INTRODUCTION

In 2017, an estimated 85% of Medicare Part D regional prescription drug plans will offer preferred pharmacy networks (Fein, 2016). Prescription plans other than Medicare Part D have also been moving to preferred networks. A preferred pharmacy network offers patients a choice of pharmacies but provides financial incentives to use a preferred pharmacy. It is not clear whether the plans choose preferred pharmacies on factors other than unit costs. However, a lack of comparative quality data likely results in plans using unit costs as the primary deciding factor. However, pharmacies with higher unit costs, but better medication adherence rates may result in lower total health care costs along with better patient care. This article describes research conducted to compare medication adherence rates among pharmacy chains in a large city in the South Central United States.

Medications remain the primary treatment for the majority of chronic conditions such as hypertension, dyslipidemia, and diabetes. Poor adherence refers to not taking the drug at the appropriate dosage and schedule prescribed and the failure to continuously refill prescriptions for the duration prescribed (Lam & Fresco, 2015).

Unfortunately, poor medication adherence has been reported to range from 25% to 50% depending on measurement method, condition, and patient types (Iuga & McGuire, 2014). For this reason, poor medication adherence may be the greatest contributor to preventable health care costs for these conditions. An estimate of the avoidable healthcare costs associated with poor medication adherence ranges from 3% to 10% of healthcare spending in the United States. These costs primarily result from greater patient morbidity and mortality, particularly hospitalizations (Iuga & McGuire, 2014). Studies have also demonstrated the negative cost impact of poor adherence on individual conditions (Bitton, Choudhry, Matlin, Swanton, & Shrank, 2013) (Wild, 2012).

Due to the high incidence of negative health consequences along with the financial strain associated with non-adherence, pharmacies have incorporated a variety of medication management services to increase adherence rates of prescribed medication regimens. Various interventions to improve adherence have produced positive outcomes, especially in those with chronic diseases, including hypertension, heart failure, depression, and asthma (Viswanathan, 2012). The most studied
interventions include reduced patient pay, increased prescription insurance coverage, medication therapy management and patient-level educational interventions including behavioral support (Zeber, et al., 2013).

From refill reminder calls to enrolling patients in automatic refill plans, community pharmacies have implemented initiatives such as these to encourage medication adherence for these disease states. Because patients interact with pharmacists upon prescription drop off and pick up, community pharmacists play a crucial role in medication therapy maintenance and adherence (Iyengar, et al., 2014).

Pharmacists and their pharmacies that offer enhanced medication management services focused on improving adherence may be able to offset more than the increased costs of providing that service. However, we were unable to find information on whether different groups of pharmacies produce higher rates of adherence over the others. This study will attempt to determine whether we can detect differences in adherence rates among different pharmacy chains. If we observe variations in adherence patterns between pharmacy chains, the information can be further analyzed to determine if the pharmacy chain with superior adherence rates has implemented an adherence program different than those of the other chains. This approach may assist prescription drug plans with selecting pharmacies for their preferred networks.

METHODS

OBJECTIVES

The primary objective of this study focused on whether adherence rates differ among different pharmacy chains. The study hypothesized that the results would not show a difference in adherence rates among pharmacy chains. Also, this article will share our approach to calculating differences in adherence rates using pharmacy claims data.

STUDY DESIGN

The study conducted an observational retrospective analysis of pharmacy claims data from May 2015 to August 2015 paid by a government employer in a South Central United States metropolitan area.

DATA MANAGEMENT

The data set included pharmacy claims for 51,757 patients. The researchers loaded the claims into a SQL Server 2012 database for analysis. The key fields extracted and used for analysis included:

- Unique patient identifier
- Age
- Gender
- National Drug Code (NDC) to identify medications
- National Provider Identifier (NPI) to identify pharmacies

PATIENT SELECTION

The patients selected included those 20 years or older, used medicine in the category of antihypertensive, antihyperlipidemic, and antidiabetic agents, and had a duration of therapy of 31 days or longer.

Age was grouped by decade to obtain a general understanding of how this factor plays a role in
adherence. The grouping was in 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, 80-89 years, 90-99 years, and 100+ years.

**MEDICATION SELECTION**

The research focused on medications used to treat the top three chronic conditions for this patient population; hypertension, hyperlipidemia, and diabetes. The data identified 4,321 patients with medications indicated to treat these conditions.

The system used a medication indications dataset supplied by First Databank to identify the medications indicated for those conditions and the associated patients. The dataset matches the NDC for a medication to both FDA-approved indications and indications recognized in official compendia including, but not limited to, the United States Pharmacopoeia-Drug Information (USP-DI) and the American Hospital Formulary Service-Drug Information (AHFS-DI).

The antihypertensive agents included medications in the following classes; angiotensin converting enzyme (ACE) inhibitors, ACE inhibitor combinations, angiotensin II receptor blocker (ARB), ARB combinations, beta-adrenergic blockers (beta blockers) selective and nonselective, beta blocker diuretic combinations, calcium channel blockers (CCB), diuretics (loop, loop combinations, potassium sparing, potassium-sparing combinations, aldosterone receptor antagonists, thiazides, and thiazide combinations), and vasodilators.

The antihyperlipemic agents included HMG-CoA reductase inhibitors as well as combination products.

The antidiabetic agents included insulin and oral hypoglycemic agents.

**PHARMACIES INCLUDED**

Researchers loaded National Provider Identifiers (NPI) from the National Plan & Provider Enumeration System (NPPES) into the SQL Server database. The billing address within that dataset allowed researchers to group the individual pharmacies by chain pharmacy. Matching by billing address resulted in five chain pharmacies with sufficient prescription utilization to include within the analysis.

No independent pharmacies individually, or a grouped together, accounted for a sufficient number of patients to include in the analysis.

**MEASURES OF ADHERENCE**

Although there are several ways to define medication adherence, generally it is the degree of how closely a patient follows their prescribed medication regimen (Osterberg & Blaschke, 2005) (Sattler, Sun Lee, & Perri III, 2013). A common method, the medication possession ratio (MPR), uses the days supply submitted by the pharmacy on the claim divided by the quantity of medication supplied to estimate adherence. Most studies consider patients with an MPR that exceeds 80% to be adherent. However, days supply submitted, and an assumed daily quantity prescribed may not accurately reflect the actual utilization of the medication by the patient.

This study used medication dosage modules supplied by First Databank to provide minimum defined daily dosages (DDD) of medications based on the most common medication indication, age, and gender. The total dose, based on the quantity dispensed during the study period, divided by the duration of therapy calculated an average daily dose (ADD). The study then estimated adherence by dividing the ADD by the minimum defined daily dose (DDD) within the First Databank medication dosage module.

**Example calculation:**

1) Total quantity of 10mg tablets dispensed for the patient: 120 units
2) Total dose: 120 units times 10mg = 1,200mg
3) Duration: 150 days
4) Average daily dose (ADD): 1,200mg/150 days = 8mg per day
5) Minimum defined daily dose (DDD) from First Databank: 10mg per day
6) Adherence: ADD/DDD = 8mg per day divided by 10mg per day = 0.80 (80%)

The study estimated duration by calculating the difference in days between the first and last dispensed dates plus an estimated number of days provided by the last refill quantity. In most cases, the duration of therapy for antihypertensive, antihyperlipidemic, and antidiabetic agents exceed 31 days due to the chronic nature of these conditions. A duration of therapy of 31 days or greater was included in the analysis to calculate the potential impact on adherence between pharmacy chains. By eliminating patients that did not refill their prescription after 30 days, we avoided skewed data for patients who may have had changes in therapy as well as individuals who did not continue therapy within the first month.

STATISTICAL ANALYSIS
The study compared adherence rates for each chain pharmacy while matching for medication, age, and gender.

The analysis used a one-way analysis of variance (ANOVA) to compare adherence rates among the chain pharmacy groups. Based on an estimated average of adherence rate of 0.8, a standard deviation of 0.05, an acceptable Type I error rate ($\alpha$) of 5%, and an acceptable power of 80% (1−$\beta$) an estimate sample size of 98 for each group would be required.

RESULTS
PRIMARY OBJECTIVE: ADHERENCE
Overall, the mean adherence score in this study population was 0.78 (SD = 0.41). The study revealed that the difference between the average defined daily dose of the various pharmacy chains was not statistically significant, as tested by one-way ANOVA ($p > 0.05$, power=0.909) (Table 1).

Table 1: Mean adherence per pharmacy chain

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>p*</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chain A</td>
<td>0.79 ± 0.43</td>
<td></td>
<td>1,542</td>
</tr>
<tr>
<td>Chain B</td>
<td>0.78 ± 0.40</td>
<td></td>
<td>2,443</td>
</tr>
<tr>
<td>Chain C</td>
<td>0.78 ± 0.41</td>
<td></td>
<td>144</td>
</tr>
<tr>
<td>Chain D</td>
<td>0.75 ± 0.35</td>
<td></td>
<td>109</td>
</tr>
<tr>
<td>Chain E</td>
<td>0.81 ± 0.45</td>
<td></td>
<td>83</td>
</tr>
</tbody>
</table>

* = non-significant if left blank

DEMOGRAPHICS
The study included data on a total of 4,321 patients. The mean age of participants was 57.80 years (range = 20 - 90), and 52.2% of participants were men. The analysis matched patients based on medication, age, and gender. (Tables 2 and 3)

Table 2: Mean adherence by patient age and gender

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>p*</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>0.78 ± 0.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age decade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 - 29</td>
<td>0.75 ± 0.98</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>30 - 39</td>
<td>0.67 ± 0.62</td>
<td>125</td>
<td></td>
</tr>
<tr>
<td>40 - 49</td>
<td>0.74 ± 0.39</td>
<td>425</td>
<td></td>
</tr>
<tr>
<td>50 - 59</td>
<td>0.77 ± 0.38</td>
<td>1126</td>
<td></td>
</tr>
<tr>
<td>60 - 69</td>
<td>0.81 ± 0.41</td>
<td>1401</td>
<td></td>
</tr>
<tr>
<td>70 - 79</td>
<td>0.80 ± 0.38</td>
<td>868</td>
<td></td>
</tr>
<tr>
<td>80 - 89</td>
<td>0.77 ± 0.38</td>
<td>268</td>
<td></td>
</tr>
<tr>
<td>90 - 99</td>
<td>0.72 ± 0.36</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>100 +</td>
<td>0.69 ± 0.79</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

* = non-significant if left blank

Table 3: Mean adherence by medication category

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>p*</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>0.83 ± 0.41</td>
<td></td>
<td>9,654</td>
</tr>
<tr>
<td>Category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>0.73 ± 0.49</td>
<td>5,778</td>
<td></td>
</tr>
<tr>
<td>Antidiabetic</td>
<td>1.06 ± 0.51</td>
<td>&lt;0.05</td>
<td>1,638</td>
</tr>
</tbody>
</table>

* = non-significant if left blank
DISCUSSION

These chain pharmacies showed similar adherence rates to one another which may suggest that they use similar programs to improve adherence. Overall, the average defined daily dose (DDD) for the full study population was 0.78. As a general rule, a value of 0.80 would be considered compliant in most studies using various measures of compliance.

The study attempted to detect a chain pharmacy group with a program that had helped their patients significantly improve their adherence. If detected, the researchers would request the opportunity to evaluate their program to understand better their system, training, and approach.

STRENGTHS

The study achieved sufficient sample sizes for the chain pharmacy groups to detect any statistically significant differences.

The adherence calculation used a more rigorous estimate of adherence than estimates that rely on submitted days supply and quantity rather than dosing calculations.

The inclusion of three therapeutic categories allowed estimations of adherence for two conditions with fewer short-term complications (e.g., hypertension, hyperlipidemia) and one with a higher chance of acute symptoms or complications (e.g., diabetes) that may impact patient adherence.

LIMITATIONS

The data for this study was limited to a single employer in a specific metropolitan region in the South Central United States. The results may vary based on the type of plan and region. Also, the analysis did not include independent pharmacies or the mail-service pharmacy due to a lack of sufficient sample size of patients. The study also focused on identifying differences in the retail pharmacies for the plan, not to identify whether mail-service prescription delivery would have different results. The results should not be used to assume that all pharmacies have comparable patient adherence rates.

RECOMMENDATIONS

This type of analysis may show different results in drug plans with financial incentives for improving adherence rates. In particular, this would apply to Medicare Part D prescription drug plans that receive financial incentives through the STAR rating system. The STAR rating system includes adherence measures for key medication categories. Plans that achieve an overall rating of four or five receive bonus payments of five percent (5%) (O'Neill Hayes, 2015). Further research should focus on plans that provide incentives to pharmacies for improved adherence.

CONCLUSION

We found no significant differences in adherence rates when comparing pharmacy chains in this South Central United States metropolitan area. This analysis does not indicate that these pharmacies do not help improve patient adherence only that we did not detect any differences between these pharmacy chains. The lack of financial incentives for these pharmacies to improve adherence may have influenced these results. Further research of this finding in plans with financial incentives for pharmacies can guide areas of improvement in adherence and overall pharmaceutical care.

REFERENCES

Med, Pages 357.e7-357.e27. doi:doi.org/10.1016/j.amjmed.2012.09.004


