# Assessing the Appropriate Use of Proton Pump Inhibitors in a Veteran Outpatient Population

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Researchers at the James H. Quillen VAMC in Mountain Home, Tennessee, undertook a pilot study to better understand the magnitude of potentially inappropriate proton pump inhibitor use. The study results revealed many areas for improving their proper use and patient follow-up.

Proton pump inhibitors (PPIs) are among the most prescribed medications in the U.S. This is in part due to PPIs being the most potent agents for acid suppression in diseases such as gastroesophageal reflux disease (GERD). In 2001, antiulcer drugs, including PPIs, accounted for $10.8 billion in retail sales.[1,2] Since PPIs have been made available in generic formulations, the total spending cost has decreased in recent years. However, PPIs remain the top-selling generic drugs in retail pharmacies. In 2011, omeprazole was ranked 21st of all prescription drugs dispensed in the U.S.[3] Prior to PPI therapy being available, histamine$_2$-receptor antagonists were standard therapy for acid suppression. In numerous trials, PPI therapy has been proven to be superior in the treatment of GERD and erosive esophagitis compared with histamine$_2$-receptor antagonists.[4] In addition to outpatient therapy, PPIs are widely used in stress ulcer prophylaxis in hospitalized patients.

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## BACKGROUND

Although PPI therapy is proven to be an effective treatment for various gastrointestinal conditions, the medical literature is inundated with clinical trials highlighting the adverse effects (AEs) and outcomes associated with prolonged use of PPI therapy. These trials are helping to bring to light the overuse of PPI therapy and the need for appropriate prescribing habits for practitioners. As the use of PPIs continues to grow, insuring appropriate prescribing of PPIs is critical to limiting AEs for patients.

Even in patients with appropriate indications for PPI use, this drug class has been linked to several AEs and risks to patient health. At the time of this study, recent evidence had been published debating a potential drug-drug interaction between the antiplatelet agent clopidogrel and PPIs.[5-7] In addition, the overuse of PPIs has been associated with community-acquired pneumonia infections, spine and wrist fractures, and *Clostridium difficile* infections.[8-16] These findings have ignited debate regarding the overuse of PPI therapy and its appropriate prescribing habits.

The U.S. Food and Drug Administration (FDA) has approved indications for use of each marketed PPI with correlated dosing specified for each indication.[17-20] For example, omeprazole prescribing guidance for GERD indicates a dose of 20 mg daily for 4 to 8 weeks of therapy. Despite FDA-labeled indications and dosing, PPI therapy continues to be prescribed for unapproved indications, at inappropriate doses, and as long-term treatment when not indicated. Often, PPI therapy is initiated during a hospital admission, and therapy is not reevaluated at discharge. One study found that among patients prescribed acid suppressive therapy for ulcer prophylaxis during a hospital admission, 65% of patients did not have an indication for use, and 55% of patients were discharged on therapy.[21] Another study found that 60% of patients placed on acid suppressive therapy lacked an indication for use, and 34% of these patients were discharged from the hospital on the medication.[22]

Currently, no studies have evaluated inappropriate PPI prescribing patterns or cost savings associated with the prescribing behavior of PPI

**Table 1. Patient demographics (mean age, 65)**

| | n (%) |
|---|---|
| Sex | |
| Male | 193 (97) |
| Race | |
| White | 151 (76) |
| African American | 5 (3) |
| Missing/unknown | 43 (22) |

therapy. Prescribing patterns at the James H. Quillen VAMC in Mountain Home, Tennessee, suggest the overuse and potentially inappropriate use of PPI therapy. The primary objective of this study was to assess the incidence of potentially inappropriately prescribed PPI prescriptions in an outpatient clinic population.

## METHODS

A retrospective chart review of a nondeceased outpatient population was conducted at the James H. Quillen VAMC. This VAMC is a general medical and surgical hospital with 114 medical, surgical, and psychiatric beds, a 120-bed nursing care facility, a 295-bed domiciliary, with 5 community-based outpatient clinics and 3 rural outreach clinics.

### Inclusion Criteria

- Nondeceased veterans from the outpatient clinic population
- Active outpatient prescription for lansoprazole, omeprazole, pantoprazole, or rabeprazole from 4/1/2010 to 10/1/2010

### Exclusion Criteria

- Inpatient status during study period
- Documented allergy, AE, or contraindication to PPI therapy

A randomized sample of 200 patients was chosen from the study population. Given the large study population, the study sample of 200 was determined based on preliminary data regarding PPI use and the constraints of the study time line. Randomization was performed by using Microsoft® Excel Software. The Excel formula RANDBETWEEN was used to randomize the study population. The initial study population consisted of 13,907 patients listed alphabetically in an Excel spreadsheet. Each patient was assigned a random number between 1 and 500,000, using the formula = RANDBETWEEN (1,500,000). The population was then sorted in numerical order by the random number assignment using the Excel "sort" function. The first 200 patients were then selected as the study sample population.

**Table 2. Initial PPI Rx**

| PPI Rx | n (%) |
|---|---|
| Pantoprazole | 3 (2) |
| Lansoprazole | 18 (9) |
| Rabeprazole | 47 (24) |
| Omeprazole | 131 (66) |

PPI = proton pump inhibitor.

Once patients were identified, the computerized patient record system was used to collect data from each patient's chart. The data were recorded on data collection forms and then assimilated into a Microsoft®Access database for analysis. Each patient chart review was numbered sequentially as it was reviewed, and the following information was collected: sex, age, race, weight, initial PPI prescribed, dose and frequency of the PPI prescribed, start date and duration of therapy, the initial prescription provider, the department within the VAMC in which the PPI was initiated, provider specialty, the indication for use, dates of documented therapy follow-up, presence of documentation for long-term therapy, and potential interacting medications co-prescribed with PPI therapy. Also, the chart was reviewed to determine whether the patient had been started on PPI therapy before receiving care at the James H. Quillen VAMC by a non-VA provider or at a VAMC other than the James H. Quillen VAMC. To reduce the potential for variances in the data collection technique or introduction of investigator bias, only 1 investigator was involved in the collection of data for this study.

Following the chart review, a descriptive analysis was performed to determine the incidence of inappropriately prescribed PPI prescriptions. In this analysis, *appropriate PPI prescribing* was defined as an appropriate dose and frequency of PPI therapy in relation to the patient's documented indication for use. Appropriate indications for PPI use were based on those indications published by the FDA. The indication for PPI use must have been documented in the patient chart. Each patient must have documented follow-up to therapy and assessments at 4, 8, or 12 weeks after starting PPI therapy in accordance with FDA prescribing parameters. *Appropriate documentation of follow-up* was defined as reassessment of patient symptoms or indication for PPI use and acknowledgment for patient to continue, change, or discontinue therapy. If a patient was intended to remain on therapy long-term, the patient chart must have been documented to indicate and support long-term therapy. Appropriate indications for long-term therapy were those recognized by FDA prescribing guidance for each PPI in this anal-

**Table 3. Indications for PPI use**

| Indication for use[a] | n (%) |
|---|---|
| Gastric ulcer | 2 (1) |
| *Helicobacter pylori* eradication to reduce risk of duodenal ulcer | 4 (2) |
| Risk reduction of NSAID—associated gastric ulcer | 16 (8) |
| Other[b] | 28 (4) |
| No documented indication for use | 40 (20) |
| GERD | 109 (55) |

[a]As documented in patient charts.
[b]Other indications for use documented in patient charts in < 2 occurrences include duodenal ulcer, maintenance of healing of erosive esophagitis, dyspepsia, Barrett's esophagus, esophageal varices, heartburn, gastritis, gastrointestinal (GI) bleed, abdominal pain, GI prophylaxis, chronic laryngitis, peptic ulcer.
GERD = gastroesophageal reflux disease; NSAID = nonsteroidal antiinflammatory drug; PPI = proton pump inhibitor.

**Table 4. Inappropriate PPI analysis (n = 180)**

| Reason for inappropriateness | n (%) |
|---|---|
| Dosage | 5 (3) |
| Concomitantly prescribed Rxs | 36 (20) |
| Indication for use | 45 (25) |
| Follow-up to therapy | 174 (96) |

PPI = proton pump inhibitor.

ysis. Patient symptoms must have been reassessed at least annually for long-term therapy.

## RESULTS

Of the 200 medical charts sampled for review, 1 chart was excluded from analysis secondary to possible gynecomastia associated with PPI use. Of the remaining 199 charts included in this analysis, the sample population was mostly male (97%) and had a median age of 65 years (Table 1). Among the sample, most patients were initially prescribed omeprazole therapy (66%) (Table 2). The most common indication for PPI use documented in patient charts was GERD (55%) (Table 3). Of note, 20% of the charts reviewed did not have a documented indication for use. Patient charts were analyzed to determine whether a patient's initial PPI therapy was initiated at the James H. Quillen VAMC, at another VAMC, or by a non-VA provider. The analysis showed that 22% of patients were started on a PPI by a non-VA provider, 19% of patients were started on a PPI by another VAMC, with the majority of patients being started on PPI therapy by a provider at the James H. Quillen VAMC. Patients were restarted on PPI therapy at the James H. Quillen VAMC at new patient visits. Out of all providers, primary care providers (74%) accounted for the most initiations of PPI therapy. Patient charts were assessed for documented follow-up to therapy.

Of the 199 patient charts reviewed, 69 charts (35%) did not have documented follow-up of PPI therapy. Of those charts with documented follow-up to therapy, time to first follow-up after initiation of PPI therapy was a median of 344 days. Time to second follow-up was a median of 270 days. Analysis of concomitantly prescribed medications revealed 20 patients (33%) co-prescribed clopidogrel with PPI therapy. An analysis of all charts for appropriateness of PPI therapy was also conducted based on this study's definition of appropriate PPI therapy, which included follow-up to therapy in 4 to 8 weeks after initiation of a PPI, appropriate indication for use, appropriate dose of PPI therapy, and no concomitantly prescribed drug-drug interaction medications. Ninety percent (n = 180) of PPI prescriptions were found to be potentially inappropriate. Of those 180 prescriptions, inappropriate follow-up to therapy was the most common reason for potential inappropriateness to therapy (96%) (Table 4).

## DISCUSSION

This study suggests that PPI prescribing at the James H. Quillen VAMC may have areas for improvement. Adequate follow-up after initiation of therapy is a principle area of focus. After starting therapy, providers were not reassessing patient symptoms within the FDA recommended guidelines of 4 to 8 weeks of therapy. This may be inherent to the medical system's ability to reschedule patients in a timely manner due to provider scheduling conflicts or patient travel arrangements. With 22% of patients started on a PPI after initiation by a non-VA provider and 19% of therapy being started after initiation from a VAMC other than the James H. Quillen VAMC, the process of new patient assessment may be an area to examine. The VAMC providers prescribing a PPI, originally started by another provider, may have assumed that therapy appropriateness was determined by the previous provider and, therefore, continued PPI therapy inappropriately. This assumption may explain the extended time

to follow-up of therapy for this subset of patients. However, this does not preclude a provider from assessing the appropriateness of therapy in an effort to reduce polypharmacy and potential drug-drug interactions for the veteran population. The study authors also made the observation that patient charts were missing important information, such as reassessments, known indications for therapy, and recommendations for long-term therapy.

## COST ANALYSIS

A secondary objective of this study was to assess the estimated direct cost associated with providing inappropriately prescribed PPI therapy to the veteran population. Other direct and indirect costs related to inappropriate PPI prescribing such as hospitalization, treatment of PPI-related AEs, loss of productivity, and quality of life were not captured in this study. However, by identifying potentially inappropriate PPI therapy, the risk of secondary AEs and associated costs seen with PPI use may be reduced.

To assess the cost associated with providing inappropriately prescribed PPIs, a cost analysis was conducted on the data to determine an estimated annualized cost associated with providing potentially inappropriate PPI prescriptions to patients. An estimated $5 per prescription fill was used as a multiplier to estimate the cost of each PPI prescription. The multiplier of $5 was determined by estimating the average cost of a PPI prescription at the facility per month. The analysis assumed 12 months of PPI refills per year and per patient.

Given the 180 inappropriate PPI prescriptions, an estimated $11,000 projected annual cost may be expected to provide these potentially inappropriate PPI prescriptions. If this analysis is extrapolated to the entire study population of 13,709 patients prescribed a PPI, and estimating 90% may be potentially inappropriate, an estimated $750,000 annual cost for potentially inappropriate PPI prescriptions may be expected.

The cost analysis for this study was used to give an estimate of the monetary relationship associated with providing potentially inappropriate PPI therapy to the outpatient population. This analysis was not intended to imply that if therapy was not reassessed in 4 to 8 weeks, then therapy should be stopped and deemed inappropriate. However, this analysis is intended to show the potential cost savings that may result from maximizing the appropriate use of PPI therapy in a veteran outpatient population. Although this study was not intended to assess the clinical impact associated with the inappropriate use of PPI therapy, insuring adequate follow-up to therapy, appropriate indications for use, dosages of therapy, and eliminating drug-drug interactions with PPIs may help reduce the incidence of AEs associated with PPI use.

## CONCLUSION

Some limitations of this study included the study sample size in relation to the study population. The decision to analyze 200 patient charts was based on study time constraints and the ability to determine trends in data. Also, the data were only carried out by 1 researcher. This was intended to reduce variability in data collection techniques but may have resulted in researcher bias. Subjectivity in the interpretation of provider documentation may have limited the results of this study. Overall, the results of this study suggest that PPI prescribing in the outpatient population can be improved.

Overall, improvements in follow-up to PPI therapy are an area of focus to reduce the incidence of potentially inappropriate PPI therapy. This study was designed as a pilot study to direct future investigators to better understand the magnitude of inappropriate PPI use and to create interventions that will address this issue. Potential areas for intervention include alerts for follow-up in computerized order entry packages, formalized education for prescribers, and focused pharmacy department limitations on quantity or duration of PPI prescriptions. Future research could explore reasons for the inappropriate prescriptions (perceived lack of necessity, inadequate time or systems to pursue follow-up, or others) in clinical practice and assess the implementation and effectiveness of other interventions. ●

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