

Comparison of the Medication Possession Ratio Alone and in Combination With Breakthrough Events for Classifying Patients With Acid-Related Diseases

Brook RA¹; Smeeding JE²; Joshua-Gotlib S³; Warner D⁴

¹Head, Retrospective Analysis, The JeSTARx Group, Newfoundland, NJ; ²President, The JeSTARx Group, Dallas, TX, and The University of Texas, Austin, TX; ³Associate Director, Health Economics and Outcomes Research, AstraZeneca LP, Wilmington, DE; ⁴Brand Director, Managed Markets, AstraZeneca LP, Wilmington, DE

CONCLUSIONS

- The MPR alone method outperforms the MPR in combination with the existence of BTEs in differentiating patients with ARDs.
- It is likely that GERD-specific medical encounters and diagnostic procedures may not be reflected in patient medical histories maintained by insurers.
- The simplicity of using the MPR alone as a surrogate marker for analyzing GERD severity allows health plans and other large purchasers the opportunity to explore the impact of GERD on their patient population.

OBJECTIVES

- To determine whether the medication possession ratios (MPRs) alone or in combination with breakthrough events (BTEs) were likely to show differentiation by patient groupings by:
 - Exploring differences in MPRs among users of proton pump inhibitor (PPI) therapy
 - Identifying if the existence of certain BTEs (diagnoses and procedures) in combination with MPRs are better predictors of disease severity than medication usage alone (MPR)

INTRODUCTION

- The prevalence of gastroesophageal reflux disease (GERD), defined as at least weekly heartburn, has been estimated at 20 million in the United States.¹ The number of patients who had a medical visit related to GERD in a given year has been found to be far lower.²
- Acid-Related Diseases (ARDs) include GERD and related conditions, such as esophagitis and heartburn (Table 1).

Table 1. ARD ICD-9 codes and prescription utilization

| ARD-specific condition | ICD-9 code | Prescription product | Class |
|--------------------------|------------|----------------------|-------------------|
| Hypersecretory condition | 251.5 | Esomeprazole | PPI |
| Esophagitis, unspecified | 530.10 | Omeprazole | PPI |
| Esophagitis, incomplete | 530.1 | Lansoprazole | PPI |
| Reflux esophagitis | 530.11 | Rabeprazole | PPI |
| Acute esophagitis | 530.12 | Pantoprazole | PPI |
| Other esophagitis | 530.19 | Cimetidine | H ₂ RA |
| Esophageal reflux | 530.81 | Famotidine | H ₂ RA |
| Heartburn | 787.1 | Nizatidine | H ₂ RA |
| Dysphagia, complete | 787.2 | Ranitidine | H ₂ RA |

METHODS

- Retrospective database analyses of 10.6 million adjudicated claims from the PharMetrics (Watertown, Mass) database were used to examine utilization rates and medical costs of patients with ARDs.
- The study classified ARD patients into 5 cohorts by both MPR alone and in combination with specified BTEs. Each classification method was examined to assess how well it differentiated patient types based on PPI medication use and BTEs.

- Patients at least 18 years of age with an *International Classification of Diseases*, ninth revision (ICD-9), code for GERD in their history or with utilization of medical or pharmacy services that included at least a 30-day supply of PPIs or an H₂-receptor antagonist (H₂RA) between July 1, 2001, and June 30, 2003, as listed in Table 1, were included in the study.
- Patients were excluded if they had any claims for:
 - Human immunodeficiency virus (ICD-9 codes of 042.X-044X)
 - Any neoplasms (ICD-9 codes of 140.X-239.X). Because neoplasms may not have been immediately diagnosed, persons with neoplasms identified before September 30, 2003, also were excluded.
- MPRs were calculated for all patients enrolled in the study.
- Claims during the study period were analyzed for the presence of breakthrough diagnoses and breakthrough procedures, Tables 2A and 2B, respectively.

Table 2A. Breakthrough diagnoses

| Diagnosis | ICD-9 code |
|---|------------|
| Ulcer (chronic peptic ulcer of esophagus) | 530.2 |
| Stenosis, stricture, esophagus | 530.3 |
| Abnormality of secretion of gastrin, Zollinger-Ellison Syndrome (gastric hypersecretion with pancreatic islet cell tumor) | 251.5 |

Table 2B. Breakthrough procedures

| Procedure | CPT code |
|---------------------------------|--------------------------|
| Esophagus dilation+ | 43450-43458 |
| Esophagus dilation, endoscopic+ | 43220-43226, 43248-43249 |
| Esophagus dilation, surgical+ | 43510 |

CPT, current procedural terminology.

- Figures 1 and 2 show how the study classified ARD patients by their MPRs alone and in combination with specified BTEs, respectively, into 5 cohorts. The study examined how well each classification method differentiated persons based on the following:
 - Total costs (study period and per month):** Total costs, medical visit costs, ED costs, hospitalization costs, costs for all NDC claims, costs for PPI claims, costs for H₂RA claims, costs for PPI + H₂RA claims, costs for non-PPI and non-H₂RA NDC claims
 - ED costs:** ED events classified as upper gastrointestinal (GI), other GI emergencies, noncardiac chest pain, cardiac, noninfectious respiratory, other respiratory, other emergencies
 - Ratios:** Annual and monthly ratios of the costs of PPI therapy compared with the following: all NDC drugs, total claims, hospitalizations, and medical visits
 - Utilization:** Annual and monthly utilization data (number of medical visits, ED visits, and hospitalizations, and cumulative number of days of hospital stay)
 - ARD-specific comorbidities:** Based on the ICD-9 codes from Table 1
 - Non-ARD-specific comorbidities:** Based on ICD-9 codes for asthma, obesity, depression, pain, and sleep disorders. Because of the difficulty in identifying pain and sleep disorders, these comorbidities also were assessed by the use of concomitant medications.

Figure 1. Cohort assignments based on MPR alone

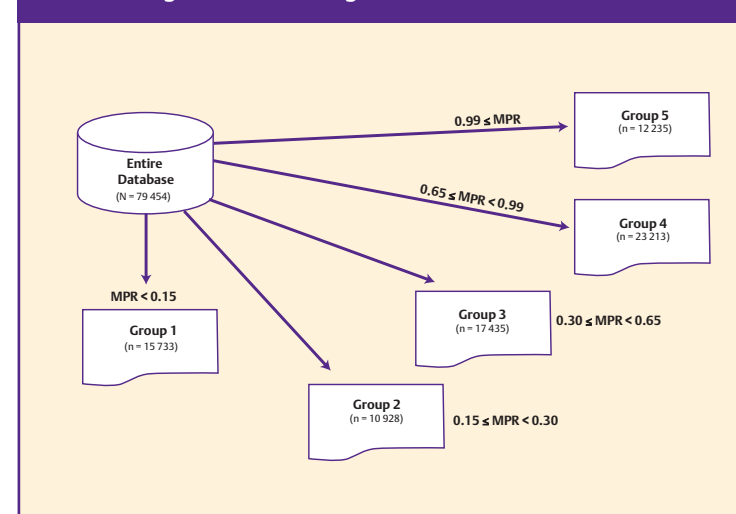
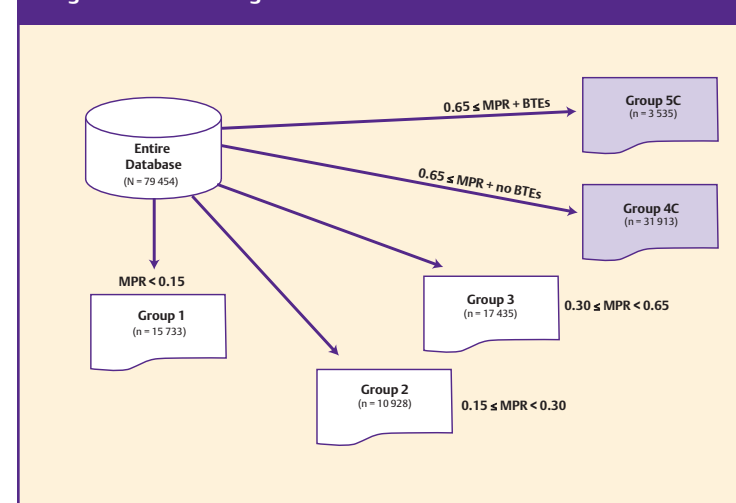


Figure 2. Cohort assignments based on MPR in combination with BTEs



- Once the patients were classified, differences between utilization and costs were compared using paired comparison tests.
 - Pairwise group comparisons of means were made between cohorts using Bonferroni's (Dunn's) method for multiple comparisons of continuous variables and χ^2 paired comparison tests for discrete variables.
 - Nonparametric Kruskal-Wallis χ^2 tests were used to compare the distributions of these data.
 - Differences were considered to be statistically significant if $P \leq .05$.
- The study specifically examined how well each classification method discriminated between all groups and additionally between the top 2 cohorts (groups 4 and 5).
- The analysis plan identified 760 possible matched pair comparisons and 43 comparisons between the top 2 cohorts.

RESULTS

- The study identified a population of 79 454 persons with 700 846 claims for PPI prescriptions during the 2-year time frame.
- Significant pairwise comparisons identified for the 2 methods follow:
 - The MPR alone method identified 523 (68.8%)
 - The MPR combination method identified 464 (61.1%)
- In comparing the top 2 cohorts (Table 3):
 - The MPR alone method identified 29 (67.4%) compared with 19 (44.2%) for the combination method.
 - The combination method outperformed the MPR alone method in comparison of the top 2 cohorts in terms of ARD-specific comorbidities and for costs incurred from ED visits.

Table 3. Comparison of classification methods: MPR alone and in combination with BTEs

| Variable type | Number of significant comparisons | | | |
|---|-----------------------------------|------------------------|--------------------|--------------------------|
| | MPR alone method | | Combination method | |
| | All groups | Group 4 versus group 5 | All groups | Group 4C versus group 5C |
| Total costs/study period (\$) | 146 | 8 | 124 | 3 |
| Total costs/month (\$) | 146 | 8 | 124 | |
| ED costs (\$) | 54 | 0 | 46 | 1 |
| Ratios (n) | 76 | 3 | 74 | 3 |
| Utilization (n) | 42 | 2 | 32 | 0 |
| Totals, economic and utilization, (n) | 464 | 21 | 400 | 10 |
| Total possible (n) | 660 | 33 | 660 | 33 |
| Performance (%) | 70.3 | 63.6 | 60.6 | 30.3 |
| Total ARD-specific comorbidities (n) | 23 | 3 | 36 | 4 |
| Total possible (n) | 50 | 5 | 50 | 5 |
| Performance, ARD-specific (%) | 46 | 60 | 36 | 80 |
| Total non-ARD-specific comorbidities (n) | 36 | 5 | 28 | 5 |
| Total possible (n) | 50 | 5 | 50 | 5 |
| Performance, non-ARD-specific (%) | 72 | 100 | 56 | 100 |
| Total comorbidities (n) | 59 | 8 | 64 | 9 |
| Total possible (n) | 100 | 10 | 100 | 10 |
| Performance, comorbidities (%) | 59 | 80 | 64 | 90 |
| Totals, above and comorbidities, (n) | 523 | 29 | 464 | 19 |
| Total comparisons (n) | 760 | 43 | 760 | 43 |
| Performance, above and comorbidities, (%) | 68.8 | 67.4 | 61.1 | 44.2 |

REFERENCES

- Shaheen N, Provenzale D. *Am J Med Sci*. 2003;326:264-73.
- IMS National Disease and Therapeutic Index (NDTI) Audit, March 2005.