Results of an Intervention in an Academic Internal Medicine Clinic to Continue, Step-Down, or Discontinue Proton Pump Inhibitor Therapy Related to a Tennessee Medicaid Formulary Change

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ABSTRACT

BACKGROUND: In July 2005, the State of Tennessee Medicaid Program (TennCare) announced formulary changes for proton pump inhibitors (PPIs) to be implemented in August 2005. Prior to these changes, pantoprazole was the only preferred PPI, and there were no restrictions to its use. The revised formulary included 3 preferred PPIs (esomeprazole, lansoprazole, and omeprazole OTC), all of which required prior authorization (PA). In order to obtain an approved PA for a PPI, the patient was required to have either (a) a diagnosis of erosive esophagitis, Barrett’s esophagus, Schatzki’s ring, a pathological hypersecretory condition (e.g., Zollinger-Ellison syndrome, multiple endocrine adenoma), grade III-IV gastropathy, significant gastrointestinal bleed; or (b) another indication for acid suppression therapy (e.g., GERD, hyperacidity in cystic fibrosis, gastric or duodenal ulcer, gastroparesis) with a history of failure of prior therapy with a histamine-2 receptor antagonist (H2-blocker). The internal medicine clinic of a regional medical center implemented an intervention to address these changes in formulary status of PPIs.

OBJECTIVE: To (a) describe the process used by an internal medicine clinic to ensure that patients requiring acid suppression therapy received appropriate treatment according to revised TennCare formulary criteria without unnecessary interruption of therapy, and (b) assess self-reported symptom control 8 months after intervention in the patients who either discontinued therapy or stepped-down to H2-blocker therapy.

METHODS: This study involved TennCare patients in an internal medicine clinic who received a new or refill prescription for pantoprazole between April 20 and June 20, 2005, from the medical center’s outpatient pharmacy. A clinical pharmacist and an internal medicine physician collaborated to develop a protocol for adjusting acid suppression therapy. A clinical pharmacist reviewed medical records for all patients identified to verify indication or documentation for acid suppressing therapy at all, and 19% had resumed PPI use.

RESULTS: Of 135 TennCare beneficiaries who were active patients of the internal medicine clinic and received a prescription from the outpatient pharmacy for PPI therapy (pantoprazole) between April 20 and June 20, 2005, 6 patients were excluded because they reported stopping PPI therapy on their own. Of the remaining 129 patients, 18 (14.0%) did not have an indication for PPI therapy and acid suppression therapy was discontinued (discontinue therapy group), 40 (31.0%) met the TennCare PA criteria for continuation of PPI therapy (PA group), and 71 (55.0%) did not meet the TennCare PA criteria and were stepped down to a H2-blocker (step-down group). At the 8-month follow-up, acid suppression therapy was assessed in 68 patients (21 patients were lost to follow-up): 13 patients (19.1%) had resumed PPI therapy; 38 (55.9%) were using an H2-blocker; and 17 (25.0%) were not using acid suppression therapy. Telephone interviews were completed for 45 of the 75 patients in the step-down and discontinue therapy groups who did not receive an escalation in acid suppression therapy after the initial intervention (i.e., who did not make a change from H2-blocker therapy to PPI therapy or from no acid suppression therapy to H2-blocker therapy or PPI therapy). Twenty-eight patients (62.2%) reported symptoms one per week or less; 14 patients (31.1%) reported symptoms more often than once weekly. Symptom control was unable to be determined in 3 patients (6.7%) because of incomplete information obtained from the patient during the interview.

CONCLUSIONS: After a proactive collaboration between physicians and clinical pharmacists in response to changes in TennCare formulary criteria for PPIs, more than one-half of patients were stepped down to H2-blocker therapy, and 14% were discontinued from acid suppression therapy. Among the step-down or therapy discontinuation patients for whom data were available at the 8-month follow-up, 81% were still using either an H2-blocker or no acid suppressing therapy at all, and 19% had resumed PPI use.


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What is already known about this subject

- Between 1999 and 2004, proton pump inhibitor (PPI) use in the United States steadily increased, while the use of histamine-2 receptor antagonists (H2-blockers) steadily decreased. PPIs are frequently prescribed for inappropriate reasons and for longer than recommended treatment periods.
- PPIs are more effective at eliminating symptoms of gastroesophageal reflux disease and healing esophagitis than are H2-blockers; however, all PPIs except omeprazole OTC are more expensive than H2-blockers. Strategies for cost-effective use of PPIs include “step-up” or “step-down” PPI therapy using H2-blockers, “on demand” PPI therapy, and adding the less costly PPI omeprazole OTC to formularies.
- Reported results of step-down therapy have been conflicting. Piterman et al. (2004) reported that approximately 70% of patients whose PPI therapy is stepped-down will have relapse of symptoms within 6 months. In contrast, Inadomi et al. (2001) reported that 58% of patients whose therapy was stepped down remained asymptomatic without PPI therapy at one year.
Proton pump inhibitors (PPIs) are the most widely prescribed class of drugs used to suppress gastric acid secretion.\(^1\) They are used to treat numerous gastrointestinal disorders, including peptic ulcer disease (PUD), gastroesophageal reflux disease (GERD), erosive esophagitis, Zollinger-Ellison syndrome, Barrett’s esophagus, and upper gastrointestinal bleeding.\(^2\)\(^,\)\(^6\)

Between 1999 and 2004, PPI use in the United States steadily increased, while the use of histamine-2 receptor antagonists (H2-blockers: cimetidine, famotidine, nizatidine, ranitidine) steadily decreased.\(^7\) PPIs continue to be prescribed more often than H2-blockers. In 2007, esomeprazole, lansoprazole, and pantoprazole were the fourth, eighth, and thirteenth leading brand name prescription drugs dispensed in the United States, with 26.4, 20.4, and 16.1 million prescriptions, respectively.\(^1\) Comparatively, ranitidine and famotidine were ranked 47th and 120th for generic drugs with 13 and 3 million prescriptions dispensed, respectively, in 2007. Neither cimetidine nor nizatidine ranked among the top 200 drugs dispensed in 2007.\(^8\)

Esomeprazole OTC was the third leading over-the-counter brand name product sold in the United States in 2007, with over $388 million in sales.\(^9\) Ranitidine and famotidine ranked 77th and 111th, respectively, in sales of nonprescription agents in 2007.\(^9\) Nonprescription cimetidine and nizatidine were not ranked among the top 200 in 2007.\(^9\)

PPIs are frequently prescribed for inappropriate reasons and for longer than the recommended treatment periods.\(^10\)\(^,\)\(^11\) They are more effective at eliminating symptoms of GERD and healing esophagitis than H2-blockers.\(^12\)\(^-\)\(^15\) However, PPIs are more expensive than H2-blockers (e.g., the generic H2-blockers ranitidine, cimetidine, and famotidine cost less than $20 per month of therapy compared with more than $120 per month for the PPIs, except omeprazole OTC [less than $30 per month]).\(^16\)

A 2005 report from the Agency for Healthcare Research and Quality showed that all PPIs at standard doses are equally effective at relieving the symptoms of GERD.\(^17\) This equivalence has led to an increase in the inclusion of less costly PPIs on many third-party formularies. West et al. reported that adding omeprazole OTC to a prescription drug formulary resulted in a 38% net savings to a state employee health plan in Arkansas.\(^18\)

Strategies to improve the cost-effectiveness of GERD treatment such as step-down, step-up, and on-demand therapy have also been recommended.\(^11\)\(^-\)\(^12\)\(^,\)^\(^22\)\(^-\)\(^24\) Step-down therapy consists of either decreasing the PPI dose or switching to an H2-blocker in patients who have achieved symptomatic relief with PPI treatment. Step-up therapy, which has been shown to be cost-effective, consists of starting with either nonprescription or standard dose H2-blockers and increasing to high-dose H2-blockers or PPIs if symptoms are not controlled.\(^23\) On-demand (intermittent) therapy is the periodic use of PPIs in response to symptom recurrence following an initial symptomatic response to PPIs.\(^22\)\(^,\)\(^24\)

Like many payers, the Tennessee Medicaid Program (TennCare) has implemented formulary changes in an effort to provide cost-effective care. In August 2005, the TennCare Program implemented formulary changes for PPIs. Prior to these changes, pantoprazole (Protonix) was the only preferred formulary PPI, and there were no PPI prescribing restrictions. To receive PPI therapy under the new formulary guidelines, all patients were required to fail a 2-week trial of H2-blocker unless 1 of several conditions was met (Table 1). These conditions included a diagnosis of erosive esophagitis, Barrett’s esophagus, Schatzki’s ring, a pathologic hypersecretory condition (e.g., Zollinger-Ellison syndrome, multiple endocrine adenoma), grade III-IV GERD, nonsteroidal anti-inflammatory drug gastropathy, or significant gastrointestinal bleed. Additionally, the prescriber was required to submit a prior authorization (PA) form via facsimile to TennCare requesting PPI therapy. For the patient to meet the H2-blocker failure criterion, the prescriber was required to document failure on the PA form.

Generic ranitidine, famotidine, nizatidine, and cimetidine were the preferred H2-blockers on the new formulary. The preferred PPIs on the revised formulary were esomeprazole, lansoprazole, and omeprazole OTC. Any of these 3 could be selected for therapy if prescribing criteria were met. TennCare allowed 30 days for prescribers to ensure that patients met the new criteria and submit the PA request. At the end of 30 days, claims for PPI therapy were rejected by TennCare for patients who did not meet the new criteria. Nonprescription (OTC) H2-blockers were not included on the TennCare formulary.

The academic internal medicine clinic at the Memphis Regional Medical Center provides approximately 15,000 patient care visits annually for about 5,100 patients. An estimated one-third of this patient population receives TennCare benefits.
Approximately 30%-40% of the clinic population obtains their prescriptions from the medical center's outpatient pharmacy. Between July 1, 2005, and December 31, 2005, the outpatient pharmacy filled 65,363 prescriptions for 5,857 patients. Patients treated at our facility rarely purchase OTC medications because of personal financial limitations.

The internal medicine clinic is staffed by attending and resident physicians who provide care to an indigent population. Clinical pharmacists manage anticoagulation, diabetes, hypertension, and hyperlipidemia. They also work collaboratively with physicians in the clinic to aid in drug selection in order to comply with numerous third-party formularies. In response to previous TennCare formulary changes, clinical pharmacists have collaborated with physicians to develop therapeutic substitution protocols for statins, angiotensin-converting enzyme inhibitors, angiotensin II receptor blocking agents, nasal corticosteroids, and inhaled corticosteroids. These protocols were used in the outpatient pharmacy to avoid interruptions in therapy.

The purpose of this article is to (a) describe the process used by an internal medicine clinic to ensure that patients requiring acid suppression therapy receive appropriate treatment according to revised TennCare formulary criteria without unnecessary interruption of therapy, and (b) assess self-reported symptom control 8 months after intervention in the patients who either discontinued therapy or stepped down to H2-blocker therapy.

This project was approved and granted an exempt status by the University of Tennessee Health Science Center Institutional Review Board. Because the internal medicine clinic utilizes a paper-based medical chart system, it was not possible to use medical charts to identify all TennCare patients treated by the internal medicine clinic who were receiving PPI therapy. Therefore, PPI therapy for TennCare patients was identified from prescription dispensing records in the medical center's outpatient pharmacy. A list of TennCare patients receiving new or refill prescriptions for PPI therapy with pantoprazole between April 20 and June 20, 2005, was generated from the outpatient pharmacy database. This 2-month time frame was chosen to ensure the identification of all clinic patients on PPI therapy including those who may not have adhered to obtaining prescription refills at 30-day intervals. Because pantoprazole was the only preferred PPI on both the TennCare and medical center's formularies prior to the changes implemented in 2005, it was the only agent used to identify patients on PPI therapy.

Clinical pharmacists and the director of the internal medicine clinic collaborated to develop a protocol for adjusting acid suppression therapy (Figure 1). The protocol was designed to meet TennCare criteria. A gastroenterologist reviewed the protocol and was available for any questions that arose. A clinical pharmacist evaluated each patient identified, excluding those who were not patients of the internal medicine clinic. A medical record review was conducted to verify medication history and indications for acid suppression therapy. If the medication history or indication for acid suppression therapy were not documented in the medical record, patient telephone interviews were conducted to obtain the indication and medication history.

Three groups of patients were defined. Patients with an indication for PPI therapy that met TennCare criteria were continued on PPI therapy after obtaining a PA (PA group). All patients in the PA group were converted from pantoprazole to esomeprazole because it was the only PPI available on both the medical center's formulary and the revised TennCare formulary. A one-to-one dose conversion was used in the transition from pantoprazole to esomeprazole. Patients with a documented indication for acid suppression therapy that did not meet the TennCare criteria for PPI therapy were changed to H2-blocker therapy (step-down group). Because ranitidine was the only H2-blocker on both the institution's and TennCare formularies, the step-down patients were converted to ranitidine 150 milligrams (mg) twice daily or 150 mg once daily for those patients with a creatinine clearance of less than 50 milliliters (mL) per minute. Patients without a documented indication for acid suppression therapy were discontinued from therapy (discontinue therapy group).

This process was completed by July 2005, and all changes were documented in the medical record. In March 2006, a follow-up review was conducted of patients who had discontinued acid suppression therapy or stepped down to H2-blocker therapy. The review was limited to these patient groups because it was assumed that patients who had continued on PPI therapy

### TABLE 1

**Tennessee Medicaid Clinical Criteria for Use of Proton Pump Inhibitors**

- Erosive esophagitis-Grade II or higher diagnosed on endoscopy within 2 months
- Barrett’s esophagus, Schatzki’s ring – diagnosed on endoscopy within last 2 years
- Pathological hypersecretory condition – diagnosed by serum gastrin and serum secretin stimulation test
- GERD-Grade III-IV diagnosed on endoscopy within last 2 years OR upper GI series or barium swallow within 1 year
- Continuing, symptomatic GERD OR atypical GERD with symptoms of chronic laryngitis, hoarseness, or cough due to reflux – failed 2-week trial of H2-blocker. *Diagnosed by endoscopy within 2 years or upper GI series or barium swallow within 1 year
- NSAID gastropathy – diagnosed by endoscopy within 2 years
- Significant gastrointestinal bleeding
- Hyperacidity associated with cystic fibrosis – recent failure of H2-blocker
- Gastric or duodenal ulcer or PUD – failed 2 week trial of H2-blocker. *Diagnosed by upper GI procedure within 1 month
- Gastroparesis – failed trial of prokinetic agent AND failed trial of more than 1 anti-emetic agent

*The 2005 prior authorization criteria for PPI therapy required attestation from the prescriber that the patient failed a trial of H2-blocker therapy.
GERD = gastroesophageal reflux disease; GI = gastrointestinal; H2 = histamine-2; NSAID = nonsteroidal anti-inflammatory drug; PPI = proton pump inhibitor; PUD = peptic ulcer disease.
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FIGURE 1 Protocol for Evaluating Patients on PPI Therapy

Active clinic patients (estimated 5,100)

TennCare beneficiaries with prescription for pantoprazole at outpatient pharmacy
n = 135

Patient terminated PPI therapy
n = 6

Patients included in evaluation
n = 129

Indication for PPI therapy

Yes
n = 111

TennCare criteria for PPI therapy met
n = 40

PA group
( PA obtained for esomeprazole)

TennCare criteria for PPI therapy not met
n = 71

Step-down group
(Changed to H2-blocker)

Discontinue therapy group

No
n = 18

Follow-up group
n = 89

Chart review
n = 68

Telephone interview
n = 45

Unable to determine level of symptom control
n = 3

Adequate symptom control
n = 28

Inadequate symptom control
n = 14

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*a* 184 TennCare patients had a prescription filled for pantoprazole at the medical center’s outpatient pharmacy between April 20 and June 20, 2005. After medical record review, 49 patients were eliminated because they were not active internal medicine clinic patients.

*b* To receive PPI therapy under the new TennCare guidelines, patients were required to meet 1 of the criteria in Table 1. The prescriber was also required to submit a written request for prior authorization of PPI therapy to the TennCare Program.

*c* The follow-up group included patients who received a step-down from PPI therapy to H2-blocker therapy or were discontinued from acid suppression therapy.

*d* Of 89 patients eligible for follow-up, 14 were excluded from telephone interviews because they received an escalation in acid suppression therapy after the initial intervention. Of the remaining 75 patients, 45 could be reached by telephone.

*e* Adequate control was defined as patient report of symptoms once per week or less.

*f* Inadequate control was defined as patient report of symptoms more than once weekly. These patients were referred to their resident physician for evaluation.

H2 = histamine-2; PPI = proton pump inhibitor.
TABLE 2

<table>
<thead>
<tr>
<th>Indication</th>
<th>PAa</th>
<th>Step-Downb</th>
<th>Discontinuec</th>
<th>All Patients</th>
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<tbody>
<tr>
<td>GERD</td>
<td>37</td>
<td>60 (84.5)</td>
<td>0 (0)</td>
<td>97 (75.2)</td>
</tr>
<tr>
<td>GUD/PUD</td>
<td>2</td>
<td>7 (9.9)</td>
<td>0 (0)</td>
<td>9 (7.0)</td>
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<td>Acute necrotizing inflammation of esophageal mucosa</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
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<tr>
<td>Colitis</td>
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<td>1 (1.4)</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
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<tr>
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<td>1 (1.4)</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>0</td>
<td>1 (1.4)</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
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<tr>
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<td>1 (1.4)</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
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<tr>
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<td>0</td>
<td>0 (0)</td>
<td>18 (100.0)</td>
<td>18 (14.0)</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>71 (100.0)</td>
<td>18 (100.0)</td>
<td>129 (100.0)</td>
</tr>
</tbody>
</table>

aPA group = Patients with an indication for a PPI, who were continued on PPI therapy by obtaining a prior approval for the therapy.
bStep-down group = Patients with an indication for acid suppression therapy who did not meet the criteria for a PPI. These patients were changed to a histamine-2 receptor antagonist therapy.
cDiscontinue group = Patients without an indication for acid suppression therapy. These patients were discontinued from any form of acid suppression therapy.

Results

Between April 20 and June 20, 2005, 184 patients filled a prescription for pantoprazole therapy at the medical center's outpatient pharmacy. After medical record review, 49 patients were eliminated because they were not active internal medicine clinic patients, and 6 patients were eliminated because they reported stopping acid suppression therapy on their own. Thus, 129 patients receiving pantoprazole were identified and included in this evaluation (Figure 1). The indications for acid suppression therapy for each of the groups as well as all of the groups combined are listed in Table 2. The majority (75.2%) of patients were receiving PPI therapy for GERD.

Of the 129 patients evaluated, 119 (92.2%) were receiving pantoprazole 40 mg once daily. The remaining 10 patients (7.8%) were receiving pantoprazole 40 mg twice daily. Forty patients (31.0%) met criteria for PPI therapy. After PA was successfully obtained for these patients, their PPI therapy was changed to esomeprazole 40 mg daily or twice daily as indicated (PA group).

Seventy-one patients (55.0%) did not meet TennCare criteria for PPI therapy and were changed to H2-blocker therapy (step-down group). Of these 71 patients, 53 (74.6%) were changed to ranitidine 150 mg twice daily; the remaining 18 patients (25.4%) were changed to ranitidine 150 mg daily because of a creatinine clearance of less than 50 mL per minute. Acid suppression therapy was discontinued in 18 patients (14.0%) because no indication was identified (discontinue therapy group).

At the March 2006 follow-up evaluation of the step-down and discontinue therapy groups, post-intervention acid suppression therapy was unable to be determined in 21 of the 89 patients because they had no clinic visits after the intervention (Table...
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3. Post-intervention acid suppression therapy could be assessed in 68 (76.4%) of the 89 patients. Of the 68 patients, 13 (19.1%) had resumed PPI therapy, and 55 (80.9%) were either using an H2-blocker (n = 38) or no acid suppression therapy (n = 17).

Perceived symptom control in the step-down and discontinue therapy groups was assessed through telephone interviews. Patients who received an escalation in acid suppression therapy after the initial intervention (n = 14; from H2-blocker to PPI therapy [n = 11], from no acid suppression therapy to PPI therapy [n = 2], or from no acid suppression to H2-blocker therapy [n = 1]) were excluded from this assessment. Of the remaining 75 patients, 45 could be reached by telephone; of these, 28 (62.2%) reported symptoms less than or equal to once weekly (adequate control), and 14 (31.1%) were determined to have symptoms more than once weekly (inadequate control). Symptom control was unable to be determined in 3 patients (6.7%) because of difficult interviews or irregular use of acid suppression therapy. All patients reporting symptoms more than once weekly were referred to their resident physician for evaluation. They were provided assistance in making appointments with their physician if needed. The next course of action was then left to the physician’s discretion.

Discussion

PPIs are more effective at eliminating symptoms of GERD and healing esophagitis than H2-blockers; however, they are also more expensive.12-16 Overuse of PPIs is evidenced by Naunton et al., who evaluated PPI use at the Royal Hobart Hospital in Australia, using chart review and patient interview.10 They found that only 37.1% of 200 inpatients taking PPIs met prescribing criteria according to the Schedule of Pharmaceutical Benefits and other standard therapeutic guidelines in Australia.10 Clinical criteria for PPI therapy have been established by many health system institutions.9,10,11 Pohlnd et al. evaluated adherence to institutional guidelines for twice daily lansoprazole use at the Veterans Affairs Pittsburgh Healthcare System.11 The authors reviewed the pharmacy database, electronic medical records, and interviewed patients via telephone. They reported that only 34% of 248 patients taking twice daily lansoprazole met institutional prescribing criteria and recommended step-down therapy in 48%.11 Reports regarding the outcomes of step-down therapy have been conflicting. In a 2004 review, Piterman et al. reported that approximately 70% of patients whose PPI therapy is stepped down will have relapse of symptoms within 6 months.23 In contrast, Inadomi et al. reported that in a Veterans Affairs Health Care facility, 41 (58%) of 71 patients with GERD were asymptomatic 1 year after PPI therapy was discontinued; 34% required an H2-blocker, 7% required a prokinetic agent, 1% required both H2-blocker and prokinetic agents, and 11 (15%) of the 71 patients remained asymptomatic without any acid suppression therapy. Quality of life was not affected by these changes, and treatment costs were decreased by 37%.26

This report describes how clinical pharmacists collaborated with physicians to proactively implement new formulary mandates established by TennCare to avoid unnecessary interruption in acid suppression therapy. Because of this intervention, approximately 31.1% were successfully switched to a preferred PPI to avoid interruption in therapy. While 68.9% of patients did not meet criteria for PPI therapy, 55.0% were switched to H2-blocker therapy and 14.0% did not require acid suppression therapy.

Limitations

The primary limitation of this study is the large number of patients who were lost to follow-up. Unfortunately, many Medicaid patients face financial difficulties and frequently relocate, making follow-up difficult. The “no show” rate in the clinic is approximately 30%, further decreasing the follow-up rate. Second, only patients receiving PPI therapy at the medical center’s outpatient pharmacy could be identified proactively. A larger number of patients received their medications in outside community pharmacies. Without an electronic medical record (EMR), all patients receiving PPI therapy could not be identified. An EMR would also allow one to easily identify indications as well as previous therapies. Other organizations with an EMR could identify all patients receiving PPI therapy and apply a similar methodology to transition patients in response to third-party formulary changes. Third, the TennCare formulary was limited to esomeprazole, lansoprazole, and omeprazole OTC. Omeprazole OTC is the least expensive PPI therapy option. However, TennCare had special contracts with the manufacturers and received rebates from them. TennCare does not release information about the amount of money saved via these rebates. Fourth, the survey used for the telephone interviews was not validated; however, it does reflect real-world practice. A strength of this report is that the results are based on real-time data, including chart review and patient interview, not a retrospective analysis of administrative data. Fifth, information that could have helped explain acid suppression use, such as diet, comorbidities, and concomitant medications was not obtained because those data were beyond the scope of this project. Finally, because the majority of patients were being treated for GERD, outcomes may not be transferable to other conditions.

Conclusions

This report describes a proactive collaboration between physicians and clinical pharmacists in response to changes in TennCare formulary criteria for PPIs. Patients with indications for acid suppression therapy were prescribed formulary acid suppressive medications to avoid interruption of therapy. Additionally, many patients had been prescribed PPI therapy for conditions not warranting PPI use. This finding reinforces the notion that a percentage of PPI prescriptions may be unnecessary given the availability of H2-blocker therapy.
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DISCLOSURES

There was no external funding for this research. Hamann was responsible for the study concept and design with assistance from Sprabery. Data collection was performed by Ramser with the assistance of Will and Sprabery. Data interpretation was performed by Hamann and Ramser with the assistance of George. Writing and revision of the manuscript were performed by George, Ramser, Sprabery, and Hamann.

REFERENCES