Medical Utilization and Cost Impact of Significantly Reducing Proton Pump Inhibitor Coverage: An Actuarial Analysis

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EXECUTIVE SUMMARY

As particular prescription drugs receive over the counter (OTC) approval, health benefit plans may continue coverage for a short or long term period. In some cases, coverage will be available at strengths and for indications different from the OTC product, although sometimes coverage continues even when the prescription and OTC strength are identical. Payers may recognize cost savings from significantly restricting or dropping coverage for prescription drugs that have an OTC option, particularly since OTC medicines are considered safe, clinically effective and convenient and do not require a health care provider visit to obtain a prescription.

Concern is raised by some about the real-world comparable effectiveness of prescription and OTC products. For example, there could be adverse clinical and medical cost consequences if significantly restricted or dropped coverage leads to reduced adherence with prescribed drug therapies that have an OTC option. Reduced adherence could occur if patients choose not to access the OTC option or simply delay refilling their RX product due to higher out-of-pocket costs.

In the case of proton pump inhibitors (PPIs), the concern would be that non adherence could lead to an increase in particular gastrointestinal conditions (gastrointestinal bleeding, gastritis, heartburn etc.) and an increase in utilization of physician office visits, GI procedures and GI related ER visits or inpatient admissions. In addition, use of prescription or OTC alternatives such as H2 receptor antagonists could increase. Two studies have examined this issue, one focused on restricting coverage for PPIs and another for H2 receptor antagonists. Neither study identified an adverse clinical or cost impact from restricting coverage for prescription PPIs or H2 receptor antagonists. [1, 2]

It is also important to consider the impact that significantly reducing or dropping PPI coverage could have over an extended period of time and that long term studies should be considered to fully understand the impact that this type of change could have on the plan and the patient. This paper investigates the issue further for PPIs.

The authors conducted a claim based longitudinal analysis of plan contributors to the Thomson Reuters MarketScan® Commercial Database who significantly restricted or dropped coverage of PPIs. We examined the frequency of PPI sensitive medical conditions and services in the year before and after significant restriction or dropping of PPI prescription benefit coverage to determine if there were adverse impacts on services or medical cost.

KEY FINDINGS

Our analysis identified no statistically significant difference in the utilization of 15 key PPI sensitive metrics after coverage was significantly restricted or dropped including:

- Inpatient admissions for GI bleeds or complicated peptic ulcer
- Diagnostic radiologic upper GI procedures or upper endoscopy procedures
- Physician office visits for PPI sensitive conditions
- Use of H2 receptor antagonists
- Prevalence of esophageal cancer

The finding of no detectable adverse impact in any of the 15 metrics could indicate that those who were being prescribed PPI therapy in the "pre" period were still accessing a PPI therapy in the "post" period, although we do not have data to test this hypothesis. Examples of how patients could continue to access a PPI after a restriction in benefit coverage include:

- After discussing with their doctor, purchasing an OTC PPI, for the treatment of frequent heartburn
- Seeking a medical exemption from their plan through an authorization or appeal process that allows the patient to continue to receive coverage of the RX PPI as part of their current benefit design
- After discussing with their doctor, deciding to pay out-of-pocket for the prescription PPI
- Receiving free samples from their doctor
- Receiving free product directly from the manufacturer as part of a patient assistance program

It is also possible that some patients may discontinue PPI use. However, these results suggest that adverse outcomes, if any, are not likely to be apparent for a typical large employer. The Methodology section contains details on the statistical testing we performed.

For more details on the cost associated with PPI coverage, see the Milliman white paper titled "*Proton Pump Inhibitors: A High Cost Employee Benefit with Over-the-Counter Alternatives"*, available at www.otcbenefitadvisor.com, which examines PPI benefit coverage from the perspective of employers and the potential for savings from shifting utilization to OTC.

OTC PPIs are indicated to treat frequent heartburn with a 14-day course of treatment no more than once every 4 months unless otherwise directed by a physician. It is important to balance cost effectiveness of OTC PPIs with the needs of patients for whom an OTC PPI therapy is not an appropriate option. In considering coverage decisions for PPIs, each employer should consult medical experts to determine which patients may use OTC products. PPIs are not interchangeable. They differ in dose, indication, contraindications, and directions for use. All patients should talk with their doctor before stopping or starting any medication therapy and to ask whether an OTC PPI is right for them, and if so, which one(s).

This paper was commissioned by Procter & Gamble, which markets an OTC PPI. This report reflects the findings of the authors and does not represent a position or endorsement by Milliman of any product or policy. As with any economic study, the information contained in this report cannot consider all possible factors, and our information may not be suitable for use in certain situations. Particular employers or insurers may have results that differ significantly from the averages presented here.

BACKGROUND

HISTORICAL PERSPECTIVE OF PRESCRIPTION DRUGS MOVING TO OTC

Proton Pump Inhibitors (PPIs) were available only by prescription until 2003, when the first PPI became available as an OTC. Today, three branded PPIs are available as OTC products. The wide availability of OTC PPIs, combined with the high use and cost of brand PPIs, raises the potential for drug savings under certain circumstances for both employers and employees. Many employers have already seen the cost of the PPI category decline due to wide spread generic use and the increased availability of OTC options (including FDA approvals for two additional OTC PPIs in the second half of 2009) [3] but significant opportunity exists to further reduce spending in this prescription drug class.

Over-the-counter (OTC) medicines are considered safe, clinically effective, cost effective, and convenient. While they may be used without a prescription, depending on the patient's condition or symptoms, it may still be appropriate to discuss OTC treatment options with their physician prior to stopping or starting an OTC product. Millions of Americans use these products daily to treat a wide variety of symptoms. There are many OTC products available that previously were available only by prescription. Surveys indicate that 92% of American consumers consider OTC drugs effective; 83% consider OTC drugs safe; and 73% report that they prefer to treat symptoms themselves with OTC drugs. [4]

When an ingredient is first approved, it is typically approved to be marketed by a manufacturer as a prescription medicine. After a sufficient amount of time has passed to enable the manufacturer to gather appropriate scientific information on the product, the manufacturer may elect to submit a new drug application to the Food and Drug Administration (FDA) for consideration for OTC status. Drug manufacturers or citizen groups can petition the FDA to switch an approved prescription medication to OTC status. The same safety and product efficacy standards apply as for prescription products. The main criteria considered by the FDA for a proposed switch are 1) whether the product has a high safety profile and 2) if labeling can be clear, accurate and understood by the lay person. Consumers must be able to self-diagnose, self-treat, and self-manage their condition. Essentially the FDA weighs the risks and benefits of the proposed switch.[5] The FDA does not however, consider the economic implications of allowing OTCs into the market.

PPIs are a highly utilized class of medication and have long been a top volume prescription category. Prescription PPI's are categorized as "ulcer drugs" a Top 10 cost category with several large PBM's. Express Scripts 2009 Drug Trend Report (published April 2010) indicates that the "ulcer disease drug class", of which PPIs contribute 91% of the utilization and 94% of the cost, is the 6th most costly therapeutic class with 5.7% of the spending. According to the report, 8.2% of members have one or more scripts for ulcer drugs, and this category contributes $45.75 Per Member per Year (PMPY) to total PMPY spending. [6] CVS-Caremark reported in 2009 Ulcer Medications as the 2nd most expensive therapeutic class representing 7.3% of total Rx spending. [7] In "Walgreens Health Initiative 2009 Trend Report", Ulcer Disease was ranked 4th in spending representing 6.3% of total pharmacy spending. [8]

The PPI class, once comprised of blockbuster brand drugs, more recently includes a mix of generic competitors as well as three available Branded OTCs. Health plans and employers have promoted lower-cost PPI generics and OTC drugs for the treatment of frequent heartburn by changing brand PPIs from a preferred tier to a non-preferred tier – with a higher copayment.[9] Additionally, in an effort to mitigate PPI costs, many insurers are using medical management and other formulary restrictions to control PPI use. Some insurers have imposed many common utilization management techniques to control costs, the most common of which are prior authorization, step edits and limits on duration of therapy. [10]

It's possible that some employers may see costs decline in the PPI category through effective formulary and benefit design management and educational outreach regarding the appropriate use of OTC PPIs used in the treatment of frequent heartburn. However, employers should carefully

consider the potential for increases in medical costs due to changes in compliance, if changes in benefit coverage occur, and while medical costs do not appear to rise in this analysis, additional analysis is needed to understand longer term financial impact to the plan as well as to their members' health.

POTENTIAL ADVERSE IMPACT OF PROTON PUMP INHIBITORS MOVING TO OTC

Concern is raised by some about the real world comparable effectiveness of prescription and OTC products. For example, there could be adverse clinical and medical cost consequences if significantly limiting or dropping prescription coverage leads to reduced adherence with prescribed drug therapies. Reduction in adherence could occur if patients do not access the OTC option for the treatment of frequent heartburn when prescription coverage is restricted and an OTC PPI is indicated.

Concern is also raised for patients who are under a doctor's care and have moved to an OTC PPI for the treatment of frequent heartburn based on their doctor's recommendation. There is some risk that these patients could choose to no longer routinely follow up with their doctor. Therefore, plans considering significantly restricting or dropping coverage are highly encouraged to recommend ongoing and active communication between the patient and their doctor.

With PPIs, the concern would be that non adherence could lead to an increase in particular gastrointestinal conditions (gastrointestinal bleeding, gastritis, heartburn, etc.) and an accompanying increase in utilization of physician office visits, GI procedures and GI related ER visits or inpatient admissions. Use of prescription or OTC alternatives such as H2 receptor antagonists could also increase. A few studies have investigated these issues. A time-trend study of British Columbia residents (age 66 or older) found that coverage restriction of 3 leading PPIs led to substantial PPI utilization changes and savings, without increased noncompliance or clinical complication.[1] A study of the impact of introducing a H2 receptor antagonist OTC identified a reduction in the number of prescriptions dispensed for these and all gastrointestinal agents without an increase in physician visits overall or for GERD. [2]

FINDINGS

2005-2009 THOMSON REUTERS MARKETSCAN® COMMERCIAL DATABASE

This retrospective claims analysis utilized data from the Thomson Reuters MarketScan® Commercial Claims databases for the period 2005-2009. These data included health insurance claims across a continuum of care (e.g., inpatient, outpatient, outpatient pharmacy, carve-out behavioral healthcare) as well as enrollment data from large employers and health plans across the United States who provide private health coverage for about 27 million commercially insured employees, spouses, and dependents. This administrative claims database includes a variety of fee-for-service, preferred provider organizations, and capitated health plans. MarketScan® is a registered trademark of Thomson Reuters (Healthcare) Inc. See Appendix A for more information about the MarketScan® Commercial Database.

DEFINING PPI SENSITIVE MEDICAL SERVICES AND CONDITIONS

Based on a literature review, we identified PPI sensitive medical services and conditions that could be impacted by reduced adherence with prescribed PPI therapy. We used claim data logic described in the Methodology section to identify each of the specific PPI sensitive metrics. These services include, GI diagnostic testing, physician visits, ER visits and inpatient admissions for GI related conditions, incidence of GI cancers and utilization of H2 receptor antagonist (limited coverage of PPIs could result in a shift to increased utilization of H2 receptor antagonists). We examined costs for H2 receptor antagonists along with day supply per member per month (PMPM). We examined utilization for the other PPI sensitive medical services but did not include a cost analysis in our results. Cost varies according to provider negotiated reimbursement rates and could produce higher or lower costs after PPI benefit change, even when utilization is unchanged.

The following table lists the 15 PPI sensitive metrics we analyzed:

H2 receptor antagonist Day Supply PMPM
H2 receptor antagonist Allowed $PMPM
Inpatient Admits for GI bleeds per 1000 lives/year
Inpatient Admits for Complicated Peptic Ulcer per 1000 lives/year
Physician office/ER Visits for Gastritis and Duodenitis w/o Hemorrhage per 1000 lives/year
Prevalence of Esophageal Cancer Patients per 1000 lives
Diagnostic Radiology Upper GI Procedures per 1000 lives/year
Upper Endoscopy Procedures per 1000 lives/year
Physician office/ER Visits for GERD per 1000 lives/year
Physician office/ER Visits for Erosive Esophagitis per 1000 lives/year
Physician office/ER Visits for Barrett's Esophagus per 1000 lives/year
Physician office/ER visits for Hiatal Hernia per 1000 lives/year
Physician office/ER Visits for Peptic Ulcer per 1000 lives/year
Physician office/ER Visits for Heartburn per 1000 lives/year
Physician office/ER Visits for Dyspepsia per 1000 lives/year

LONGITUDINAL ANALYSIS

For the longitudinal study, we identified employer plans that appeared to significantly restrict or drop coverage of prescription PPIs from one calendar year to the next and compared the utilization of PPI sensitive medical services and conditions in the year before and after the PPI coverage changed. We chose employer plans with at least 10,000 member months (or approximately 1,200 member lives) in both the index year and subsequent year.

We identified an employer plan as significantly restricting or dropping PPI prescription benefit coverage if the PPI days supply per member per month (Day Supply-Per Member Per Month PMPM) was:

- At least 0.6 PPI Day Supply-PMPM in the index year, and
- Less than 0.6 PPI Day Supply-PMPM in the subsequent year, and
- At least 50% lower Day Supply-PMPM in the subsequent year than in the index year.

We chose the 0.6 PPI Day Supply PMPM based on expected PPI claims for a plan that has typical PPI prescription coverage. Considering approximately 6% of a commercially insured population has one or more scripts for a PPI, our threshold assumed at least a 10 day supply on average per PPI user which would be equivalent to 0.6 PPI Day Supply across all commercial members. We did not use a PMPM cost threshold to identify employer plans that significantly restricted or dropped coverage as movement to generics significantly reduces PPI spending without a reduction in paid days supply.

Table 1 profiles the plans that met our criteria. The smallest plan contributor had approximately 1,200 lives and the largest had approximately 47,000. The lives were slightly more female (54%) and the average age was 38. The majority of lives were from PPO plans and the plans had members in regions that were nationally representative. To avoid the bias that could be introduced if PPI users left the plan after coverage was restricted, we examined PPI lapse rates (portion of insured population leaving the plan) for PPI users and used only plans with PPI lapse rates similar to that of total plan population lapse rates. The average population lapse rate for the 18 plans is 27%, which is very similar to the 30% lapse rate for PPI users.

Table 1: Summary Description of Qualified Plans - MarketScan® 2005-2009

		PPI Day Supply PMPM		Average Age	Portion that are Female
Covered Lives:	Year X	Year X	Year X+1		
Less than 10,000	2005	1.1	0.5	33.7	49%
Less than 10,000	2005	1.4	0.4	41.2	46%
Less than 10,000	2005	1.1	0.5	34.0	56%
Less than 10,000	2005	0.6	0.0	28.8	39%
Less than 10,000	2006	0.8	0.0	30.2	42%
Less than 10,000	2006	1.0	0.4	33.4	50%
25,000+	2006	1.5	0.6	28.0	56%
Less than 10,000	2006	1.2	0.5	30.4	47%
Less than 10,000	2007	1.6	0.4	32.4	41%
Less than 10,000	2007	1.0	0.0	50.2	51%
Less than 10,000	2007	1.1	0.0	49.3	51%
Less than 10,000	2008	1.3	0.0	47.2	80%
Less than 10,000	2008	2.2	0.0	52.9	51%
Less than 10,000	2008	0.6	0.0	29.8	49%
Less than 10,000	2008	1.4	0.0	45.6	78%
Less than 10,000	2008	2.5	0.0	52.2	51%
10,000-24,999	2008	0.7	0.0	28.3	50%
Less than 10,000	2008	4.8	0.0	40.1	49%
Total 18 Plans (~ 140,000 lives)		**1.4**	**0.2**	**38.2**	**54%**

We examine PPI sensitive medical services and conditions across all lives in each of the qualified plans in the year prior to and after significant restriction or dropping of PPI prescription benefit coverage. Table 2 provides the average utilization for each metric. For most of the metrics, the statistic is actually lower in the year after PPI prescription coverage is significantly restricted or dropped. We do not attribute the lower (or higher) values to the change in coverage, as these changes were not statistically significant (Table 3).

The finding of no detectable adverse impact could indicate that those who were being prescribed PPI therapy in the index year were still accessing PPIs in the subsequent year, although we do not have the data to test this hypothesis. Examples of how patients could continue to access a PPI after a restriction in benefit coverage include:

- After discussing with their doctor, purchasing an OTC PPI, for the treatment of frequent heartburn
- Seeking a medical exemption from their plan through an authorization or appeal process that allows the patient to continue to receive coverage of the RX PPI as part of their current benefit design
- After discussing with their doctor, deciding to pay out-of-pocket for the prescription PPI
- Receiving free samples from their doctor
- Receiving free product directly from the manufacturer as part of a patient assistance program

It is also possible that some patients may discontinue use of their PPI. However, these results suggest that adverse outcomes, if any, are not likely to be apparent for a typical large employer.

Table 2: PPI Sensitive Metrics Before and After Significant Restriction or Dropping of Prescription PPI Coverage. Average of 18 plans

PPI Sensitive Metric	Index Year	Subsequent Year	Average Difference
PPI Day Supply PMPM	1.40	0.24	-1.16
PPI Allowed $ PMPM	$5.37	$1.08	-4.29
H2 receptor antagonist Day Supply PMPM	0.15	0.04	-0.11
H2 receptor antagonist Allowed $PMPM	$0.10	$0.04	-$0.06
Inpatient Admits for GI bleeds per 1000 lives/year	0.40	0.25	-0.15
Inpatient Admits for Complicated Peptic Ulcer per 1000 lives/year	0.03	0.01	-0.02
Prevalence of Esophageal Cancer Patients per 1000 lives	0.12	0.09	-0.03
Diagnostic Radiology Upper GI Procedures per 1000 lives/year	5.65	5.22	-0.43
Upper Endoscopy Procedures per 1000 lives/year	18.80	19.47	0.67
Physician Office/ER Visits per 1000 lives/year for:			
Gastritis and Duodenitis w/o Hemorrhage	47.58	42.01	-5.57
GERD	32.72	29.25	-3.47
Erosive Esophagitis	2.85	2.15	-0.70
Barrett's Esophagus	0.65	0.72	0.07
Hiatal Hernia	0.74	1.03	0.29
Peptic Ulcer	0.53	0.41	-0.12
Heartburn	1.46	1.44	-0.02
Dyspepsia	2.36	2.52	0.16

Milliman analysis of MarketScan® 2005-2009; Year X = comprehensive PPI benefit coverage; Year X+1=first year of significantly restricted or dropped PPI prescription benefit coverage.

To indicate the statistical significance of the difference in PPI sensitive metrics, we calculated a 90th percentile confidence interval around the difference from the index year (X, year before restricted or dropped coverage) to the subsequent year (X + 1, year after restricted or dropped coverage) for

each of the PPI sensitive metrics. For all metrics, we found that the 90th percentile confidence interval includes zero, which is why we conclude there was no statistically significant difference in the rate of PPI sensitive metrics before and after PPI prescription coverage was significantly restricted or dropped.

Table 3: Confidence Interval of the Difference in PPI Sensitive Metrics Before and After Significant Restriction or Dropping of PPI Prescription Coverage

PPI Sensitive Metric	Difference from Year X to Year X + 1		
	Lower Bound (90th %-ile confidence interval)*	Upper Bound (90th %-ile confidence interval)*	Confidence Interval includes zero?
PPI Day Supply PMPM	-2.8042	-0.6164	No
H2 receptor antagonist Day Supply PMPM	-0.1972	-0.0121	No
H2 receptor antagonist Allowed $PMPM	-$0.144	-$0.021	No
Inpatient Admits for GI bleeds per 1000 lives/year	-1.1018	1.3193	Yes
Inpatient Admits for Complicated Peptic Ulcer per 1000 lives/year	-0.1448	0.1364	Yes
Prevalence of Esophageal Cancer Patients per 1000 lives	-0.3803	0.0141	Yes
Diagnostic Radiology Upper GI Procedures per 1000 lives/year	-3.8449	3.9578	Yes
Upper Endoscopy Procedures per 1000 lives/year	-10.5557	11.3145	Yes
Physician Office/ER Visits per 1000 lives/year for:			
Gastritis and Duodenitis w/o Hemorrhage	-13.5359	11.9557	Yes
GERD	-10.9312	10.3829	Yes
Erosive Esophagitis	-0.6843	1.4218	Yes
Barrett's Esophagus	-1.3294	1.0633	Yes
Hiatal Hernia	-0.6124	2.5727	Yes
Peptic Ulcer	-0.8169	2.3882	Yes
Heartburn	-1.4614	1.0667	Yes
Dyspepsia	-1.7306	1.7764	Yes

*The 90th percentile confidence interval = 90% of the time, the true value for the difference from year X to year X+1 for a given PPI sensitive metric is likely to be contained within the interval. See Methodology section of this report for a description of the confidence interval calculation. Year X = comprehensive PPI benefit coverage; Year X+1=first year of significantly restricted or dropped PPI prescription benefit coverage.

Inherent limitations with claim based analyses could apply to this analysis including unreliable coding and the lack of clinical data. In addition, two PPI sensitive metrics, Barrett's esophagus and esophageal cancer, may take years to develop from untreated gastroesophageal reflux disease (GERD), so their inclusion in a 2 year study is questionable.

We note that our sample of 18 geographically distributed PPO type plans with approximately 140,000 total lives may not be representative of particular employer groups or health plans.

IMPLICATIONS FOR PAYER/EMPLOYERS

In considering coverage decisions for PPIs and the implications of restricting PPI prescription benefit coverage, employers should first understand their current PPI utilization and spending. This includes analyzing the covered PPI users' age and gender mix, the PPI-related disease conditions, as well as the PPI drug mix and the annual PPI frequency or days supply. This information will inform an employer of the potential opportunity for savings by making a PPI benefit design change. In particular, the portion of PPI users that are chronic users should be examined as this would be the population that would likely be impacted. In a previous analysis we identified that 60% of the PPI takers had a 6 month supply or less during a calendar year. Additional details about the necessary steps to making a PPI benefit coverage change can be found in the Milliman white paper titled "*Proton Pump Inhibitors: A High Cost Employee Benefit with Over-the-Counter Alternatives"*, and available at www.otcbenefitadvisor.com.

Two published reports and our claim data analysis did not detect a material impact on utilization of PPI sensitive medical conditions or services from significantly restricting or dropping coverage for prescription PPIs. Employers or insurers who restrict or eliminate PPI prescription coverage and who are concerned about adverse medical and cost consequences, can monitor their own experience using the data methodology we describe.

Other windows to potential impacts of a PPI benefit design change include,

- Complaints from members or physicians
- A high volume of requests for prescription PPIs through a precertification process, especially if such requests are approved
- Shifts in membership out of plans with restricted PPI coverage and into plans with relatively generous coverage.

Several PPIs are now available as OTC products and whether a plan restricts PPI benefit coverage or not, members can shift to using OTC PPIs for appropriate treatment of frequent heartburn. This OTC PPI use will likely not be captured in the employer's claims data. The movement toward OTC products and very low cost retail generics (e.g., $4 generics) that fall below plan copays may mean that increasing numbers of prescriptions will fall outside claims databases. Employers and plans may need to reconsider the accuracy of using prescription data to identify individuals with certain conditions – or their compliance with particular drug therapies.

METHODOLOGY

We examined the impact of significant restriction or dropping of PPI prescription benefit coverage for the following PPI sensitive metrics:

H2 receptor antagonist Day Supply PMPM
H2 receptor antagonist Allowed $PMPM
Inpatient Admits for GI bleeds per 1000 lives/year
Inpatient Admits for Complicated Peptic Ulcer per 1000 lives/year
Physician office/ER Visits for Gastritis and Duodenitis w/o Hemorrhage per 1000 lives/year
Prevalence of Esophageal Cancer Patients per 1000 lives
Diagnostic Radiology Upper GI Procedures per 1000 lives/year
Upper Endoscopy Procedures per 1000 lives/year
Physician office/ER Visits for GERD per 1000 lives/year
Physician office/ER Visits for Erosive Esophagitis per 1000 lives/year
Physician office/ER Visits for Barrett's Esophagus per 1000 lives/year
Physician office/ER visits for Hiatal Hernia per 1000 lives/year
Physician office/ER Visits for Peptic Ulcer per 1000 lives/year
Physician office/ER Visits for Annual Heartburn per 1000 lives/year
Physician office/ER Visits for Dyspepsia per 1000 lives/year

CODING FOR PPI SENSITIVE METRICS

The following section provides detailed coding for the select PPI sensitive metrics presented in this report. We identified a PPI claim or an H_2 receptor antagonist claim using NDC codes. The complete list of PPI and/or H_2 receptor antagonist NDCs used is available upon request.

Gastritis or Duodenitis without hemorrhage events were identified as one or more ER visit or physician evaluation and management (E&M) outpatient claim with any of the following ICD9 diagnosis codes in the primary position of the claim:

- 530.1x
- 530.2x
- 530.4x
- 530.7x
- 530.8x
- 531.x - 535.x

Esophageal cancer patients were identified as individuals having one or more inpatient admission, ER visit or physician E&M outpatient claim with ICD9 diagnosis codes of either 150.x or 151.0 coded in the primary position of the claim.

Upper GI diagnostic radiology utilization was identified by claims with the following CPT-4 procedure codes:

- 74210 – Contrast x-ray exam of throat
- 74220 – Contrast x-ray exam of esophagus
- 74240 – X-ray exam, upper GI tract
- 74241 – X-ray exam, upper GI tract
- 74246 – Contrast x-ray exam, upper GI tract
- 74247 – Contrast x-ray exam, upper GI tract

Upper GI endoscopic procedures were identified by claims with the following CPT-4 procedure codes: 43200 – 43259 (excluding 43246)

Physician office or ER visits for selected PPI sensitive GI conditions were identified if the physician E&M claim had one of the following ICD-9 diagnosis codes in the primary position of the claim:

Disease Condition	ICD9 Diagnosis Code(s)
Barrett's Esophagus	530.85
Dyspepsia	536.8
GERD	530.11, 530.81
Erosive Esophagitis	530.20, 530.21, 530.82, 530.10, 530.12, 530.19
Heartburn	787.1
Hiatal Hernia	552.3, 553.3
Peptic Ulcer	531.x, 532.x, 533.x, 534.x

Inpatient admissions for GI bleeds were identified if any one of following ICD9 diagnosis codes were in the primary position of the inpatient claim:

- 530.21
- 531.0x, 531.2x, 531.4x, 531.6x
- 532.0x, 532.2x, 532.4x, 532.6x
- 533.0x, 533.2x, 533.4x, 533.6x
- 534.0x, 534.2x, 534.4x, 534.6x
- 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61
- 537.83
- 578.x

Inpatient admissions for complicated peptic ulcers included inpatient claims with any one of the following ICD9 diagnosis codes in the primary diagnosis position:

- 531.1x, 531.3x, 531.5x
- 532.1x, 532.3x, 532.5x
- 533.1x, 533.3x, 533.5x
- 534.1x, 534.3x, 534.5x

An office visit was flagged using the following CPT-4 procedure codes:

- 99201-99205
- 99211-99215
- 99241-99245
- 99341-99350
- 99499

ER visits were identified using standard place of service code 23.

PPI BENEFIT COVERAGE

Our starting population of plan contributors to Marketscan excluded contributors without a pharmacy benefit and excluded HMO and capitated plans since all claims may not be captured under these plan types. Qualified plans for the longitudinal analysis had at least 10,000 member months (approximately 1,200 members) and a PPI user lapse rate that was not significantly higher or lower than the average population lapse rate. In addition, to qualify for the longitudinal analysis, each plan had at least 0.6 Day Supply-PMPM in the base year and less than 0.6 Day Supply-PMPM in the subsequent year with at least a 50% reduction in the Day Supply-PMPM. A drop of this magnitude was defined as indicative of a change in PPI benefit design coverage.

Using the above PPI benefit coverage logic, we identified 18 plans that qualified for the longitudinal study representing approximately 140,000 members with more than 1 million member months. Half of the 18 plans had a base year of 2008 in the study, while the rest had base years of 2005, 2006 or 2007.

CONFIDENCE INTERVAL

The purpose of the confidence intervals of the difference in PPI sensitive metrics before and after significant restriction or dropping of PPI prescription coverage is to illustrate meaningful differences in the outcomes we studied. We measured 15 PPI sensitive services (see Coding for PPI Sensitive Outcomes section above) for the 18 plans included in our study. Our general formula for the outcomes is:

$$MVi\ PMPM(X) = \frac{\sum_c \sum_m MVi_m^c}{\sum_c \sum_m MMOS_m^c}$$

Where,

X: Year
MVi: Value of the i-th PPI sensitive outcome (i=1 to 17)
$MMOS$: Member Months
m: Index of Members
c: Index of Plans

The results are in Table 3 of the Findings section of this report.

For the PPI sensitive outcomes, we calculated the difference of the 18 plans between year X+1 and year X. The histograms of those differences are approximately symmetric and bell-shaped. The Central Limit Theorem assures that the distribution of the metric values by plans is normal for any metric (i.e. the stochastic value $\left\{\frac{\sum_m MVi_m^c}{\sum_m MMOS_m^c}\right\}_c$ is normally distributed) and the confidence interval is an interval estimate that can be used as an indicator for the reliability of the estimates. We computed the confidence intervals as from 5 percentile to 95 percentile.

PRIMER ON PPI DRUG THERAPY

PPI INDICATIONS

Proton pump inhibitors (PPIs) are a class of drugs that decrease acid production in the stomach by blocking an enzyme needed for acid production. Acid is produced by the stomach to assist with food break down making food easier to digest, but, in some circumstances, acid can irritate the lining of the esophagus, stomach, and duodenum causing indigestion and possibly ulcers.

PPIs are considered very effective and generally safe medicines. They are recommended to treat acid related disorders including but not limited to heartburn, gastroesophageal reflux disease (GERD), and gastric ulcers. OTC PPIs are approved for the treatment of frequent heartburn (occurring 2 or more days a week).

Heartburn is described as a burning sensation which begins behind the breastbone and may extend up the esophagus to the throat. It is caused by temporary relaxation of the lower esophageal sphincter which permits abnormal reflux of gastric contents into the esophagus. Treatment includes lifestyle changes (i.e., weight loss, avoiding large meals, alcohol, spicy food, and smoking) and drug therapy including antacids, histamine$_2$ receptor antagonists H_2RAs and proton pump inhibitors.[11] 20% of adults are reported to experience heartburn or acid regurgitation weekly and 40% experience these symptoms at least once a month.[12] Occasional heartburn is not a cause for worry. However, if the symptom persists and does not respond to self-treatment with an acid reducing product and life style changes, a physician may need to be consulted. Persistent heartburn that is unresponsive to self-management with an OTC acid reducer or antacids may be a symptom of a more serious problem.[11]

According to a Neilson survey, the majority of heartburn sufferers self treat and use OTC acid reducing products. The 2008 survey of 17,412 people who had experienced heartburn during the previous 12 months reports that 55% of respondents used only OTC treatment for their symptoms and 61% had not discussed their heartburn with a physician. Of the 39% who did discuss their symptoms with their doctor, about 44% received a recommendation for an OTC product and 13% were given a prescription. Many were advised to change their diet, lose weight, quit smoking or modify their lifestyle. 94% of those who used OTC products reported they were satisfied.[13]

Gastroesophageal reflux disease (GERD) is defined as persistent heartburn or acid reflux that occurs more than twice a week. GERD is characterized by symptoms and/or tissue damage that results from repeated or prolonged exposure of the lining of the esophagus to acidic contents from the stomach and occurs when the lower esophageal sphincter (LES) does not seal off the esophagus from the stomach. The prevalence of GERD is estimated to be 10-26% of adults.[14]

Treatment for GERD includes lifestyle changes, acid suppression therapy with PPIs and promotility therapy in selected patients especially as an adjunct to acid suppression treatment.[15] Untreated GERD can cause serious complications (i.e., damage to and bleeding in the lining of the esophagus). About 64 million prescriptions for GERD were filled in 2004 for a retail cost of nearly $7.7 billion. Proton pump inhibitors comprised the majority of the volume and cost of these prescriptions.[16] The direct medical cost of GERD was estimated to be $12 billion in 2004, more than half of which was attributed to prescription drug costs.[16]

There are seven available PPIs on the market today. Three are available as both prescriptions and OTCs. Four are available as brand-name and generic drugs. The remaining three are only available as prescription brand drugs.

APPENDIX A: DESCRIPTION OF KEY DATA SOURCES AND THEIR APPLICATION

2005-2009 Thomson Reuters MarketScan® Commercial Claims Database - The MarketScan® database contains individual-level, de-identified, healthcare claims information from employers, health plans, hospitals, Medicare, and Medicaid programs for about 27 million commercially insured employees, spouses and their dependents annually. The MarketScan® database is one of the largest collections of de-identified patient-level data in the nation. The MarketScan® database links paid claims and encounter data to detailed patient information across sites and types of providers, and over time. The annual medical database includes private sector health data from approximately 100 payers. These data represent the medical experience of insured employees and their dependents for active employees, early retirees, COBRA continues, and Medicare-eligible retirees with employer-provided Medicare supplemental plans. No Medicaid or Workers Compensation data are included.

Member identification codes are consistent from year to year and allow for multiyear longitudinal studies. Information includes diagnosis codes, procedure codes, DRG codes, NDC codes along with site-of-service information, and the amounts paid by commercial insurers. For this study, we used annual MarketScan® Commercial databases for the period 2005-2009.

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