2004.
- Patients also were required to have one or more pharmacy claim for a PPI (identified based on NDC) during the calendar years of 2003 and 2004 (the first observed PPI was set as the index date).

- Exclusion criteria: patients with erosive esophagitis (ICD-9-CM diagnosis code 530.20, 530.21) or Barrett's esophagus (ICD-9-CM diagnosis code 530.85) diagnosis were excluded from the study population.
- Two patient cohorts were identified: the QD cohort consists of selected GERD patients who had a once-daily initial PPI dosing regimen, and the BID cohort consists of selected GERD patients who had a twice-daily initial PPI dosing regimen.

## **Study Measures and Data Analysis**

- Healthcare resource utilization and associated direct costs by component in the 12 months following the index date were determined. Components include inpatient services (i.e., hospitalization), outpatient services (i.e., community-based physician visits and emergency room visits), and prescription medications.
- Student *t*-tests were used to test the statistical difference between the QD and BID cohorts.
- Multivariate analysis technique was employed to examine the effects of initial PPI dosing regimen on total healthcare costs after accounting for baseline patient demographic and clinical characteristics

## **RESULTS**

- The total sample size was 242,376 patients, including 219,365 patients (90.5%) in the QD cohort and 23,011 patients (9.5%) in the BID cohort.
- Baseline demographics were similar between the two cohorts, although there were fewer males in the BID cohort than in the QD cohort (see Table 1).

**Table 1: Baseline demographic characteristics, by dosing frequency**

Characteristic	Dosing frequency		p-value
	Q.D.	B.I.D.	
<b>Number of patients</b>	219,365	23,011	
<b>Mean (SD) age</b>	56.6 (15.0)	56.7 (14.4)	0.15
<b>Female (%)</b>	59.1%	62.6%	<0.01
<b>Plan types (%)</b>			<0.01
Comprehensive	32.3%	34.5%	
HMO	11.7%	12.4%	
PPO	40.9%	38.0%	
Other*	15.0%	15.0%	
<b>Geographic region (%)</b>			<0.01
Northeast	7.7%	8.0%	
North Central	36.3%	40.1%	
South	40.5%	35.1%	
West	15.3%	16.6%	
Unknown	0.3%	0.2%	

\* Other insurance types include: EPO, POS, and POS with capitation.

- In the pre-index period, patients in the BID cohort had clinical characteristics that indicated more severe GERD than patients in the QD cohort. Patients in the BID cohort also had more comorbid conditions (Table 2).

**Table 2: Clinical characteristics in the pre-index period, by dosing frequency**

Characteristic	Dosing frequency		p-value
	Q.D.	B.I.D.	
<b>Number of patients</b>	219,365	23,011	
<b>Patients with esophageal stricture or hemorrhage (%)</b>	2.6%	3.6%	<0.01
<b>Patients with endoscopy procedures (%)</b>	18.8%	30.7%	<0.01
<b>Mean (SD) Charlson comorbidity score</b>	1.0 (1.6)	1.2 (1.7)	<0.01
<b>Distribution of Charlson comorbidity score</b>			<0.01
0	54.2%	46.5%	
1	23.7%	26.2%	
2	10.9%	12.6%	
3+	11.3%	14.6%	
<b>Patients with PPI treatment (%)</b>	41.6%	52.2%	<0.01
<b>Patients with H2RA treatment (%)</b>	3.8%	4.9%	<0.01
<b>Patients with any hospitalization (%)</b>	16.7%	21.5%	<0.01
<b>Mean (SD) total healthcare expenditures</b>	\$5,923 (\$13,538)	\$8,290 (\$17,288)	<0.01

- Patients on BID regimens had significantly higher levels of GERD-related and overall resource utilization during the post-index period. Differences were observed in percentage of patients who required hospitalization, ER visits and GERD-specific and overall medication burden (see Table 3).

**Table 3: Inpatient and physician resource use in the post-index period, by dosing frequency**

Component of healthcare service	Dosing frequency		p-value
	Q.D.	B.I.D	
<b>Number of patients</b>	219,365	23,011	
<b>Hospitalization admissions:</b>			
GERD-related:			
Percentage of patients	0.9%	1.7%	<0.01
Mean (SD) length of stay	0.0 (0.6)	0.1 (0.8)	<0.01
Overall:			
Percentage of patients	16.6%	19.6%	<0.01
Mean (SD) length of stay	1.1 (6.6)	1.4 (6.1)	<0.01
<b>Patients with any ER visit (%)</b>	18.3%	19.5%	<0.01
<b>Mean (SD) number of community based physician visits</b>	12.4 (12.3)	14.5 (14.1)	<0.01
<b>Mean (SD) number of PPI prescriptions</b>	1.7 (2.7)	2.1 (2.9)	<0.01
<b>Mean (SD) number of H2RA prescriptions</b>	0.1 (0.6)	0.1 (0.6)	0.42
<b>Mean (SD) number of total prescriptions</b>	8.8 (6.6)	11.0 (7.8)	<0.01

- Direct treatment costs during the post-index period were significantly higher for the BID cohort relative to those in the QD cohort for inpatient services, outpatient services, pharmacy services and total and GERD-related healthcare costs (Table 4).

**Table 4: Annual healthcare costs for GERD patients in the post-index period, by dosing frequency**

Component of healthcare cost	Dosing frequency		p-value
	Q.D.	B.I.D	
<b>Number of patients</b>	219,365	23,011	
<b>Mean (SD) inpatient costs:</b>			
Any Condition	\$1,754 (\$11,086)	\$2,437 (\$13,897)	<0.01
GERD-related	\$60 (\$1,291)	\$143 (\$1,952)	<0.01
<b>Mean (SD) outpatient costs:</b>			
Any Condition	\$3,570 (\$9,040)	\$4,491 (\$9,277)	<0.01
GERD-related	\$252 (\$919)	\$337 (\$1,465)	<0.01
<b>Mean (SD) total medical costs:</b>			
Any Condition	\$5,324 (\$16,273)	\$6,928 (\$18,885)	<0.01
GERD-related	\$311 (\$1,641)	\$480 (\$2,571)	<0.01
<b>Mean (SD) pharmacy costs:</b>			
All Medications	\$2,845 (\$3,398)	\$4,174 (\$5,129)	<0.01
PPIs	\$871 (\$585)	\$1,452 (\$994)	<0.01
<b>Mean (SD) total healthcare costs</b>	<b>\$8,169 (\$17,140)</b>	<b>\$11,102 (\$20,382)</b>	<b>&lt;0.01</b>
<b>Mean (SD) total GERD-related healthcare costs</b>	<b>\$1,187 (\$1,898)</b>	<b>\$1,941 (\$3,088)</b>	<b>&lt;0.01</b>

- In multivariate analysis, we controlled for patient demographics, clinical characteristics, prior PPI usage, and prior GERD-related expenditures.
- After adjusting for baseline patient characteristics, the BID cohort was associated with approximately \$1,500 (p<0.01) in additional total healthcare expenditures and \$450 (p<0.01) in additional GERD-related healthcare expenditures.
- Significant predictors for higher costs among BID patients include age, male gender, region, Charlson comorbidity score, pre-index diagnosis of esophageal stricture or hemorrhage, and pre-index use of PPIs.

## LIMITATIONS

- Retrospective study design
- Without access to patients' actual medical records, the study could not sufficiently assess the severity of GERD conditions in study patients

- The study did not have access to patients' history of over-the-counter medication utilization

## **CONCLUSION**

- Patients prescribed once-daily PPIs had significantly lower levels of resource utilization and incurred lower healthcare costs in both the pre-index and post-index periods compared to those dispensed twice-daily PPIs.
- After adjusting for patient demographic and clinical characteristics at baseline, the cost for the twice-daily PPI dosing regimen was \$1,500 ( $p<0.01$ ) higher for all healthcare expenditures and \$450 ( $p<0.01$ ) higher for GERD-related expenditures compared to once-daily PPIs.

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